

Original Research Article

Role of uterine artery color doppler assessment in first and second trimester for early detection of IUGR and preeclampsia

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Abstract:

Aim and Objective:

To predict the risk factor for intra uterine growth retardation and preeclampsia in pregnant women with the help of uterine artery Doppler screening and associated indices (pulsatility index and diastolic notching) of sensitivity and specificity

Method: Prospective, Descriptive study uterine artery Doppler assessment was carried out at 12 to 14 weeks and 20 to 26 weeks gestation in unselected women with singleton as well as multiple pregnancies, attending for routine antenatal care in a primary care center. The Diastolic notching, pulsatility index (PI) and its relationship to preeclampsia as well as IUGR were evaluated at first and second trimester.

Results: Uterine artery diastolic notch detection had a sensitivity (preeclampsia=52% ; IUGR=18.92%) and a specificity (preeclampsia= 76.8 %; IUGR=66.27%) of in the first trimester whereas a sensitivity (preeclampsia=68% ; IUGR=27.03%) and a specificity (preeclampsia= 89.5%; IUGR=79.52%) in the mid trimester. The pulsatile index detection had a sensitivity of (preeclampsia= 48%; IUGR=35.14%) and a specificity (preeclampsia=49.5% ; IUGR=43.37) of in the first trimester whereas a sensitivity (preeclampsia=40% ; IUGR=29.73%) of 40% and a specificity(preeclampsia= 55.59%; IUGR=50.60%) of in the mid trimester.

Conclusion: Uterine artery Doppler sonography fulfill all the requirements for screening in prediction of pre-eclampsia and IUGR. Our results are comparable to the results of other studies.

1. INTRODUCTION

Preeclampsia has been identified as the primary factor in both maternal and foetal morbidity and mortality.¹ Eclampsia and preeclampsia are thought to be accountable for more than 14% (58,000) of maternal deaths globally each year, however in affluent nations, it primarily affects the foetus.² Approximately 15% of preterm births are caused by preeclampsia.³

In the absence of other causes of increased blood pressure (BP) (140/90 mmHg measured 2 times with at least a 6 h interval) in previously normotensive women, pregnancy-induced hypertension (PIH) occurs after 20 weeks of pregnancy. Pre-eclampsia is the term used when PIH is accompanied by substantial proteinuria (protein in urine 0.3 g/in 24 h) and multi-organ

failure. Pre-eclampsia is classified as eclampsia when it is accompanied with grand mal seizures and/or coma.¹ The serious effects of pregnancy-induced hypertension include pre-eclampsia and eclampsia.

By the eighth week, the trophoblast usually begins to infiltrate the decidual part of the spiral arteries, and by the twelfth week, this invasion is typically finished. After this, the second stage of spiral artery invasion begins, during which the trophoblast similarly invades the myometrial part of the spiral arteries. Normally, this is finished in 18 to 19 weeks, but it could take up to 22 or 24 weeks longer. The spiral artery bed does not change in the great majority of preeclampsia patients. Blood cannot flow as easily into the intervillous area as a result.

The main causes of illness and death in mothers and infants are still pre-eclampsia and intrauterine development restriction.⁴⁻⁶ Coagulopathy, liver and kidney failure, and stroke are among the maternal consequences of pre-eclampsia.⁴ Intrauterine growth restriction in utero increases the chance of developing cardiovascular disease, hypertension, and type 2 diabetes in adults.^{7,8}

The aberrant placenta development that characterises pre-eclampsia and intrauterine growth restriction⁹ leads to insufficient uteroplacental blood supply. This gave rise to the concept of using Doppler ultrasound as part of routine ultrasound screening to gauge the rate at which blood is flowing through the uterine artery.¹⁰ In women who are not pregnant or in their first trimester, the waveforms of uterine artery blood flow are characterised by low end-diastolic velocities and an early diastolic notch. A diastolic notch or aberrant flow velocity ratios have been associated with insufficient trophoblast invasion beyond 24 weeks of pregnancy.¹¹

Uterine artery Doppler resistance indices in the mid trimester and the later development of IUGR have been linked in numerous studies. However, studies reveal that uterine artery blood movement can also be detected with a Doppler, is when trophoblasts are most intrusive during first trimester.¹²

The uterine artery waveform is the most reliable indirect indicator of the spiral artery bed.³ Doppler ultrasonography measurements of raised uterine artery velocity during the first and midtrimesters should give unplanned signal of this method and act as a screening tool for preeclampsia. It is more accurate to predict unfavourable pregnancy outcomes when uterine artery Doppler scans are performed at 23-26 weeks of pregnancy rather than 19-22 weeks of pregnancy.¹³

