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Accuracy Of Uterine Artery Doppler In Determining Pre- Eclampsia And Adverse Pregnancy Outcomes In 2nd Trimester

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Abstract

Preeclampsia is considered as one of the most important causes of death among pregnant women all around the world. This study aimed to study the predictive value of uterine artery Doppler ultrasonography in the incidence of preeclampsia and the adverse pregnancy outcomes in pregnant women who attended MTH & Mujahid hospital. This study was performed by the prospective cohort method and the statistical population included 40 pregnant women, in their 13-24 weeks of pregnancy, with a singleton pregnancy who referred to the Madina teaching Hospital & Mujahid hospital Faisalabad o during 2021-2022. Flow velocity waveforms of right and left uterine artery were imaged with the patient in the semi recumbent position and uterine artery was identified in the longitudinal scan, lateral to uterus. Resistive index, pulsatility index and presence and absence of diastolic notch was considered. Out of 40 cases studied, 19 patients showed abnormal uterine artery Doppler results and among these 19(47.5%) developed preeclampsia, 4(21.0%) had adverse effect on fetus. Therefore, Doppler ultrasonography of the uterine artery has a predictive value in preeclampsia among pregnant women.

Introduction

Preeclampsia (PE) is a multisystem, pregnancy-specific disorder that is characterized by the development of hypertension (Blood pressure-140/90 mmHg) and proteinuria (300 mg/24 hours) after 20 weeks of gestation followed by organ perfusion with extreme vascular spasm [1,2].

In Preeclampsia there is insufficient invasion of maternal spiral arteries by the trophoblast early in gestation, so the transformation of these vessels from high resistance low volume to low resistance high volume non-responsive vessels does not take place.[3]

Pre-eclampsia is a leading cause of maternal and perinatal mortality and morbidity throughout the world, particularly in developing countries [3]. The prevalence of pre-eclampsia in developing countries ranges from 1.8% to 16.7% [4].

Medical Doppler ultrasound is commonly used to assess blood flow in the body's major and minor vessels [7]. Doppler ultrasonography of uterine artery is a noninvasive modality that is used to determine vascular perfusion of utero-placental area. It is regarded as an indirect evaluation of trophoblastic development during pregnancy. Most Doppler studies show that preeclampsia can be predicted as placental perfusion is initially impaired [8]. In the second trimester, a Doppler examination is performed using a Transabdominal approach. Uterine artery waveforms are easily accessible in more than 95 percent of patients [5].

Uterine artery Doppler has been widely study for the prediction of Pr**e-**eclampsia in the involvement of defective trophoblastic invasion [9]. The uterine arteries are a measure of the uteroplacental flow and a branch of the anterior division of the internal iliac artery [6].

Type	**Ratio**
Type I (mild)	>0.58
Type II (moderate)	Mild notching
Type III (severe)	Severe notching + >0.64

Uterine Artery Doppler findings for pre-eclampsia categorization

Elevated resistive index (RI), pulsatility index (PI) or systolic to diastolic (S/D) ratios and the presence of a diastolic notch are considered as abnormal uterine artery flow velocity disorders [10]. A PI or RI > 90%-Interval or the presence of any diastolic notch is defined as pathological and is related to multiple adverse pregnancy outcomes [6].

Studies were classified into 4 groups according to how the abnormal uterine artery flow velocimetry waveform was defined:

those that used flow waveform ratios (resistance index, pulsatility index, systolic/diastolic ratio, diastolic/systolic ratio)

those that used the presence or absence of any diastolic notch

those that used the presence or absence of bilateral diastolic Notches

those that used flow waveform ratios and presence of diastolic notches [3].

Resistive index is a parameter for characterizing arterial wave form at Doppler ultrasound. It is calculated as peak systolic velocity-end diastolic velocity/peak systolic velocity. The mean resistive index of the uterine artery was 0.50 ± 0.08 in normotensive participants and 0.64 ± 0.09 in pre eclamptic women, with the p-value <0.001. [8,10]

Pulsatility index was taken as a measure of the variability of blood velocity in vessel. It is equal to the difference between the peak systolic velocity and end diastolic velocity divided by mean velocity during cardiac cycle [8]. Mean uterine artery PI

(mean UAPI) is commonly measured at 13+6 weeks to predict adverse pregnancy outcomes including hypertensive disorder [11]

The aim of this study is to determine that either the uterine artery doppler is a standard parameter for the evaluation of pre-eclampsia in high-risk women at early stage to avoid the risk factors and adverse pregnancy outcomes.

