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Original Research Article

Study of uterine artery doppler at 11 to 14 weeks of gestation and maternofetal outcome

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Abstract

Background: Pre eclampsia (PE) is defined as a clinical syndrome which involves multi-organ system and is one of the major cause of maternal and perinatal morbidity and mortality. Doppler assessment of feto-placental circulation is one of the method for evaluation of pre eclampsia, which is a non-invasive screening tool without affecting the pregnancy. In the current study, uterine artery doppler waveform is assessed. A high pulsatility index and persistent diastolic notch helps in prediction of pre eclampsia and IUGR.

Aims and Objectives: 1) To assess the relation between uterine artery doppler indices (pulsatility index and diastolic notching) and maternofetal outcome of pregnancy. 2) To assess the sensitivity and specificity of uterine artery doppler indices in diagnosis of pre eclampsia.

Methodology: 82 antenatal women of between 11 and 14 weeks of gestation were selected after considering inclusion and exclusion criteria. Women booking to antenatal care will be subjected to uterine artery Doppler scan between 11 and 14 weeks of gestation. The bilateral uterine artery doppler indices assessed i.e., pulsatility index, diastolic notching. All patients are assessed for fetomaternal outcome.

Results: Out of 82 women, 19.5% of women developed PE. In the current study 14.6% of women had pathological uterine artery PI in those 66.7% developed pre eclampsia and 16.66% delivered FGR babies. 7.3% of women had diastolic notching in those 33.3% had pre eclampsia and 16.66% delivered FGR babies. Uterine artery doppler pulsatility index has sensitivity of 50%, specificity of 93.94%, PPV of 66.67% and NPV of 88.57%.

Conclusion: Thus high uterine artery Pulsatility Index and persistent diastolic notching in doppler waveform at between 11 and 14 weeks of gestation has shown to predict pre eclampsia which is non-invasive and cost effective test.

Keywords: Pre eclampsia, FGR, Pulsatility Index, Diastolic notch.

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1. Introduction

Prevalence of preeclampsia (PE) is around 2-5%. PE is the leading cause of morbidity and mortality in pregnant mother and neonate. Doppler is used for assessment of circulation between mother and fetus. Doppler is being used widely as it is a non invasive tool. Elevated PI in the uterine artery is one of the screening tests for prediction of PE.¹ Uterine artery Doppler helps in assessing utero-placental circulation at an early gestation. Uterine artery Doppler is a screening method for predicting pre-eclampsia, fetal growth restriction (FGR), placental abruption, and stillbirth.²

Antenatal care aims at early recognition and management of high risk pregnancy. When trophoblast invades the myometrium and decidua via spiral arteries completely, normal plantation takes place. This converts the circulation in low resistance and high blood flow vascular system is created. In complete trophoblastic invasion leads to high resistance low flow vascular bed leading to decreased perfusion through placenta eventually leading for development of pre-eclampsia(PE).³ 1st trimester Doppler is a more accurate method for predicting early onset than with late onset pre-eclampsia. Multiparametric predictive models

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have shown that first trimester uterine artery pulsatile index along with maternal features and biochemical markers can achieve a detection rate of over 90% for early onset pre eclampsia.⁴

Apart from Doppler indices biomarkers like VEGF-1, PLGF, PAPP, beta-hCG have been studied in prediction of preeclampsia. Preeclampsia and intrauterine growth restriction (IUGR) are both more likely to develop when P.I. is higher.⁵

Therefore, this "study of uterine artery Doppler indices at 11-14 weeks of gestation and fetomaternal outcome" is intended to concentrate that on using Doppler ultrasound in the first trimester, which will offer an excellent opportunity to assess for these pregnancy complications at an early stage, when intervention may be feasible.

2. Materials and Methods

This is a prospective cohort study which was done over a period of 18 months among women consulting for antenatal care at Ramaiah Medical College and Hospital, Bangalore, Karnataka, during the period of March 2021 to October 2022.

2.1. Inclusion criteria

All the pregnant woman aged >18 yrs with singleton pregnancy.