Non-pregnant women was having highest velocity in early diastolic notch and modest. At 18 - 20 weeks, there is strong flow and no diastolic notch. When there is a high resistance uteroplacental waveform with a diastolic notch, which is a sign of arterial vessel tone and the uterine artery flow thought to be low. It goes disappear in the mid trimester. High resistance patterns are linked to an enlarged risk of pregnancy problems, including a 70% chance of proteinuric hypertension and a 30% chance of a small-for-gestational-age foetus coexisting.¹⁴

Although uterine artery Doppler has been used in several studies to screen for preeclampsia and foetal development restriction in unassigned patients, its effectiveness is still debated. Sensitivities vary based on the kind of Doppler used, where the sample is taken, what is meant by abnormal uterine artery resistance, how far along the pregnancy is when the test is done, and what the end goal is.¹⁴ Therefore, we want to study the early detection of preeclampsia and IUGR with the help of uterine colour Doppler sonography in the first and mid trimester stages of pregnant women.

2. MATERIAL AND METHOD:

This prospective, observational study, conducted at our institute was approved by Institutional ethics committee. Our tertiary care centre is seeing 120 pregnant women with gestational ages ranging from 12 to 14 weeks and 20 to 26 weeks for routine antenatal care. All women with a pregnancy attending for routine first-trimester nuchal translucency ultrasound Doppler assessment were offered the option to participate in the study. Written informed consent was obtained from them, and the study was approved by the local ethics committee. Transabdominal uterine artery Doppler assessment was performed by the sonographer at the time of the nuchal translucency scan. Uterine artery Doppler indices were measured as described previously. Pulsed-wave Doppler was used to obtain uterine artery waveforms. When three similar consecutive waveforms were obtained, the presence of a protodiastolic notch was recorded and the PI was measured.

12 to 14 weeks and 20 to 26 weeks.

We were enrolled 120 pregnant women with reliable dating of pregnancy with known LMP as well as given informed written consent whereas multiple pregnancies, anomalous fetus as well as not given consent form were excluded from our study.

Procedure:

Using a General Electric Voluson 730 ultrasound equipment with an endovaginal probe and a convex abdominal probe with a frequency range of 2.0-5.0 MHz, ultrasonography was carried out (4–10 MHz). For the technique, the angle between the incident ultrasound beam and the vessel under study had to be less than 60°. Indicators were derived using samples of at least 5 waves that appeared identically and had a distinct spectral shape.

Color Doppler, power Doppler, and pulsed Doppler were used to identify uterine and foetal vessels, followed by quantitative and qualitative evaluation. The maternal side of the maternal-fetal-placental unit's hemodynamic peculiarities are reflected in the velocimetric examination of the uterine artery.

At 11–14 weeks, a sagittal section of the cervix was acquired as part of normal ultrasonography. The paracervical plexus was located after a lateral sweep of the probe. The uterine artery was located at the cervico-corporeal junction using colour Doppler. Before the uterine artery splits into the arcuate arteries, measurements were taken at this location. Bilateral pulsatility indices were measured, and the mean PI was computed. Bilateral early diastolic notches' existence or absence was also noted.

Statistical Analysis:

Data was analysed using SPSS, version 26.0 (SPSS Inc., Chicago, IL, USA). Quantitative data was expressed as mean plus-minus SD whereas qualitative data was expressed in percentage by using SPSS. Comparisons between the groups were done using chi square test or chi square test wherever appropriate. Sensitivity and specificity was calculated with the help of diagnostic calculator. A p value <0.05 was considered statistically significant.

3. RESULTS

Table :1

		Sensitivity	Specificity	PPV	NPV
Preeclampsia (First Trimester)	Diastolic Notch	52%	76.84%	37.14%	85.88%

	Pulsatile index	48%	49.47%	20%	78.33%
Preeclampsia (Second Trimester)	Diastolic Notch	68%	89.47%	62.96%	91.40%
	Pulsatile index	40%	55.79%	19.23%	77.94%
IUGR (First Trimester)	Diastolic Notch	18.92%	66.27%	20%	64.71%
	Pulsatile index	35.14%	43.37%	21.67%	60%
IUGR (Second Trimester)	Diastolic Notch	27.03%	79.52%	37.04%	70.97%
	Pulsatile index	29.73%	50.60%	21.15%	61.77%