Pre-eclampsia (PET), which affects about 2% of pregnancies, is a major cause of perinatal and maternal morbidity and mortality [12-14]. Routine antenatal care has evolved with the aim of identifying women at high risk for subsequent development of PET.

The likelihood of developing PET is increased by a number of factors in the maternal history, including Afro-Caribbean race, nulliparity, high body mass index (BMI) and personal or family history of PET [15-16]. However, screening by maternal history may detect only about 30% of those that will develop PET for a false-positive rate of 10%.

A more effective method of screening for PET is provided by uterine artery Doppler velocimetry at 22 weeks' gestation either alone or in combination with maternal history, with detection rates of 52% and 57%, respectively [16-17]. Indeed, Doppler is particularly effective in screening for severe PET that necessitates iatrogenic delivery before 34 weeks, with a detection rate of 85% for a false-positive rate of 10% [16].

Identification of women at high risk for PET during the second trimester could potentially improve pregnancy outcome because intensive maternal and fetal monitoring in such patients would lead to an earlier diagnosis of the clinical signs of the disease and the associated fetal growth restriction and avoid the development of serious complications through such interventions as the administration of antihypertensive medication and early delivery.

Another important reason for the early identification of these high-risk women would be to determine whether the administration of prophylactic therapy would prevent or significantly ameliorate these conditions. However, attempts at the prevention of PET by the prophylactic use of drugs from mid-gestation have been largely unsuccessful in the case of calcium and antioxidant vitamins, or they have had a small effect (10%) in the case of low-dose aspirin [17-20].

It is uncertain whether pharmacological interventions starting from the first rather than the second trimester would prove to be more effective in the prevention of PET, but before this can be investigated it is essential to develop a method of effective and early identification of the high-risk group.

Literature review

Preeclampsia (PE) is a multisystem, pregnancy-specific disorder that is characterized by the development of hypertension (Blood pressure-140/90 mmHg) and proteinuria (300 mg/24 hours or 1 + dipstick) after 20 weeks of gestation.

The incidence of pre-eclampsia is higher in primigravida women, and in those who have a family or history of hypertensive pregnancy. Pre-eclampsia is heterogeneous disorder with variable maternal and fetal manifestations [22]. Pre-eclampsia complicates 3%-8% of pregnancies worldwide, overall, 10- 15% of maternal deaths are associated with preeclampsia and eclampsia [23].

Even in the era of modern obstetrics, pre-eclampsia remains as a major complication of pregnancy which can lead to significant incidences of maternal and neonatal mortality and morbidity. Despite advances in medical research, reliable screening test for prediction of these adverse complications still lacking [22].

In the mother, pre-eclampsia may cause premature cardiovascular disease, such as chronic hypertension, ischemic heart disease and stroke later in life, while children born after preeclamptic pregnancies and who are relatively small at birth, have an increased risk of stroke, coronary heart disease and metabolic syndrome in adult life [22]

Pre-eclampsia is defined as the development of hypertension, proteinuria, or both, after 20 weeks in women with previously normal blood pressure [24]. It may be associated with many other signs and symptoms such as edema, visual disturbances, headache and epigastric pain [25]. The fundamental cause of pre-eclampsia is thought to be the abnormal uteroplacental circulation resulting from the failure of second wave of trophoblastic invasion into spiral arterioles, this will result in increased resistance to flow within the uterine arteries and decreased placental perfusion as well as due to imbalance between the prostacyclin and thromboxane A2 production [26].