2.2. Exclusion criteria

1. Exclusion of fetus with sonologically detectable congenital anomalies.
2. Woman with cardiovascular pathology, renal disease, pre-gestational diabetes.
3. Those with known congenital uterine malformations in the previous scan.
4. Multi fetal gestation.

2.3. Sample size

82.

With the reference from Neravi and Udayshree study has observed that sensitivity of predicting pre-eclampsia by uterine artery notch and RI was 85.71%. In the present study expecting similar results with 95% confidence interval and relative precision of 7% the study requires a minimum of 82 subjects.

2.4. Study design

Prospective study.

2.5. Procedure

82 antenatal women between 11 to 14 weeks period of gestation were included in the study after considering the inclusion and exclusion criteria. Women attending for routine antenatal care between 11 and 14 weeks were advised abdominal ultrasound as a method of screening for chromosomal defects, pre eclampsia and FGR. Pulsatility

index, diastolic notching were assessed by uterine artery doppler. Increased resistance to blood flow on uterine artery Doppler leads to appearance of diastolic notch and increase in indices. All participants were followed upto delivery to assess maternofetal outcome. Subjects with pathological uterine artery PI were advised take low dose aspirin (75mg) between 11 to 14 weeks of gestation after screening for uterine artery Doppler.

Pre eclampsia was defined as Hypertension in Pregnancy as Systolic blood pressure \geq 140mmhg and/or the diastolic blood pressure \geq 90mmhg on at least two occasions four hours apart developing after 20 weeks of gestation in previously normotensive women. Hypertension should be accompanied by proteinuria of >300mg in 24 hours or 2 readings of at least ++ on dipstick analysis. FGR is defined as EFW of <3rd centile or EFW < 10th centile with abnormal doppler findings.

2.6. Transabdominal ultrasound technique

The curvilinear transabdominal transducer used is 5 or 3.5 MHz. Midsagittal section of the uterus and cervical canal is imaged and paracervical vessels are identified. Doppler for colour flow is used. Next to the cervix, the uterine arteries are visible. The Doppler sampling gate was set at 2 mm, flow velocity waveforms are obtained from the ascending branch of the uterine artery at the location closest to the internal os. To obtain the highest systolic and end-diastolic velocities smallest angle of insonation (30°). Once similar wave forms are obtained the PI can be calculated. The average reading from both sides is added together to determine the mean PI.

Doppler wave forms can be obtained at the crossing of uterine artery with external iliac artery. The probe is directed towards the pelvis and is positioned about 2-3 cm inside the iliac crests. Uterine arteries are recognised using colour flow Doppler. 1 cm above crossing of uterine artery and the external iliac artery, Doppler is used and indices are measured. This ensures that the main uterine artery trunk is used to obtain Doppler velocities.^{6,7}

2.7. Statistical analysis

Data was analyzed using SPSS 22 version software. The data was computed in the form of Frequencies and proportions. Chi-square test or Fischer's exact test (for 2x2 tables only) was used as test of significance for qualitative data. Continuous data was represented as mean and standard deviation.

3. Results

In the present study about 50% women were in the age group of 20-30 years, 3.7% were in the age group between 18-20 years, 30.5% were in the age group between 21-25 years, 15.9% were in the age group between > 30 years. P value computed was 0.703, which was not statistically significant. Hence there was no relation between preeclampsia and age

(Table 1). About 65.9% were multigravida and 34.1% were primigravida there was no significant statistical difference found between Preeclampsia and parity.25% of primigravida and 16.70% of multigravida patients developed pre eclampsia. There was a significant difference found between Preeclampsia and BMI. 45.5% of women with pre eclampsia had BMI of >30kg/m2.

19.5% of participants developed pre eclampsia in which 2.5% had severe pre eclampsia, 17.07% had non severe pre eclampsia and 80.5% were normotensive.

