



STUDY ON UTERINE ARTERY DOPPLER INDICES AND PLACENTAL VOLUME IN 11-14 WEEKS OF GESTATION AS A PREDICTOR OF INTRAUTERINE GROWTH RESTRICTION AND PRE -ECLAMPSIA

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ABSTRACT **Aims and objectives:** To determine the reference values for the first-trimester uterine artery Doppler indices and placental volume in 11-14 weeks gestation. To assess the role of uterine artery Doppler and placental volume at 11-14 weeks of pregnancy for prediction of preeclampsia and intrauterine growth restriction and to evaluate the perinatal outcome in patients with deranged uterine artery doppler and placental volume. **Materials and methods:** Conducted in the Department of Obstetrics and Gynecology of MLB Medical college, Jhansi over a period of 18 months. 200 women with singleton pregnancies between 11 to 14 weeks were enrolled. Uterine artery Doppler waveforms and placental volumes were studied. These women were again rescanned at 26-30 weeks of gestation and further followed up for development of preeclampsia and IUGR. **Results:** Out of 200 patients, 19% developed preeclampsia and 13% patients had IUGR. In our study 33% of women had uterine artery diastolic notching with mean RI of 0.60 ± 0.071 and mean PI of 1.47 ± 0.347 at 11-14 weeks. When only diastolic notch at 11-14 weeks was considered, 39.39% of women developed preeclampsia and 24.24% had IUGR. When uterine artery diastolic notch and $RI > 0.65$ was also included, detection rate increased to 77.77% for pre-eclampsia and 66.66% for IUGR. When only notch was considered sensitivity for preeclampsia was 68.40% and specificity was 77.01%, for IUGR sensitivity was 61.53% and specificity was 72.82%. When notch and $RI > 0.65$ considered together, specificity increased to 97.59% for preeclampsia and 96.66% for IUGR. The sensitivity of low placental volume in predicting preeclampsia was 35.29% and 30.76% for IUGR. 39.39% had IUGR and 33.33% required NICU admission within 72 hours of delivery among patients with deranged Doppler. **Conclusion:** Findings suggest that impaired placentation as demonstrated by increased mean RI and mean PI is implicated in development of pregnancy complications like preeclampsia and IUGR.

KEYWORDS : Intrauterine growth restriction (IUGR), Small-for-gestational age (SGA), Resistance Index (RI), Pulsatility Index (PI)

INTRODUCTION

Small for gestational age fetuses are generally healthy, suffering only a slight increase in perinatal mortality and morbidity in comparison to normally grown fetuses. In contrast, intrauterine growth restriction (IUGR), as a consequence of chronic uteroplacental insufficiency, is associated with a high risk of perinatal mortality and morbidity^[1-3]. It is very important to detect pregnancies at risk of IUGR, as the antenatal identification of reduced fetal growth has been shown to significantly reduce perinatal morbidity and mortality, by four to five fold^[4-5].

There is evidence to demonstrate that trophoblast invasiveness is maximal in the first trimester, when it is also possible to assess uterine artery blood flow by Doppler. The definition of SGA as birth weight below the 10th or 5th centile includes a large spectrum of smallness, ranging from constitutionally small, healthy infants delivered at term to those with severe placental impairment requiring emergency preterm delivery^[6-8]. Moreover, these studies did not differentiate isolated IUGR cases from those associated with pre-eclampsia, which may have an independent influence on uterine artery doppler indices^[7-9].

Pre-eclampsia (PE) is a pregnancy-specific syndrome that can affect virtually every organ system. It affects 5-10% of pregnancies worldwide and 4.6% of pregnancies in India^[9-10]. It forms one member of the deadly triad, along with hemorrhage and infection that contribute greatly to maternal morbidity and mortality (14% worldwide, 29.54% in India)^[11-12].

Poor placentation is associated with an imbalance of circulating vasoactive factors and, in turn, leads to maternal vascular maladaptation with associated systemic endothelial dysfunction^[13-14].

