

Role of Uterine Artery Doppler in Prediction of Preeclampsia and Associated Adverse Outcomes Between 12-20 Weeks in Low Risk Pregnancies

Original
Article

Asmaa Ibrahim Ogila, Abdalla Medhat Sayed, Manal Hamdy, Hadeer Meshaal and Yossra Sameh Lasheen

Department of Obstetrics and Gynecology, Faculty of Medicine, Cairo University, Egypt

ABSTRACT

Objectives: To assess the role of uterine artery Doppler done between 12 – 20 weeks pregnancy in prediction of preeclampsia and associated adverse outcomes.

Material and Methods: The study was designed as prospective observational case control study. 100 pregnant patients were selected from the maternity hospital outpatient with Doppler ultrasound done in fetal medicine unit by a consultant, only 92 patients completed their antenatal follow up. The participants then were allocated into two groups, one group with abnormal uterine artery indices (n=6) and the other group with normal uterine artery indices (n=86). The two groups were compared regarding development of preeclampsia, fetal growth restriction, oligohydramnios and NICU admissions.

Results: Among the 92 patients who completed their follow up period, of the 6 patients with abnormal uterine artery indices 4 developed preeclampsia, two of which had fetal growth restriction. While in the group with normal Doppler indices, no maternal or fetal complications developed.

Conclusion: Screening with Doppler and especially inclusion of an early diastolic notch is a good predictive test of preeclampsia. The test offers a good sensitivity in the prediction of preeclampsia, it is also a good negative test and thus it can exclude cases that don't need frequent examination. This may allow more appropriate targeting of antenatal care.

Key Words: Doppler, early pregnancy, preeclampsia.

Received: 21 April 2024, **Accepted:** 22 April 2024

Corresponding Author: Asmaa Ibrahim Ogila, Department of Obstetrics and Gynecology, Faculty of Medicine, Cairo University, Egypt, **Tel.:** +2 010090650463, **E-mail:** ogilaasma@gmail.com

ISSN: 2090-7265, May 2024, Vol.14, No. 2

INTRODUCTION

Preeclampsia is a pregnancy specific complication characterized by high blood pressure and signs of damage to another organ system, most often the liver and kidneys. Preeclampsia usually begins after 20 weeks of pregnancy in women whose blood pressure had been normal^[1].

Preeclampsia and fetal growth restriction are major causes of perinatal mortality and morbidity, and a major cause of maternal morbidity and mortality as well^[2].

Several studies have shown that a generalized endothelial dysfunction is associated with these complications. Clinical trials have shown that pregnant women who demonstrate high resistance in uteroplacental blood flow are at high risk of preeclampsia^[3].

The increased resistance to uteroplacental flow in cases of preeclampsia arises from the insufficient invasion of the maternal spiral arteries by the trophoblasts early

in gestation. This defect in invasion results in failure of converting the high resistance low volume vessels into low resistance high volume ones^[4].

Subsequent to this state of high resistance in the uteroplacental circulation secreted factors from the ischemic placenta cause generalized endothelial cell injury, compromised vascular integrity and an atherosclerosis like process in small arteries resulting in occlusion and necrosis^[5].

As there is no effective treatment for this complication, the identification of women who are at risk of developing preeclampsia would be of great value. Clinicians could then identify women who require closer antenatal surveillance and allow early referral for timely delivery, when signs or symptoms occur^[6].

So our study focuses on the role of uterine artery Doppler done between 12-20 week gestation for prediction of preeclampsia and associated adverse outcomes in low risk pregnancies.

AIM OF THE WORK

The aim of this study is to determine the role of Doppler assessment of the uterine arteries at 12-20 weeks of gestation in predicting the subsequent development of preeclampsia and associated adverse outcomes.

PATIENTS AND METHODS

This study was conducted at Kasr El Aini Hospital, Cairo University in the period from September 2019 to March 2020 on 100 pregnant women who attended the obstetric out-patient clinic for routine antenatal care examination at 12-20 weeks of gestation using a model using a curvilinear transabdominal multi-frequency (3-7 MHz) transducer (Voluson 730 Pro, GE Healthcare, USA) ultrasound apparatus at the fetal medicine unit.

Inclusion criteria

Singleton pregnancies with a gestational age from 12-20 weeks.

Exclusion criteria

Multifetal pregnancies, Diabetes Mellitus, Hypertension before 20 weeks.

Renal disorders, Cardiac disorders, Women known with antiphospholipid syndrome.

Patients included in this study will have the following done:

Each patient will sign a written consent after explaining to her, the aim of the study, what it involves, intended benefits and anticipated risks.