The crucial issue to understand is that the prime mover of pre-eclampsia is abnormal placentation. Two common theories appear to be interlinked, ie, a genetic theory and an immunological theory [27]. Pre-eclampsia can be perceived as an impairment of the maternal immune system that prevents it from recognizing the feto-placental unit [28] . This concept has led to the idea of using Doppler assessment of uterine artery flow velocity waveform as a screening test for predicting preeclampsia [29]. Doppler examination of uterine arteries is a noninvasive tool that can be used to indirectly assess trophoblast development and uteroplacental perfusion [29]. Uterine artery Doppler sonography which is done during the second trimester can accurately predict preeclampsia, Resistance Index (RI), pulsatility index (PI) which are considered indirect measures of uteroplacental circulation [30]

Around one-tenth of maternal deaths in Asia are associated with hypertensive disorders, among them eclampsia and preeclampsia have the greatest impact on maternal and newborn morbidity and mortality. Preeclampsia is considered as the onset of a new episode of hypertension during pregnancy, characterized by persistent hypertension (Diastolic blood pressure ≥ 90 mmHg) and substantial proteinuria (>0.3g/24 hours).

Preeclampsia ranges from mild to severe as per the clinical characteristics and it is 5-8% in worldwide but it is one in every 10 pregnant women in India and varies from urban to rural, rural Indian women experiences higher incidences in getting preeclampsia than the urban Indian. In 2009,EmmanuelBujoldMD proposed that ASA treatment initiated early in pregnancy is an efficient method of reducing the incidence of preeclampsia and its consequences in women with ultrasonography evidence of abnormal placentation diagnosed by uterine artery Doppler studies.

In Mar 1994 North RA[1],Ferrier C,Long D proposed that Although abnormal uterine artery Doppler is associated with an increased risk of preeclampsia and FGR, the positive predictive values do not support its introduction as a routine screening test in nulliparous women.

July 2006FàtimaCrispiMD[a]suggested that In early-onset preeclampsia and intrauterine growth restriction, placental growth factor was lower and soluble fms- like tyrosine kinase–1 and vascular cell adhesion molecule–1 higher than in control subjects, although all changes were more pronounced in preeclampsia. In late-onset preeclampsia, those patients with abnormal uterine artery Doppler indices had higher soluble fms-like tyrosine kinase–1 and vascular cell adhesion molecule–1 level. In May 2018 Daniel Lorber Rolnik proposed that the use of uterine artery Doppler as a single predictive test for PE and FGR has poor accuracy. However, its combined use in predictive models is promising, being more accurate in detecting preterm PE than FGR.

In September 2007 W. Plasencia,N. Maiz,S. Bonino,C. Kaihura suggested that Maternal variables together with uterine artery PI at 11 + 0 to 13 + 6 weeks' gestation provide sensitive prediction of the development of PET, especially of severe early-onset PET. In 2004 Aris T Papageorghiou MBChB suggested that in normal pregnancy, impedance to flow in the uterine arteries decreases with gestation, and histopathological studies suggest that this is due to trophoblastic invasion of the spiral arteries and their conversion into low-resistance vessels. Failure of trophoblastic invasion is associated with complications of uteroplacental insufficiency. Several

Doppler screening studies, both in the second and more recently in the first trimester of pregnancy, have demonstrated an association between increased impedance to flow in the uterine arteries and subsequent development of pre-eclampsia, FGR and perinatal death.

Jeltsje S. Cnossen MD proposed that abnormal uterine artery waveforms are a better predictor of pre-eclampsia than of intrauterine growth restriction. A pulsatility index, alone or combined with notching, is the most predictive Doppler index. These indices should be used in clinical practice. Future research should also concentrate on combining uterine artery Doppler ultrasonography with other tests.

In 2013 S. Karger AG, Baselsuggest that In a normal pregnancy, uterine artery PI is affected by maternal characteristics, and in PE, uterine artery PI MoM is related to the severity of the disease. To determine maternal characteristics affecting uterine artery pulsatility index (PI) in normal pregnancies at 20–24 weeks' gestation and examine in pregnancies with preeclampsia (PE) the relation between uterine artery PI multiple of the median (MoM) and severity of disease.

In october2018 Maysaa A. Chyad, Enas A. Azab, Mennatallah H.Shalaby, Ahmad A. Aly can conclude that uterine artery Doppler between 14-20 weeks of gestation is a simple rapid non-invasive procedure and it can be used as a reliable indicator for prediction of preeclampsia to use it as a screening test.