Pathological mean uterine artery PI was seen in 14.60% of subjects. P value was calculated and was 0.001. There was a significant difference found between Preeclampsia and uterine artery PI. 66.7% of women with pathological mean uterine artery PI had pre eclampsia among them 16.66% developed severe and 83.34% developed non severe preeclampsia. (Table 2)

7.31% of women had bilateral uterine artery notching. There was a significant difference found between Preeclampsia and Diastolic notching. 33.3% of women with bilateral uterine artery notching had preeclampsia. P valve 0.005.(Table 3)

Pathological mean uterine artery PI was seen in 14.6% of subjects and they were started with low dose aspirin. P

value was <0.001, there was a significant difference found between Preeclampsia and low dose aspirin. (Table 4)

Of 82 study participants 51.2% of them underwent vaginal delivery and 48.8% of them underwent LSCS. 9.8% of newborns were low birth weight in which 37.5% of them had pathological mean uterine artery PI, 25% of them had bilateral uterine artery diastolic notching. 90.2% of them were of normal birth weight.

There was no significant difference (p valve 0.183) found between Preeclampsia and birth weight. 18.8% and 81.3% of newborns born to preeclamptic are low birth weight and normal birth weight respectively. There was no significant difference (P value 1) found between Preeclampsia and NICU admission. 6.3% of NICU admissions were seen in the newborn born to pre eclamptic women. (Table 5)

3.7% of newborns had stage 1 FGR. There was no statistical significance between FGR with uterine artery PI and diastolic notching. How ever there was statistical significance between Aspirin and FGR (P value less than 0.001).(Table 6)

There was a statistically significant difference found between uterine artery PI and preeclampsia. The mean uterine artery PI of 1.61 found in normotensive and 2.02 in patients with pre eclampsia. (Table 7)



Figure 1: Transabdominal scan showing uterine artery doppler waveforms

Table 1: Distribution of subjects according to age and preeclampsia

Age Group	Non Pre eclampsia		Preeclampsia	
	N	%	N	%
<20yrs	2	66.7%	1	33.3%
21-25yr	19	76%	6	24.0%
26-30yrs	35	84.4%	6	14.6%
>30 yr	10	76.9%	3	23.1%

Table 2: Distribution of subjects according to preeclampsia and uterine artery PI

PI	Non pre eclampsia		Preeclampsia	
	N	%	N	%
Normal	62	88.6%	8	11.4%
Abnormal	4	33.3%	8	66.7%

Table 3: Distribution of subjects according to diastolic notching

Diastolic Notch	Non pre eclampsia		Preeclampsia	
	N	%	N	%
Absent (76)	62	81.6%	14	18.41%
Present (06)	4	66.7%	2	33.3%

Table 4: Distribution of subjects according to low dose aspirin

Received Low Dose Aspirin	Non pre eclampsia		Preeclampsia	
	N	%	N	%
Yes (70)	62	88.6%	8	11.4%
No (12)	4	33.3%	8	66.7%

Table 5: Distribution of preeclampsia based on birth weight and NICU admission

	Non Pre-eclampsia N	Non Pre-eclampsia %	Preeclampsia N	Preeclampsia %
Low birth weight	62	88.8%	8	11.4%
Normal	4	33.3%	8	66.7%
NO NICU admission	5	7.6%	3	18.8%
NICU admission	61	92.4%	13	81.3%

Table 6: Distribution of FGR in uterine artery PI, diastolic notching and aspirin

	Non Pre-eclampsia N	Non Pre-eclampsia %	Preeclampsia N	Preeclampsia %
Normal uterine artery PI	69	98.57%	1	1.53%
Abnormal uterine artery PI	10	83.3%	2	16.6%
Absent diastolic notch	74	97.36%	2	2.64%
Present diastolic notch	5	83.3%	1	16.6%
Aspirin received	10	83.3%	2	16.6%
Aspirin not received	69	98.57%	1	1.42%

Table 7: Comparison of mean uterine artery PI among subjects with preeclampsia and without preeclampsia

	Mean	Standard Deviation	p value
Non preeclampsia	1.61	0.44	0.002
Preeclampsia	2.02	0.71	

Table 8: Comparison of sensitivity, specificity, positive predictive value, negative predictive value, accuracy of uterine artery PI, diastolic notching and both combined

Statistic	Uterine artery PI	Diastolic Notching	Combined
Sensitivity	50%	12.5%	50%
Specificity	93.94%	93.94%	92.42%
Positive predictive value	66.67%	33.33%	61.54%
Negative predictive value	88.57%	81.58%	88.41%
Accuracy	85.37%	78.05%	88.15%

4. Discussion

The current study was conducted among 82 women visiting for antenatal care at Ramaiah Medical college and Hospital over a period of 18 months were analyzed for uterine artery Doppler changes between 11 and 14 weeks of gestation and all the subjects included in the study criteria were followed up till delivery and details of pregnancy events, delivery and neonatal outcome were studied.