Full History Taking Including: Name, age, Obstetric history and 1st day of last menstrual period (LMP), gestational age documentation, medical and surgical history.

Thorough Clinical Examination

Height (in cm) and weight (in kg) measurements, Obstetric palpation (Maneuvers of Leopold): Fundal level, Fundal grip to detect the part of the fetus occupying the fundus.

Umbilical grip to detect the back and fetal limbs.

First pelvic grip to detect part of the fetus occupying the lower uterine segment and to detect engagement.

Ultrasound

Complete transabdominal ultrasonographic examination including confirmation of gestational age, fetal number, viability, presentation, estimated fetal weight, position and grade of placenta, amount of liquor.

Uterine artery Doppler

All pregnant women underwent transabdominal uterine artery Doppler assessment. Blood flow velocity waveforms were obtained with a pulsed wave Doppler ultrasound using a curvilinear transabdominal multi-frequency (3-7 MHz) transducer (Voluson 730 Pro, GE Healthcare, USA) apparatus.

The uterine artery was easily identified by its characteristic flow velocity waveform. At each examination the patient was in a semi-recumbent position with her head and chest supported at approximately 45° to the Horizontal.

The maximum systolic and minimal diastolic velocities were computed by electronic caliber and produced the systolic diastolic ratio, the resistance index and pulsatility index of the two vessels. The RI, PI and the presence or absence of a diastolic notch (unilateral- or bilateral) were noted. Waveform profiles were obtained without uterine contraction (lax abdominal wall).

Women with a mean PI of ≥ 1.45 , a mean RI of ≥ 0.58 and those with unilateral or bilateral uterine artery notches were considered as screen positive group, while those with PI of less than 1.45, RI less than 0.58 and with no uterine artery notches were considered as screen negative group.

Both groups were followed up till delivery in the form of routine antenatal care with special concern for blood pressure measurement, urine analysis for proteinuria and more frequent ultrasound for fetal growth scan monitoring.

Sample size calculation

According to the results reported in previous publication (3), and using a Confidence Interval (margin of error) of 4.50% and a Confidence Level of 95%, we calculated that the minimum proper sample size was 90 women. To compensate for possible drop-out, the final sample size included was 100 women. Sample size calculation was done using online Sample Size Calculator (<https://www.calculator.net/>).

Ethical approval

Local ethical committee approval was obtained before enrollment of women into the study.

Code: MS-256-2019

Statistical methodology

Data was collected, tabulated, coded then analyzed using SPSS computer software version, numerical variables were presented as mean and standard deviation on other hand categorical variables were presented as number of cases and percent.

Student-t-test was used for between groups comparison of numerical variables. Chi-square test or fisher exact test were used, whenever appropriate, for comparison between groups as regard categorical variables.

RESULTS

100 pregnant females were included in the study. These females were recruited from Kasr El Aini obstetric outpatient clinic for routine antenatal care in the period from September 2019 to March 2020.

All females included in the study had transabdominal Doppler ultrasonography for assessment of the presence of diastolic notch & its laterality & assessment of resistance index (RI) and pulsatility index (PI) in both uterine arteries. Uterine artery Doppler was considered abnormal if uterine artery $PI \geq 1.45$, $RI \geq 0.58$, presence of unilateral or bilateral diastolic notch.

The age range of the study population was 20-42 years with mean of 31 years. 65 cases (65 %) were primigravidas and 35 cases (35 %) were multiparas. The range of gestational age at the first time visit was 10 - 20 weeks with mean of 18 weeks and the ages of the patients were 20-30 years (53 cases) , 31-40 years(43 cases) and 4 cases between 40-42 years. All pregnant women were followed up till delivery for development of preeclampsia & IUGR.

92 cases completed their follow up program while 8 cases were lost and so were considered as drop out cases (1 patient developed IUFD at 27 weeks & 7 patients did not fulfill their antenatal follow up schedule) (Table 1).

Table 1: shows summary for the results in the two groups with abnormal and normal Doppler flow