MATERIALS AND METHODS:

The study was conducted from september2021 to June 2022 in department of diagnostic Radiology, Madina teaching Hospital& Mujahid Hospital, Faisalabad. The sample size of 40 was calculated. Consecutive non-probability sampling was used. All women coming for routine second trimester anomaly scan were included. Uterine artery assessment was done transabdominally. Each uterine artery was sampled soon after the crossing of the iliac vessels. Color Doppler gives a map of blood flow superimposed on the normal 2D image and is used to identify a particular blood vessel and sample the blood velocity within that vessel. Spectral Doppler gives a graph of blood velocity versus time- the Doppler waveform. This waveform is analyzed to detect changes in resistance to the blood flow. Pulsatility Index, Resistive Index values and presence or absence of diastolic notching were noted. These patients were followed up till delivery and maternal and neonatal outcome was noted.

Women with twin pregnancy, anomalous fetus or medical comorbidities like cardiovascular diseases, diabetes, chronic kidney, or liver diseases were excluded from study. Uterine artery Doppler sonography was conducted upon the women coming for routine anomaly scan. Flow velocity waveforms of right and left uterine artery were imaged with the patient in the semi recumbent position and uterine artery were identified in the longitudinal scan, lateral to uterus. In this position bifurcation of common iliac artery were identified and recording was made at the point where uterine artery and external iliac artery have crossed each other as detected by the color flow doppler. Pulsed wave doppler was used to obtain three consecutive waveforms. Resistive index, pulsatility index and presence and absence of early diastolic notch and its depth in terms of notch index were calculated.

Women were followed regarding development of pre-eclampsia. Uterine Artery Doppler findings for pre-eclampsia were categorized as: Type I: Resistive index >0.58; Type II: Mild notching of uterine artery at beginning of diastole; Type III: Severe notching + abnormal Resistive index (>0.58).

Resistive Index was taken as an indicator of resistance of an organ to perfusion. It is parameter for characterizing arterial waveform at Doppler ultrasonography. It is calculated as Peak systolic velocity-End diastolic velocity/Peak systolic velocity. Pulsatility index was taken as a measure of the variability of blood velocity in vessel. It is equal to the difference between the peak systolic velocity and end diastolic velocity divided by mean velocity during cardiac cycle. The mean Pulsitility index

from the left and the right uterine arteries were calculated. If the mean PI was more than 1.45 were considered abnormal. There is not much difference between the abnormal PI values of uterine artery doppler from 16-19 week of gestation. Notch index was the result of increase in the resistance to the blood flowing into placenta.
Pre-eclampsia was defined by high blood pressure and excess of patient's urine after 20 weeks of pregnancy. It can lead to eclampsia if left untreated. According to the international society for study of hypertension pre-eclampsia is diagnosed if previously normotensive women have diastolic blood pressure above 90 mmHg measured twice 4 hours apart and with proteinuria of>300mg in 24 hours urine specimen or 02+ protein dipstick test twice 04 hours apart.
True Positive cases were cases which showed uterine artery doppler findings suggestive of pre-eclampsia and subsequently develops pre-eclampsia. The qualitative variables like true positives, types of abnormal uterine artery Doppler flow were expressed as frequency and proportions. Accuracy, sensitivity, specificity, negative and positive predictive values were calculated.

RESULTS

Uterine artery Doppler were studied in all 40 cases and the outcome of pre- eclampsia was studied and statistical analysis was carried out using sensitivity specificity and predictive values. The results showed that among the study population of 40, 19 patients developed pre-eclampsia, thus a prevalence of 52.5% was noted. Abnormal uterine artery Doppler was described by Doppler indices having a mean PI>1.45, mean RI>0.7 and persistence of diastolic notch. In our study of 40 gravid women, 11 patients had PI>1.45, 6 patients had RI>0.7, and 7 patients had persistence of diastolic notch.