Uterine artery Doppler waveforms were assessed for Pulsatility Index and Diastolic notching at 11-14 weeks of gestation. Among 82 subjects 14.6% of them had pathological uterine artery PI and 9.8% had diastolic notching between 11 and 14 weeks of gestation. 66.7% of women with pathological mean uterine artery PI developed pre eclampsia (16.66% developed severe and 83.34% developed non severe preeclampsia) which is high compared to Martin et al⁹ where 5% and 18.6% of subjects had pathological mean uterine artery PI and bilateral diastolic notching respectively in which 27% of women developed pre eclampsia and similarly seen in the study conducted by Bindal et al reported 35% of them had diastolic notching of that 42.8% had pre eclampsia.²⁰ Harrington K et al¹⁴ who described pre-eclampsia in 15.16% of women with bilateral notching at first trimester which is low compared to current study. Among 82 subjects studied 19.5% women developed pre-eclampsia which similar to study conducted by Oancea et al⁶ i.e., 21.6%, Neravi et al¹ is 22%, Das et al.¹² is 17.6% and high prevalence compared to that quoted by Das et al¹² which is 12.7%, Gomez et al¹³ is 2.2%, Harrington K et al¹⁴ is 4.7%.

The mean uterine artery PI was found out to be 1.64 in normotensives and 2.02 in pre-eclamptic subjects which is statistically significant when compared to non preeclamptic subjects and hence uterine artery PI helps in early prediction of pre eclampsia which is similar to Martin et al where the mean uterine artery PI is >2.5.⁹ Bilateral uterine artery notching seen in 7.3% of cases of which 33.3% had pre eclampsia and 16.66% had FGR, compared to Gomez et al.¹³ where 29.5% had diastolic notching at 13-14 weeks and 48.2% at 11-12 weeks, similarly with Bindal et al the mean uterine artery PI was 1.179 in normotensive and 1.44 in patients with pre eclampsia.²⁰

Both Uterine artery PI and Diastolic notching were pathological in 6.09%, 40% had pre eclampsia and 20% had FGR. In our study 16.66% of subjects who had pathological mean uterine PI and notching delivered growth restricted baby which is similar in the study conducted by Martin et al which is 12%.⁹

One of the factor in the etiopathogenesis of pre eclampsia is imbalance in production of vasoconstrictor substances such as prostacyclin and thromboxane. Thromboxane is a vasoconstrictor and stimulant of platelet aggregation. This is the rationale of using Low aspirin might prevent or delay development of pre eclampsia. Early

detection of PE and starting prophylactic therapy may help to prevent PE and its severe complications. Use of calcium and antioxidant vitamins for prevention of PE from mid-gestation has been unsuccessful as they have small effect i.e, around 10%.⁸

Subjects with pathological uterine artery PI were advised take low dose aspirin (75mg) among them 16.7% developed severe and 50% developed non-severe which is statistically significant similarly seen in the study conducted by Bower et al the incidence of pre eclampsia was 29% in subjects received aspirin (60mg) and 41% in the placebo group.¹⁵ 16.66% of women were on low dose aspirin among them 16.67% delivered growth restricted baby. In the study conducted by Ebrashy et al¹⁶ women who were on low dose aspirin 35% developed pre eclampsia and 19% developed FGR, in control group 62% developed pre eclampsia and 19% developed FGR. Meta-analysis conducted by Doorn et al¹⁷ (<81mg, 81 mg, 100mg, 150mg) showed that there is significant reduction of preterm pre eclampsia i.e., 62% and in group who were on aspirin dose < 150mg did not show any significant reduction.