	Patients with abnormal uterine artery Doppler (n=6)	Patients with normal uterine artery doppler.(n=86)	p-value
Mean age (years)	28.5	31	0.3 (NS)
BMI (kg\m ²)	32	29	0.7 (NS)
Number of primigravidas	3(50%)	57(66.2%)	0.4 (NS)
Number of multigravidas	3(50%)	29(33.7%)	
Number of cases that develop hypertension without albuminuria	0	0	-
Number of cases with pre eclampsia	4(66.6%)	0(0%)	0.000 (significant)
Number of cases with oligohydramnios	2(33.3%)	0(0%)	0.004 (significant)
Numberof cases with IUGR	2(33.3%)	0(0%)	0.004 (significant)
Number of IUFD	0	0	-
Mean gestational age at delivery (weeks)	33.7	39	0.04 (significant)
Number of cases that delivered vaginally	3(50%)	56(65.1%)	
Number of cases that delivered by Cesarean section due to fetal distress	1(16.6%)	0(0%)	0.03 (significant)
Mean estimated fetal weight at delivery (Kgs)	2.4	3.2	-
Neonates with Apgar score less than 7 at 5 minutes	3(50%)	3(3.4%)	0.003 (significant)
Number of neonatal deaths	0	0	-
Number of NICU admissions	2(33.3%)	3(3.4%)	0.03 (significant)

In the 92 cases who continued the antenatal care till delivery, the following was observed:

4 pregnancies (4.34%) developed uterine artery Doppler changes with complications: 2 patients developed preeclampsia only & 2 patients developed both preeclampsia & IUGR.

2 pregnancies (2.17%) developed uterine artery Doppler changes with no complications.

86 pregnancies (93.4%) neither developed uterine artery Doppler changes nor developed complications

For statistical analysis, we divided the females subjected to this study into the following groups: preeclampsia group (n=4): preeclampsia group without IUGR (n=2), IUGR group (n=2) & non complicated group (n=88).

Demographic & clinical characteristics of the studied groups: The mean age of preeclampsia group was 28.5 years & in the non-complicated was 31 years. The difference was statistically insignificant (P= 0.2) .

The mean age of IUGR group was 28.5 years & in the non-complicated group was 31 years. The difference was statistically insignificant ($P = 0.2$).

A comparison between preeclampsia group & non-complicated group regarding gestational age mean value at examination time shows that the mean GA was 17 weeks in preeclampsia group and 19 weeks in non-complicated group that denotes a non-significant difference.

There was a statistically significant difference with p value = 0.043 between preeclampsia group & non-complicated group regarding gestational age mean value at the time of delivery that as 34.5 weeks in preeclampsia group & 39 weeks in non-complicated group.

There was statistically significant difference with (p value = 0.01) between IUGR group and non-complicated group regarding gestational age mean value at the time of delivery that was 33.5 weeks in IUGR group and 39 weeks in non-complicated group.

The diastolic notch was present in 6 cases (6.5%) of the study population.

All cases of the preeclampsia group (4 cases) showed the presence of the diastolic notch while only 2 cases (2.3%) of the non-complicated group showed the presence of diastolic notch and the difference was statistically significant (P value = 0.02) as shown in (Table 2)

Table 2: Comparison between the preeclampsia group & non-complicated group regarding presence or absence of diastolic notch

	Preeclampsia group (n= 4)	Non-complicated group (n=88)
Absent		
Count	0	86
Percent	0	97.7%
Present		
Count	4	2
Percent	100%	2.3%
<i>P</i> value	0.02	

The percentage of patients with +ve diastolic notching in IUGR group was significantly higher than those in non-complicated group (P value = 0.045) as shown in (Table 3).

Table 3: Comparison between IUGR group & non-complicated group regarding presence or absence of diastolic notch

	IUGR group (n= 2)	Non-complicated group (n=88)
Absent		
Count	0	86
Percent	0	97.7%
Present		
Count	2	2
Percent	100%	2.3%
<i>P</i> value	0.045	

Percentage of patients with bilateral notching was significantly higher in preeclampsia group than in non-complicated group (P value = 0.33)

Percentage of patients with bilateral notching was significantly higher in the IUGR group than in non-complicated group (P value = 0.027).

The mean of both RI and PI of the right uterine artery was lower in the non-complicated group when compared with the preeclampsia group and the difference was statistically significant (P value = 0.021 for PI and 0.037 for RI) as shown in (Table 4).

Table 4: Comparison between the preeclampsia group & non-complicated group regarding the mean value of Rt. uterine artery RI and PI

	Preeclampsia group (n = 4)		Non complicated group (n = 88)	
	RI	PI	RI	PI
Range	0.6-0.68	1.47-1.59	0.43-0.52	0.9-1.2
Mean	0.64	1.53	0.47	1.05
SD	+/-0.02	+/-0.01	+/-0.03	+/-0.05
<i>P</i> value	0.021 for PI and 0.037 for RI			

The mean of both RI and PI of the right uterine artery was lower in the non-complicated group when compared with the IUGR group and the difference was statistically significant (P value = 0.047 for RI and 0.035 for PI).