Faulty trophoblastic invasion of the spiral arteries results in diminished placental perfusion and upstream increased uterine artery resistance indices.

Preeclampsia is commonly divided into early-onset (diagnosed and requiring delivery < 34 weeks" gestation) and late-onset disease (diagnosed and requiring delivery >34 weeks" gestation). Early-onset preeclampsia results from impaired trophoblast invasion into the spiral

arteries, leading to placental ischemia and oxidative stress.

Considering the common origins of IUGR and preeclampsia (especially early-onset PE) in defective placentation and consequent uteroplacental insufficiency, first-trimester doppler assessment of the uterine circulation may identify women with high risk for developing obstetric complications such as preeclampsia and IUGR secondary to placental insufficiency who require more intensive surveillance during pregnancy. A good screening test for preeclampsia and IUGR should be safe, simple, quick, inexpensive and acceptable to the patients. Placental size has also been associated with abnormal pregnancy outcomes such as preeclampsia, IUGR, placental abruption and placental insufficiency.

AIMS AND OBJECTIVES

- To determine the reference values for the first-trimester uterine artery doppler diastolic notch, pulsatility index, resistance index and placental volume in 11-14 weeks gestation.
- To assess the role of uterine artery doppler at 11-14 weeks of pregnancy for prediction of preeclampsia.
- To assess the role of uterine artery doppler at 11-14 weeks of pregnancy for prediction of intrauterine growth restriction.
- To study the role of placental volume as a predictor of preeclampsia and intrauterine growth restriction at 11-14 weeks of gestation.
- To evaluate the perinatal outcome in patients with deranged uterine artery doppler and placental volume.

MATERIAL AND METHODS

A Prospective observational study was conducted in the Department of Obstetrics and Gynecology of Maharani Laxmi Bai Medical College, Jhansi over a period of 18 months in association with the Department of Radiology among women attending the out-patient department for antenatal care at MLB Medical College, Jhansi, during the period of April 2019 to September 2020.

200 women with singleton pregnancies between 11 to 14 weeks gestation were enrolled. Uterine artery doppler waveforms and

doppler indices and placental volume were studied. These women were again rescanned at 26-30 weeks of gestation and further followed up with transabdominal USG and uterine artery doppler. Blood pressure was recorded and urine was examined for albuminuria in the third trimester and these patients were followed clinically till delivery for development of preeclampsia and intrauterine growth restriction. The utero placental circulation was measured by various uterine artery doppler indices, Resistance Index (RI), Pulsatility Index (PI) and appearance of bilateral diastolic notches. The volume of the placenta was acquired by the transabdominal ultrasonography and recorded.

Inclusion criteria

- All pregnant women between 11-14 weeks of gestational age with singleton pregnancy.

Exclusion criteria

- Women with essential hypertension and history of preeclampsia, eclampsia
- Multi-fetal pregnancy
- Foetus with congenital anomaly
- Women having diabetes mellitus
- Missed abortion
- Chronic renal diseases
- Cardiac diseases
- Not willing to participate

RESULT

Table 1: Prevalence of Pre-eclampsia and IUGR

Condition	Subjects	Percent
Normal subjects	144	72.00%
Gestational hypertension	6	3.00%
Preeclampsia	24	12.00%
Preeclampsia with IUGR	14	7.00%
IUGR	12	6.00%
Total	200	100

Table 2: Distribution of cases according to presence of uterine artery Doppler end diastolic notching

Variables	Notching at 11-14 weeks	Percent	Notching at 26-30 weeks	Percent
Present	66	33.00%	34	17.00%
Absent	134	67.00%	166	83.00%
Total	200	100%	200	100%

Table 3: Association of uterine artery diastolic notch with development of preeclampsia and IUGR