Pre- eclampsia Status		**Development of Pre-eclampsia**		**Total**
		Yes	No	
Uterine Artery Findings	Yes	15	4	19
	No	0	21	21
Total		15	25	40

Parity Distribution

Gravida	**No. of patient**	**Percentage**
G1	8	20%
G2	15	37.5%
G3 and more	17	42.5%
Total	40	100%

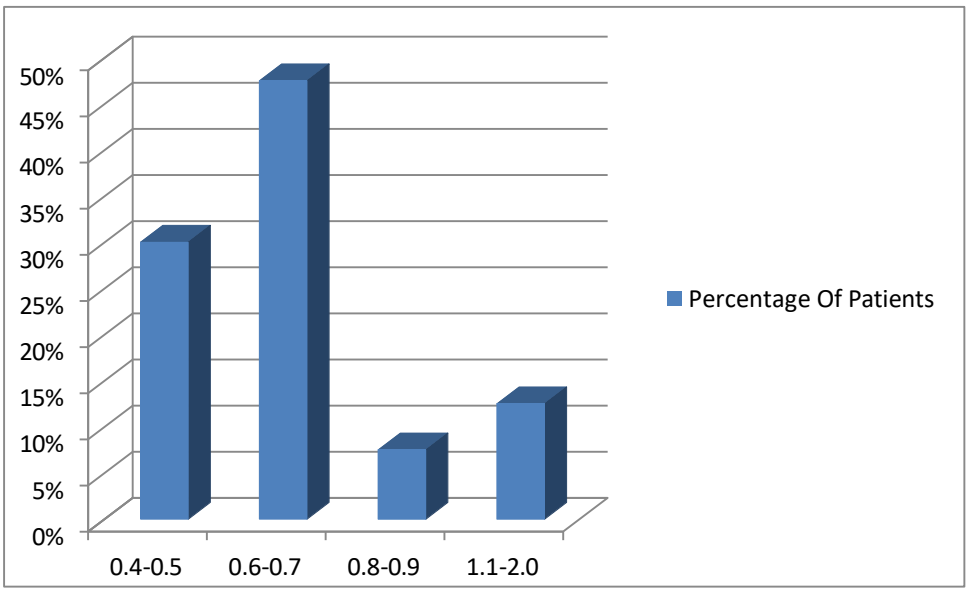
In the pre-eclampsia patient group, it was noted that 72.5% had normal pulsatility index (PI<1.45) and 27.5% had pulsatility index >1.45.

Positivity Index (PI)	Preeclampsia		Total
	Yes	no	
>1.45	8	9	17
<1.45	8	15	23
Total	16	24	40

The age distribution showed that all women were in the age range of 18-40 years. Uterine artery doppler finding in second trimester in determining preeclampsia showed abnormal findings in 19(47.5%) women in which19(47.5%) had type I (Resistive index >0.58), 36.8% (7/19) type II (Mild notching of uterine artery at beginning of diastole) and 63.2%had type III [(Severe notching + abnormal Resistive index (>0.58)]

Resistive Index (RI)	Preeclampsia		Total
	Yes	No	
>0.7	9	3	11
<0.7	10	18	29
Total	19	21	40

After the follow-up of each patient, we found that pre-eclampsia was developed 47.5% (19/40) cases.



Clustered column chart represents percentages of patients fall in different ranges of RI

DISCUSSION

Pre-eclampsia affects about 2% of total pregnancies. It is one of the major causes of fetomaternal morbidity and mortality. Due to improvement of antenatal care, the targeted approach of identifying women at high risk for subsequent development of

preeclampsia is very beneficial. The likelihood of developing preeclampsia is affected by a number of factors like race, obesity, nulliparity, and personal or family history of preeclampsia, hypertension. During second trimester, screening for women at high risk of developing pre-eclampsia is of utmost importance. The early diagnosis and prompt treatment leads to excellent fetomaternal outcomes. The fetal demise, growth restriction can be avoided by early antihypertensive therapy and early delivery [31].

Doppler ultrasonography of uterine artery is a noninvasive modality that can be used to determine vascular perfusion of utero-placental area. So it can be considered as indirectly assessment of trophoblast development during pregnancy. The Doppler modality has better prediction of preeclampsia in preterm rather than term cases. Similarly, the prediction is more accurate in the second trimester [32].

Our study has predicted pre-eclampsia with a good specificity and sensitivity. It is seen that uterine artery notching and increased pulsatility index (PI) is good predictor of pre-eclampsia and increased resistive index (RI) for intrauterine growth restriction. The accuracy, sensitivity, specificity, positive predictive value and negative predictive value of uterine artery Doppler were 85.7%, 88.2%, 84 %, 78.94% and 91.3% respectively. Pre-eclampsia complicates approximately 2–8% of pregnancies worldwide and remains one of the leading causes of maternal and perinatal morbidity and mortality, particularly in low- and middle-income countries. Despite advances in obstetric care, pre-eclampsia continues to pose significant challenges due to its unpredictable onset and progressive nature. Improvements in antenatal surveillance have highlighted the importance of a targeted approach to identify women at high risk of developing pre-eclampsia, allowing for closer monitoring and timely intervention [33].