The mean of both RI and PI of the left uterine artery was lower in the non-complicated group when compared with the preeclampsia group and the difference was statistically significant (P value = 0.033 for RI and 0.019 for PI)

The mean of both RI and PI of the left uterine artery was lower in the non-complicated group when compared with the IUGR group and the difference was statistically significant (P value = 0.041 for RI and 0.029 for PI)

4 cases developed Preeclampsia with changes in PI, RI, unilateral or bilateral notching as stated before and had termination of pregnancy at a period of 33-36 weeks. (Table 5) shows correlation between cases with Preeclampsia and degree of albuminuria and their gestational age of delivery and detected changes on Doppler u/s.

However 2 cases all through the study developed changes in PI, RI & notching but did not develop preeclampsia or IUGR and had termination of pregnancy at a period of 38 & 40 wks. (Table 6) shows correlation between these cases and their gestational age of delivery and detected changes on Doppler ultrasound.

Table 5: Correlation between cases with preeclampsia and degree of severity and their gestational age of delivery and detected changes on Doppler u/s

PRE-ECLAMPSIA	GA	PI	RI	Notching	P VALUE (between detected changes and GA)	P VALUE (between detected changes and Preeclampsia)	r Coefficient
Severe	32 weeks	1.59	0.68	Bilateral	< 0.04	< 0.05	-0.61
Severe	33 weeks	1.53	0.65	Bilateral	< 0.027	< 0.033	-0.83
Severe	34 weeks	1.55	0.63	Bilateral	< 0.027	< 0.033	-0.83
Non-severe	36 weeks	1.47	0.6	Unilateral	< 0.035	< 0.042	-0.77

Table 6: Correlation between cases with Doppler changes that did not develop complications and their gestational age of delivery and detected changes on Doppler u/s

PRE-ECLAMPSIA	Albuminuria	GA	PI	RI	Notching	P VALUE (between changes & GA)	P VALUE (between changes & preeclampsia)
Absent	(-)	38 Weeks	1.48	0.61	Bilateral	> 0.03	> 0.1
Absent	(-)	40 Weeks	1.46	0.59	Unilateral	> 0.04	> 0.2

All cases that developed changes in Doppler U/S were treated by conservative measures, followed up closely and more frequently with blood pressure monitoring and ultrasound scanning. The changes detected were assumed to herald the occurrence of preeclampsia and hence this aided to prolong the gestational period.

Sensitivity & specificity

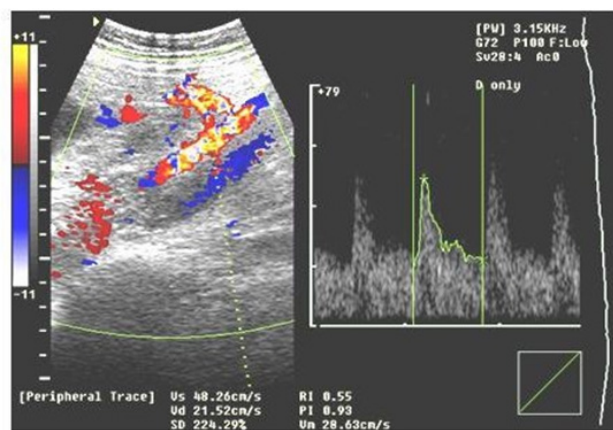


Fig. 1: Normal Rt. uterine artery waveform.