Variable		Present		Absent	
		Number	%	Number	%
Notch at 11-14 weeks (n=66)	Preeclampsia (n=38)	32	48.48%	6	0.90%
	IUGR (n=26)	16	24.24%	10	15.15%
Notch at 26-30 weeks (n=34)	Preeclampsia (n=38)	26	76.47%	12	35.29%
	IUGR (n=26)	16	47.05%	10	29.41%

Table 4: Association of resistance indices in preeclampsia and IUGR

Resistance indices (Mean Gestational age)	Preeclamptic females (Mean±SD)	Females with IUGR (Mean±SD)	Normal females (Mean±SD)
11-14 weeks	0.68±0.122	0.68±0.128	0.58±0.020
26-30 weeks	0.56±0.081	0.55±0.082	0.50±0.055

Table 5: Association of uterine artery Doppler pulsatility indices in preeclampsia and females with IUGR.

Pulsatility indices (Mean Gestational age)	Preeclamptic females (Mean±SD)	Females with IUGR (Mean±SD)	Normal females (Mean±SD)
11-14 weeks	1.97±0.349	1.84±0.481	1.35±0.225
26-30 weeks	1.03±1.555	0.96±0.142	0.84±0.073

Table 6: Comparison of uterine artery notch and uterine artery notch with RI >0.65 with development of preeclampsia and IUGR

Abnormal uterine artery waveform at 11-14 weeks	Preeclampsia (Number of patient)	Preeclampsia (Percentage) n=38	IUGR (number of patient)	IUGR (percent) n=26

Uterine artery notch (n=66)	26	39.39%	16	24.24%
Notch+RI>0.65 (n=18)	14	77.77%	12	66.66%

Table 7: Role of uterine artery doppler and placental volume in predicting preeclampsia and IUGR at 11-14 week

Variables	Sensitivity	Specificity	PPV	NPV
End diastolic notch (N=66)	68.4%	77.01%	56.52%	91.78%
Notch + RI>0.65 (N=18)	36.84%	97.59%	77.77%	87.09%
PI>95 th centile (N=20)	23.68%	93.64%	45.00%	84.48%
PI>95 th centile + notching (N=16)	23.68%	95.85%	56.25%	84.48%
S/D Ratio >95 th centile (N=22)	26.31%	93.10%	45.45%	85.26%
Placental vol<45 ml	35.29	97.59	75.00	88.04
Placental volume<45 ml + notching	29.41	97.59	71.42	87.09
Placental volume<45 ml + notching+RI>0.65	22.22	98.78	80.00	85.26

Table 8: Role of uterine artery doppler and placental volume in predicting IUGR

Variables	Sensitivity	Specificity	PPV	NPV
End diastolic notch (N=66)	61.53%	72.82%	24.24%	92.53%
Notch + RI>0.65 (N=18)	46.15%	96.66%	66.66%	92.55%
PI>95 th centile (N=20)	42.30%	95.08%	55.00%	92.06%
PI>95 th centile + notching (N=16)	30.76%	95.60%	50.00%	90.62%
S/D Ratio >95 th centile (N=22)	30.76%	92.55%	36.36%	90.62%
Placental vol<45 ml	30.76%	95.60%	50.0%	90.62%
Placental volume<45 ml + notching	30.76%	96.66%	57.14%	90.62%
Placental volume<45 ml + notching+RI>0.65	30.76%	98.86%	80.6%	90.6%

Table 9: Perinatal outcome in patients with abnormal uterine artery doppler at 11-14 weeks (n=66)

Variables	Number	Percent
IUGR	16	24.24%
Intrauterine death	2	3.03%
NICU Admission	14	21.21%
Respiratory complications	8	12.12%
APGAR<7 at 5 minutes	25	37.87%
Meconium strained liquor	6	9.09%

DISCUSSION

In our study it was found that maximum 76 (38.00%) patients were between 21-25 years of age.

Most of the subjects 111 (55.50%) were Primi-gravida. Maximum of the subjects i.e. 109 (54.50%) belonged to class IV socioeconomic class according to the Modified Prasad classification.