The risk of developing pre-eclampsia is influenced by several maternal and obstetric factors, including race, obesity, nulliparity, advanced maternal age, and a personal or family history of pre-eclampsia or chronic hypertension. These risk factors are thought to contribute to abnormal placentation and impaired maternal cardiovascular adaptation. Screening during the second trimester is particularly critical, as this period corresponds to the stage when abnormal placental perfusion becomes clinically detectable but before overt disease manifestation. Early identification of high-risk women allows the implementation of preventive strategies such as low-dose aspirin, enhanced surveillance, and timely delivery planning, which have been shown to significantly improve fetomaternal outcomes [34].

Early diagnosis and prompt management of pre-eclampsia are associated with a reduction in severe complications, including eclampsia, placental abruption, fetal growth restriction, and intrauterine fetal demise. Evidence suggests that optimized antihypertensive therapy and judicious timing of delivery can substantially decrease perinatal morbidity and improve neonatal survival, especially in preterm pregnancies [35]. Uterine artery Doppler ultrasonography is a well-established, noninvasive technique for assessing uteroplacental circulation. It provides indirect information about trophoblastic invasion and spiral artery remodeling, which are central to the pathophysiology of pre-eclampsia. In normal pregnancies, progressive trophoblastic invasion leads to reduced vascular resistance and increased uterine blood flow. In contrast, inadequate invasion results in persistently high resistance indices, reflected as increased pulsatility index (PI), resistive index (RI), and the presence of early diastolic notching [36].

Multiple studies have demonstrated that uterine artery Doppler has superior predictive value for early-onset and preterm pre-eclampsia compared to term disease, likely because early-onset pre-eclampsia is more strongly linked to placental dysfunction. Additionally, Doppler assessment in the second trimester has been shown to provide better predictive accuracy than first-trimester evaluation, as abnormal placental vascular resistance becomes more pronounced during this period [37]. In the present study, uterine artery Doppler demonstrated good diagnostic performance in predicting

pre-eclampsia, with high sensitivity and specificity. The presence of uterine artery notching and elevated PI emerged as strong predictors of pre-eclampsia, consistent with the hypothesis of impaired uteroplacental perfusion. Furthermore, an increased RI was found to be a reliable predictor of intrauterine growth restriction, reinforcing the association between high vascular resistance and compromised fetal growth. The overall accuracy, sensitivity, specificity, positive predictive value, and negative predictive value of uterine artery Doppler in this study were 85.7%, 88.2%, 84%, 78.94%, and 91.3%, respectively, highlighting its usefulness as a screening tool in routine antenatal care [38].

Inclusion criteria:

In inclusion Criteria pregnant females of aged between 18 to 40 years and having 13 to 24 weeks of gestation are included.

Exclusion criteria:

Those pregnant females who had diabetes or hypertension before pregnancy or females who had fetal anomaly were excluded in our study

Conclusion:

In conclusion, second-trimester uterine artery Doppler is a valuable, cost-effective, and noninvasive modality for the early prediction of pre-eclampsia and related adverse pregnancy outcomes. When combined with maternal risk factor assessment, it can significantly enhance early detection, guide clinical decision-making, and ultimately improve maternal and perinatal outcomes. Utero-placental circulation can be assessed noninvasively by Doppler study of uterine arteries as abnormal Doppler study is associated with outcomes such as pre- eclampsia, intrauterine growth restriction and perinatal mortality. Increased pulsatility index (PI), persistence of uterine artery notch and increased resistive index (RI) can be a good predictor of pre-eclampsia and intrauterine growth restriction.

Hence, Doppler analysis of uterine arteries should be included along with routine biometry in second trimester ultrasound for early prediction of pre-eclampsia and to avoid subsequent perinatal morbidity and mortality.

Limitations:

Motion artifact is one of the limitations in this study.

The absolute value of the uterine artery PI and RI have not been validated for early pregnancy.

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