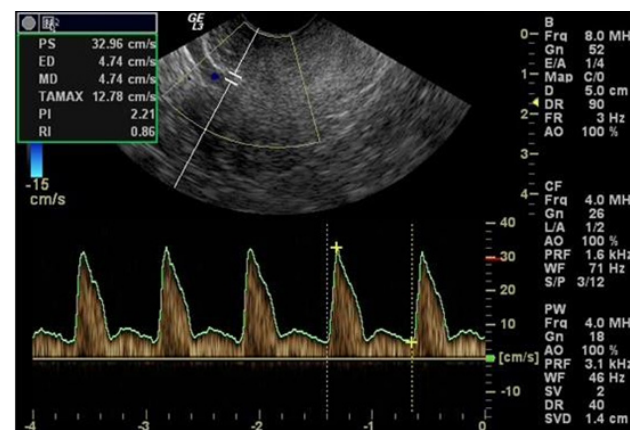


Fig. 2: Abnormal Rt. uterine artery waveform

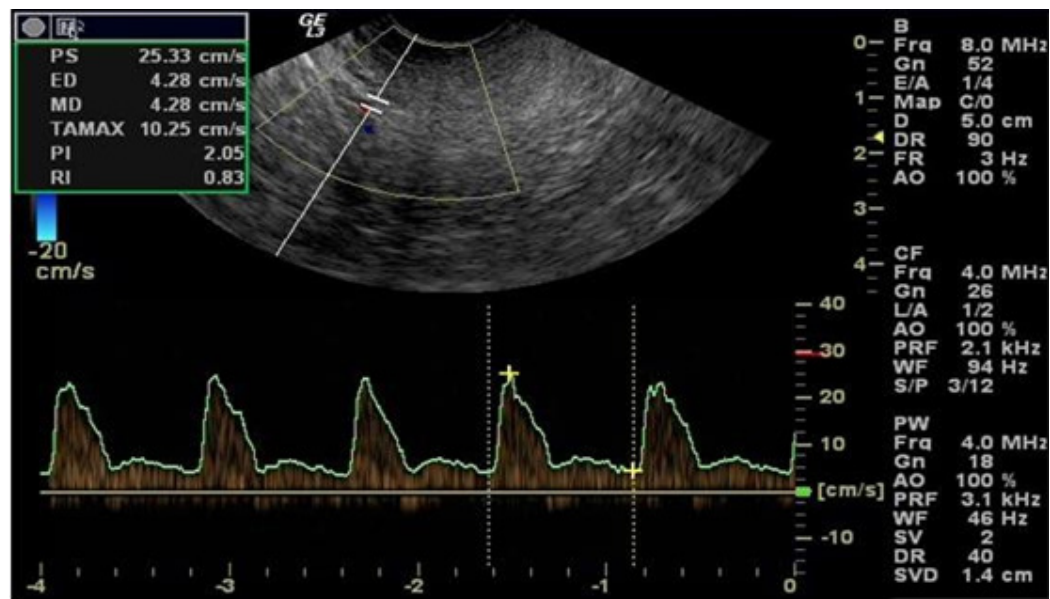


Fig. 3: Abnormal Lt. uterine artery waveform

DISCUSSION

Preeclampsia and intrauterine growth restriction remain important causes of maternal and perinatal morbidity and mortality. Maternal complications of preeclampsia include coagulopathy, renal and liver failure, and stroke^[7]. Adults who were affected by intrauterine growth restriction in utero are at increased risk for cardiovascular disease, hypertension and type II diabetes^[8].

The conversion of spiral arteries into uteroplacental artery plays a basic role in the establishment of the physiology of placental blood supply. The reduced uteroplacental blood flow due to inadequate trophoblastic infiltration of placental vascular bed can be the cause of variety of pregnancy complication as IUGR and preeclampsia^[9].

Preeclampsia and intrauterine growth restriction are characterized by abnormal placental formation which results in inadequate uteroplacental blood flow. This has led to the idea of using Doppler ultrasound to assess the velocity of uterine artery blood flow as part of routine ultrasound screening. Low end-diastolic velocities and an early diastolic notch characterize the waveforms of uterine artery blood flow in women who are not pregnant or are in their first trimester. Persistence of a diastolic notch (beyond 24 weeks' gestation) or abnormal flow velocity ratios have been associated with inadequate trophoblastic invasion^[10].

Accurate prediction of preeclampsia and intrauterine growth restriction is crucial to allow judicious allocation of resources for monitoring and preventive treatment to improve maternal and perinatal outcomes. However, studies investigating the predictive accuracy of uterine artery Doppler indices have revealed considerably varied results. Thus, it is questionable whether uterine artery

Doppler ultrasonography should be used as a predictive test^[11].

Impaired uteroplacental blood flow as reflected by abnormal uterine artery Doppler flow velocities remains the most important cause for severe pregnancy complications as preeclampsia & IUGR. This has led to the idea of uterine artery Doppler as a screening test for adverse pregnancy outcomes. Variations in Doppler techniques, measurement parameters & study protocols have resulted in disappointing results in the prediction of preeclampsia & IUGR. The clinical value of Doppler as a screening tool is defined by the high -ve predictive value of abnormal uterine artery Doppler waveforms^[12].

The impairment of trophoblastic invasion of uterine vessels with resultant placental hypoxia likely causes preterm preeclampsia (prior to 37 weeks), however the development of term preeclampsia is likely related to a separate mechanism^[13].

In our study, gestational age at delivery for the majority of our patients who did not develop preeclampsia was 37-41 weeks with mean value 39 weeks, and for those who developed preeclampsia was 33-36 weeks with mean value 34.5 weeks.

This is in agreement with the work made by Verma, D *et al* 2016 who reported that the mean value for gestational period at delivery for unaffected cases was 40 weeks, however, for those who developed preeclampsia was 37 weeks.

This difference might be due to that most of our patients who developed preeclampsia had severe degree and had to be terminated prematurely^[14].