In SPREE trial, screening for preterm PE was done combining maternal factors, mean arterial pressure, uterine artery pulsatility index and serum placental growth factor identified a high risk group. The study had about 46% of SGA neonates < 10th percentile born at < 37 weeks and 56% of those born at < 32 weeks the overall screen positive rate was 12.2%.¹⁸ In the ASPRE trial, use of aspirin (150mg) reduced the overall incidence of SGA < 10th centile by about 40% in babies born at <37 weeks and about 70% in babies born at < 32 weeks. Aspirin didn't have significant effect on incidence of for those born after 37 weeks SGA.¹⁹ There are no studies comparing 60-80mg and 150mg. However NICE guidelines recommend 75mg of aspirin in the women who has more than 1 moderate risk for pre eclampsia.

The combined sensitivity (uterine artery PI + diastolic notching) was 50%, specificity was 92.42%, PPV 61.54%, NPV 88.41%. Alone uterine artery PI has sensitivity of 50%, specificity 93.94%, positive predictive value of 66.67%, negative predictive value of 88.57% (**Table 8**) which is similar to study conducted by Martin A M et al⁹ in which the uterine artery PI sensitivity is 27%, specificity is 95.4%, PPV is 11%, NPV is 98.% and similar to study conducted by Velauthar¹⁰ where the sensitivity and specificity of abnormal uterine artery PI in the prediction of early-onset pre-eclampsia were 47.8% and 92.1% , and in the prediction of fetal growth restriction were 39.2% and 93.1% respectively and Gomez et al found sensitivity is 24%, specificity is 95%, PPV is 11.3%, NPV is 97.9%.¹³ Whereas bilateral uterine artery notching showed sensitivity of 12.5%, specificity 93.94%, PPV of 33.33%, NPV is 81.58% similar to study conducted by Neravi et al¹ showed sensitivity of 34.29%, specificity of 84.62%, PPV of 54.55%, NPV of 70.51%.

5. Conclusion

Pre eclampsia is a clinical syndrome in which multi system involved in the pathogenesis. PE is the leading cause of morbidity and mortality in pregnant mother and neonate. Thus it is important for an ideal predictive test and preventive measure still remains challenging.

In the current study 14.6% of women had pathological mean uterine artery PI and 7.3% of them had bilateral uterine artery notching at 11-14 weeks of gestation. The mean uterine artery PI in normotensive was 1.61 and in pre eclamptic patients was 2.02. 66.7% of women with pathological uterine artery PI and 33.3% of women with uterine artery notching developed pre eclampsia. 14.6% of subjects had pathological uterine artery PI were on low dose aspirin among these 16.7% were growth restricted, 33.3% were low birth weight, 16.7% developed severe pre eclamptic, 50% developed non severe pre eclamptic. Mean uterine artery PI has sensitivity of 50%, specificity 93.94%, positive predictive value of 66.67%, negative predictive value of 88.57%

Hence assessment of uterine artery doppler waveforms at 1st trimester helps in early prediction of pre eclampsia and growth restriction and also helps to categorize patients as low and high risk patients. In high risk women Doppler is one of the better monitoring tool which is a non-invasive screening method for fetoplacental circulation. Thus high uterine artery pulsatility index and notching in uterine artery doppler waveform between 11 and 14 weeks of gestation has shown to predict pre eclampsia.

It is a non-invasive test and cost effective. This scan between 11 and 14 weeks is done for aneuploidy screening; during the same procedure added doppler assessment will help in prediction of pre eclampsia and growth restriction. Our results suggest that, pregnancies at risk of developing hypertensive disorders and associated complications already have an abnormally increased uterine artery PI in early pregnancy. The use of PI to screen large undefined population as a screening test has limited role and evidences. The sample size of 82 is too small to extrapolate the results on to general population. The use of uterine artery PI combined with other screening tests needs to be determined by further investigations. The etio-pathogenesis of pre eclampsia is still unclear. Hence a panel of tests for prediction of pre eclampsia and FGR can be used; in which mean uterine artery PI could be one of the tests.

6. Source of Funding

None.

7. Conflict of Interest

None.

8. Ethical Approval

Ethical No.: MSRMC/EC/PG-12/02-2021.

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