Prevalence of preeclampsia and IUGR:

Preeclampsia was found in 38 (19.00%) subjects while intrauterine growth restriction was seen in 26 (13.00%) of subjects.

Association of notching with preeclampsia and IUGR:

In our study it was found that at 11 to 14 weeks gestation, end diastolic notching was seen in 66 (33.00%) of subjects and, notching persisted in 34 (17.00%) subjects at 26-30 weeks gestation scan.

Association of uterine artery diastolic notch with development of preeclampsia and IUGR

In our study it was found that in patients with diastolic notching at 11-14 weeks gestation, preeclampsia developed in 32 (48.48%) of subjects and IUGR was seen in 16 (24.24%) of subjects. Out of 34 patients with notching at 26-30 weeks, 26 (76.47%) subjects developed preeclampsia and IUGR was seen in 16 (47.05%) of subjects.

Association of resistance indices with pre-eclampsia and IUGR:

In our study at 11-14 weeks the Mean±SD of resistance index was 0.60±0.071. The Mean ± SD of resistance indices at 11-14 weeks gestation was found to be higher i.e. 0.68 ±0.122 in pre-eclamptic females and 0.68±0.128 in females with IUGR as compared to normal subjects with a Mean ± SD of 0.58±0.020.

Association of uterine artery doppler pulsatility indices in preeclamptic and IUGR:

In our study at 11-14 weeks the Mean±SD of pulsatility index was 1.47±0.347. In our study it was found that the Mean±SD of pulsatility indices at 11-14 weeks gestation was found to be higher i.e. 1.97±0.349 in pre-eclamptic females and 1.84±0.431 in females with IUGR as compared to normal subjects with a Mean±SD of 1.47±0.347.

Comparison of uterine artery notch and notch with RI>0.65 with development of Preeclampsia and IUGR:

In our study it was found that when only end diastolic notching was considered (n=66), 26 (39.39%) subjects developed preeclampsia and 16 (24.24%) subjects had IUGR. When both diastolic notching and RI>0.65 were considered together (n=18); detection rate increased to 14 (77.77%) for preeclampsia and 12 (66.66%) for IUGR.

Role of uterine artery doppler and Placental volume in predicting Preeclampsia at 11-14 weeks:

In our study it was found that when only notching was considered the sensitivity for predicting preeclampsia at 11-14 weeks was 68.40%, specificity was found to be 77.01% with a positive predictive value of 56.52% and a negative predictive value of 91.76% similar to Gupta Shashi et al¹⁵¹.

When both notching and RI>0.65 were considered together sensitivity was 36.84%, specificity was 97.59% with a positive predictive value of 77.77% and negative predictive value of 87.09%.

The specificity increased from 77.01% to 97.59% when RI>0.65 is included with notch, similarly described by Gupta Shashi et al¹⁵¹. Sensitivity of notch for preeclampsia is 68.4%, similar to that quoted by Kurdi et al¹⁶⁰.

PI>95th centile was found in 20 subjects with a sensitivity of 23.68%, specificity of 93.64%, positive predictive value of 45.00% and negative predictive value of 84.48% in predicting preeclampsia. When B/L notching was included, specificity increased to 95.85%. Results were similar to study conducted by AM Martin et al¹⁷¹ and Pilalis A et al¹⁸¹ (2007).

S/D ratio >95th centile was seen in 10 preeclamptic subjects with a sensitivity of 26.31%, specificity of 93.10%.

In our study it was found that maximum of the subjects i.e 107 (53.50%) had central placentation. In our study the mean placental volume was found to be 55.1ml. Placental volume was found <45 ml in 12 (31.57%) subjects of preeclampsia and 8 (30.76%) of IUGR subjects.

The sensitivity of low placental volume in predicting preeclampsia was 35.29%.

In our study it was found that when placental volume <45 ml as a parameter for predicting preeclampsia was considered the sensitivity was found to be 35.29%, specificity was 97.59% with a positive predictive value of 75.00% and a negative predictive value of 88.04%.