Our study reveals that all the cases that developed preeclampsia in the group with high Doppler indices delivered preterm, which still points to the assumption that impaired trophoblastic invasion with subsequent high resistance to blood flow is the cause of early onset preeclampsia^[13].

Our study can be criticized for its small sample size, as 4 out of 92 patients (4.34%) developed preeclampsia, while in the work of Verma, D *et al* 2016, 20 out of 165 patients developed preeclampsia (12.1%) and this may be due to the relatively larger sample size.

In the present study, 2 cases had associated IUGR with severe preeclampsia (2.17%) and delivered at gestational periods of 33 & 34 weeks respectively. Verma, D *et al* 2016 stated that 10 patients had associated IUGR with Preeclampsia (6%). High proportion of pregnancies developing preeclampsia and/or SGA have increased impedance to flow in the uterine arteries at mid-gestation. Severe preeclampsia requiring early delivery is more likely to be associated with SGA than less severe preeclampsia requiring delivery at term^[14]. According to Gupta and colleagues in 2009, we used the $PI \geq 1.45$, $RI \geq 0.58$, diastolic notches as screening tools.

In our study, 6 cases showed changes with uterine artery Doppler in the form of $PI > 1.45$, $RI > 0.58$, Unilateral or Bilateral notching in which 4 cases developed preeclampsia^[15].

Among the preeclamptic group, there was a statistically significant correlation between the changes of uterine artery Doppler and the development of preeclampsia (p value < 0.05) as well there was statistically significant correlation between the same changes and gestational period at delivery (p value < 0.05).

This was consistent with the work of Razavi, M *et al* 2019 who detected similar results with statistically significant association (P value < 0.0001)^[16].

As well, Borna, S *et al* 2019 stated the presence of statistically significant relation (p value < 0.001) between the uterine artery changes on Doppler assessment at 18-22 weeks of pregnancy and the development of preeclampsia.

In our study, the cases that did not develop preeclampsia showed non-significant statistical correlation between uterine artery changes on Doppler assessment and development of preeclampsia (p value = 0.1, p value = 0.2).

This was consistent with the work of Gupta and colleagues in 2009 who stated that abnormal uterine artery Doppler findings were reported in 55% of hypertensive cases and 4% of normotensive cases^[15].

In the preeclamptic group in our study, there was an inverse association between the presence of uterine artery changes on Doppler assessment i.e. (PI, RI or notching) and the gestational period at delivery ($r = -0.61$ to -0.83).

This was consistent with the work of Razavi, M *et al* 2019 who proved an inverse association between the gestational age at delivery and prevalence of SGA ($r = -0.99$, $p < 0.0001$) and between the gestational age at delivery and mean uterine artery $PI > 1.58$ ($r = -0.51$, $p < 0.0001$)^[16].

Pedroso, M *et al* 2018 suggested that uterine artery Doppler ultrasonography predicts preeclampsia, maternal consequence of placental diseases more confidently than IUGR. Specifically an increased PI with notching in the second trimester best predicted preeclampsia over all in low and high risk patients. An increased PI or bilateral notching best predicted severe preeclampsia. An increased PI alone or in combination with notching best predicted IUGR in low risk patients, whereas the best predictor in high risk patients was RI^[17].

In the present study, the sensitivity of PI, RI or notching to predict preeclampsia was 56%, 61%, while the specificity of PI, RI or notching to predict preeclampsia was 87%, 77% respectively. For IUGR, sensitivity of PI was 59% and the specificity was 73%, while for RI or notching was 54%, 76%.

In the study made by Razavi, M *et al* 2019, the sensitivity of PI value above the 95th percentile or bilateral notching in predicting early onset preeclampsia is 73%, 62% for late onset preeclampsia and 100% of severe cases^[16].

Pedroso, M *et al* 2018 concluded that uterine artery Doppler could be useful to detect adverse pregnancy outcomes e.g. preeclampsia & IUGR. Bilateral evidence of notching and $RI > 0.7$ is associated with adverse pregnancy outcome. To improve the prediction of such changes, uterine artery Doppler changes should be combined with biochemical testing as α -fetoprotein and β -HCG^[17].

In the study made Bodovaa and colleagues in 2011, the sensitivity of PI and RI to detect adverse pregnancy outcomes was 53.8% for both and the specificity of PI and RI was 86%. It was stated that high PI, RI values associate pregnancies destined to be preeclamptic.

In a research made by Pongrojpraw and colleagues in 2010, the sensitivity of $PI > 1.58$ to detect preeclampsia was 81.4% and to predict IUGR was 81.2% with lower specificity values of 48.8% and 47.7% respectively, and so stressed that there should be a combination of uterine artery Doppler changes with biochemical testing as stated before^[12].

In a review of 30 studies made by Pedroso and colleagues in 2018, As a single predictor, uterine artery Doppler detects less than 50% of the cases of PE and no more than 40% of the pregnancies affected by FGR^[17].

Pedroso and colleagues in 2018 concluded that an increased PI with notching in the second trimester best predicted preeclampsia overall in low and high risk patients. An increased PI or bilateral notching best predicted severe preeclampsia, an increased PI alone or in combination with notching best predicted severe IUGR in low risk patients while an increased RI is the best predictor of IUGR in high risk patients. Thus it was concluded that PI and bilateral notching are the most promising Doppler indices to predict preeclampsia and IUGR^[17].

Pedroso, M *et al* 2018 showed that there are relatively low positive predictive value for uterine artery Doppler changes to predict preeclampsia & IUGR and this can be increased by the addition of a clinical parameter or biochemical testing to these changes^[17].

This is consistent with the research made by Roy, A.J. and Bhosale 2018, in their study they found Abnormal Doppler velocimetry of the umbilical artery (increased resistance, AEDV, REDV) were significantly associated with poor perinatal outcome in the form of low birth weight, APGAR of ≤ 7 at five minutes of birth, oligohydramnios and NICU admission^[18].

Comparing mode of delivery in both groups, in the preeclampsia group, two patients delivered by cesarean section (50 %), one of them because the patient had two previous cesarean sections, and the other one had an emergency cesarean section secondary to fetal distress while being on continuous CTG monitoring, the other two patients had successful vaginal deliveries after induction of labor.

No cases of maternal ICU admission in both groups, probably because no serious complications developed in the preeclampsia group as eclampsia, HELLP and retroplacental hematoma.

When comparing the APGAR score after 5 minutes in both groups, in the abnormal Doppler indices group, three neonates out of six (50%) had APGAR score less than 7 at five minutes, all related to cases diagnosed with preeclampsia, compared to 3 neonates out of 86 (3.4 %) in the group with normal Doppler indices. This is statistically significant with a p value of 0.003. There are two NICU admissions in the group with abnormal indices, both related to preeclampsia (33.3%), with three cases of NICU admissions in the normal Doppler group (3.4%), all three cases related to preterm delivery. This is statistically significant with a p value of 0.03.

In our study it's hard to determine the independent effect of preeclampsia in NICU admission, since the two neonates admitted to NICU were delivered preterm (at 32, 33 weeks) .so the effect of prematurity and preeclampsia can't be separately assessed in our study .

In 2015 Mendola, P., *et al* assessed the independent risk of preeclampsia in rates of NICU admission in 10,507 singleton pregnancies and they concluded that Preeclampsia was directly associated with adverse neonatal outcomes beyond morbidity mediated by preterm birth. Although severe neonatal outcomes were less common at later gestational ages, marginal structural models suggested elevated neonatal risk due to preeclampsia even if it was possible to deliver all infants at term^[19].

CONCLUSION

At present, uterine artery Doppler ultrasound provides a rapid, non-invasive & harmless method of detecting women at risk of developing preeclampsia.

Uterine artery PI and bilateral notching are the most promising Doppler indices that can predict the presence of preeclampsia and IUGR, and should be used in every daily clinical practice. Doppler assessment is noninvasive and thus acceptable to the patients.

Patients with notching or high RI or PI at 12-20 weeks gestation represent a risk group for adverse pregnancy outcome; on the other hand patients with normal flow velocity waveforms in uterine arteries at that time of gestation constitute a low risk group.

Screening with Doppler and especially inclusion of an early diastolic notch is a good predictive test of preeclampsia. The test offers a good sensitivity in the prediction of preeclampsia, it is also a good negative test and thus it can exclude cases that don't need frequent examination. This may allow more appropriate targeting of antenatal care.

Women with normal uterine artery Doppler results are unlikely to develop preeclampsia, and therefore do not necessarily need antenatal follow-up that is as close as that required in women with abnormal uterine artery Doppler findings who need more close observation, more frequent blood pressure monitoring, more frequent assessment of development of albuminuria, & more frequent ultrasound assessment for early detection of IUGR. Those women can receive early treatment to prevent the occurrence of preeclampsia or IUGR & to prolong the gestational period, so improve the maternal & neonatal outcomes.

CONFLICT OF INTERESTS

There are no conflicts of interest.