When placental volume <45 ml with diastolic notching was considered the sensitivity was found to be 29.41%, specificity was 97.59% with a positive predictive value of 71.42% and a negative predictive value of 87.09%.

When placental volume <45 ml with diastolic notching and RI>0.65 were considered together, the sensitivity was found to be 22.22%, specificity was 98.78% with a positive predictive value of 80.00% and a negative predictive value of 85.26%.

Role of uterine artery doppler and Placental volume in predicting IUGR at 11-14 weeks:

In our study it was found that when only notching as a parameter for predicting IUGR at 11-14 weeks was considered the sensitivity was

found to be 61.53%, specificity was found to be 72.82% with a positive predictive value of 24.24% and a negative predictive value of 92.53%. When both diastolic notching and RI>0.65 were considered together sensitivity was 61.53%, specificity was 96.66% with a positive predictive value of 66.66% and negative predictive value of 92.55%.

PI>95th centile was found in 11 subjects with IUGR with a sensitivity of 42.30%, specificity of 95.08%, positive predictive value of 55.00% and negative predictive value of 92.06% in predicting IUGR. When B/L notching was included, specificity increased to 95.60%.

S/D ratio >95th centile was seen in 8 subjects with IUGR with a sensitivity of 30.76%, specificity of 92.55%.

The sensitivity of low placental volume in predicting IUGR was 30.76% similar to study conducted by Hafner et al¹⁹¹ 2006 where the sensitivity for detection of small for gestational age was 27.1%.

When low placental volume for predicting IUGR, the sensitivity was found to be 30.76%, specificity was 95.60% with a positive predictive value of 50.00% and a negative predictive value of 90.62%. For IUGR the sensitivity for low placental volume and diastolic notch was found to be 30.76%, specificity was 96.66% with a positive predictive value of 57.14% and a negative predictive value of 90.62%.

When RI >0.65 was also included, specificity increased to 98.86% with a positive predictive value of 80.00% and a negative predictive value of 90.62%.

Perinatal outcome in patients with deranged uterine artery doppler at 11-14 weeks:

In our study it was found that in patients with deranged Doppler (n=66), 35 (53.03%) subjects had vaginal delivery, 27 (40.90%) had emergency cesarean section and 4 (6.06%) subjects were taken for elective cesarean section and maximum subjects 175 (87.5%) delivered between 37-42 weeks.

In our study maximum 136 (68.00%) babies weighed between 2.5-2.9 kilograms and 32 (16.00%) were low birth weight weighing 1.5-2.4 kgs.

In our study it was found that in patients with deranged uterine artery doppler at 11-14 weeks, IUGR was found in 16 (24.24%) of subjects, 2 subjects (3.03%) had intrauterine death, 14 (21.21%) of newborns required NICU admission within 72 hours of delivery, 8 (12.12%) newborns had respiratory complications within 72 hours of birth, 25 (37.87%) of the new borns had APGAR score <7 at 5 minutes and 6 (9.09%) of the subjects had meconium straining.

CONCLUSIONS

Preeclampsia is a complex clinical syndrome involving multiorgan systems. The research for ideal predictive test and preventive measures remains challenging. In our study the mean of all uterine artery indices showing impedance to uteroplacental circulation were significantly higher. This shows that resistance to blood flow is a more important indicator than the actual blood flow. Combination of uterine artery doppler indices and placental volume is highly specific in predicting preeclampsia and IUGR. Findings suggest that impaired placentation as demonstrated by increased mean RI and mean PI is implicated in development of pregnancy complications like preeclampsia and IUGR. Uterine artery Doppler studies between 11-14 weeks also help us to categorize our patients into low risk and high risk so that proper vigilance may be done in high risk women.

Doppler is a non-invasive method for evaluation of fetoplacental circulation without any disturbance to human pregnancy and is a useful tool for early prediction of preeclampsia, IUGR and prevention of adverse maternal and perinatal outcome.

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