REFERENCES

1. Bahado-Singh, R.O., Kovanci, E., Jeffres, A., Oz, U., Deren, O., Copel, J. and Mari, G., 1999. The Doppler cerebroplacental ratio and perinatal outcome in intrauterine growth restriction. *American journal of obstetrics and gynecology*, 180(3), pp.750-756.
 2. Melchiorre K, Wormald B, Leslie K, Bhide A, Thilaganathan B. Firsttrimester uterine artery Doppler indices in term and preterm preeclampsia. *Ultrasound Obstet Gynecol* 2016;32:133-7.
 3. Cnossen JS., Morris RK. & Riet G.: Use of uterine artery Doppler ultrasonography to predict preeclampsia and intrauterine growth restriction: a systematic review and bivariable meta-analysis. 2012; 16: 555-610.
 4. Cošta SL, Proctor L, Dodd JM, Toal M, Okun N, Johnson JA, *et al.* Screening for placental insufficiency in high risk pregnancies: is earlier better? *Placenta* 2017;29:1034-40.
 5. Chien PF., Arnott N., Gordon A., Owen P. & Khan KS.: How useful is uterine artery Doppler flow in prediction of preeclampsia, intra uterine growth restriction & perinatal death? An over view *BJOG*. 2008; 107: 196-208.
 6. Ducey J. Velocity waveforms in hypertensive disease. *Clin Obstet Gynecol* 1989;32:679- 86.
 7. Jim, B. and Karumanchi, S.A., 2017, July. Preeclampsia: pathogenesis, prevention, and long-term complications. In *Seminars in nephrology* (Vol. 37, No. 4, pp. 386-397). WB Saunders
 8. Miller, E.C., 2019. Preeclampsia and Cerebrovascular Disease: The Maternal Brain at Risk. *Hypertension*, 74(1), pp.5-13.
 9. McNally, R., Alqudah, A., Obradovic, D. and McClements, L., 2017. Elucidating the pathogenesis of pre-eclampsia using in vitro models of spiral uterine artery remodelling. *Current hypertension reports*, 19(11), p.93.
 10. Kirbas, A., Ersoy, A.O., Daglar, K., Dikici, T., Biberoglu, E.H., Kirbas, O. and Danisman, N., 2015. Prediction of preeclampsia by first trimester combined test and simple complete blood count parameters. *Journal of clinical and diagnostic research: JCDR*, 9(11), p.QC20.
 11. Anderson, U.D., Gram, M., Åkerström, B. and Hansson, S.R., 2015. First trimester prediction of preeclampsia. *Current hypertension reports*, 17(9), p.74.
 12. Pongroj paw D., Chanthasenanont A. & Nanthakomom T.: Second trimester uterine artery Doppler screening in prediction of adverse pregnancy outcome in high risk women. *J. Med. Assoc. Thai*. 2010; 93 (Suppl.7): 127-130.
 13. Sheridan, M.A., Yang, Y., Jain, A., Lyons, A.S., Yang, P., Brahmasani, S.R., Dai, A., Tian, Y., Eilersieck, M.R., Tuteja, G. and Schuŝt, D.J., 2019. Early onset preeclampsia in a model for human placental trophoblast. *Proceedings of the National Academy of Sciences*, 116(10), pp.4336-4345.
 14. Verma, D. and Gupta, S., 2016. Prediction of adverse pregnancy outcomes using uterine artery Doppler imaging at 22-24 weeks of pregnancy: A North Indian experience.
 15. Gupta AK., Holzgreve W., Huppertz B., Malek A., Schneider H. & Hahn S.: Uterine artery Doppler changes in prediction of preeclampsia. *Clin Med*. 2009; 50(11): 2187-90.
 16. Razavi, M., Rashidi Fakari, F., Jafari, F.S., Farzaneh, F. and Sargolzaei, N., 2019. The role of uterine artery doppler ultrasound in the second trimester in predicting preeclampsia. *International Journal of Pediatrics*, 7(5), pp.9405-9411.
 17. Pedroso, M.A., Palmer, K.R., Hodges, R.J., da Silva Coŝta, F. and Rolnik, D.L., 2018. Uterine artery Doppler in screening for preeclampsia and fetal growth restriction.
 18. Roy, A.J. and Bhosale, A.A., 2018. Role of Color Doppler in predicting perinatal outcome in preeclampsia. *International Journal of Reproduction, Contraception, Obstetrics and Gynecology*, 7(2), pp.652-8.
 19. Mendola, P., Mumford, S.L., Männistö, T.I., Holston, A., Reddy, U.M. and Laughon, S.K., 2015. Controlled direct effects of preeclampsia on neonatal health after accounting for mediation by preterm birth. *Epidemiology (Cambridge, Mass.)*, 26(1), p.1
-