Figure :1

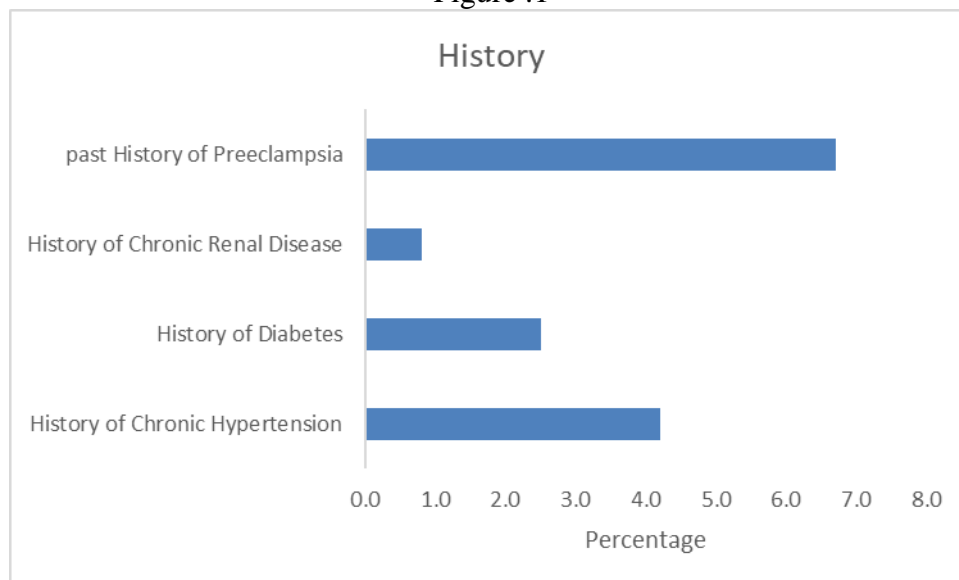
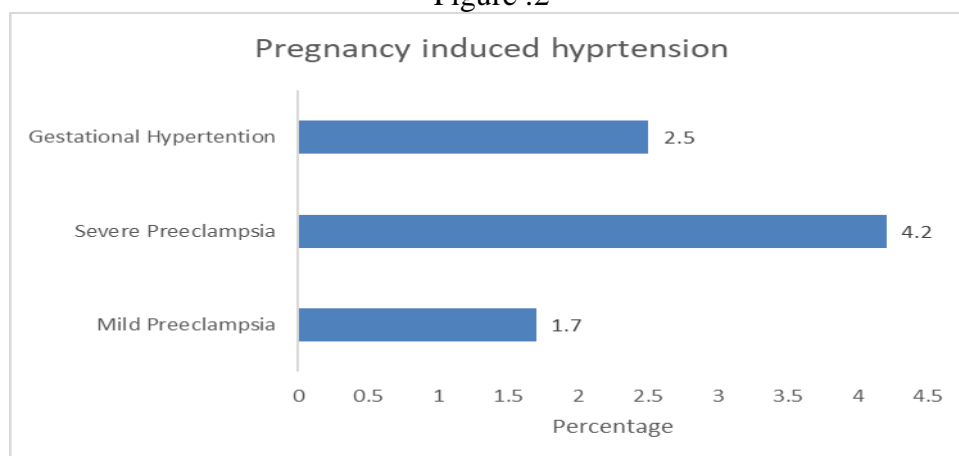


Figure :2



We enrolled 120 patients, all of whom had first-trimester pregnancy. These patients were prospectively enrolled between November 2021 and July 2022 at our institute. We selected 120 patients based on exclusion as well as inclusion criteria. According to our study population, we observed the following age groups: 1) 18-25 years: (35.84%) 2) 26-30 years: (30.84%) 3) 31-35 years old (20%) and over 36 years old (13.34%). The 18-25 age group had the highest percentage of the population (35.84%). Our study population had 48.34 % first pregnancy, 31.67% second pregnancy, 18.34% third pregnancy, and 1.67 % fourth pregnancy pregnant women enrolled for data collection.

We observed 35% of high-risk pregnancies and 65% of low-risk pregnancies. High risk and low risk were categorised based on age <20, age >35, history of hypertension, diabetes, chronic renal disease, and past history of preeclampsia.

We were observed following history in our data as history of preeclampsia (6.7%), History of chronic hypertension (4.2%), History of diabetes (2.5%) and History of chronic renal disease (0.8%)

Birth Weight:

Out of 120 pregnant women's data, 71.67% of their newly born birth weight was >2.5 kg, where as 28.33% of their newly born birth weight was ≤ 2.5kg.

Preeclampsia

First trimester:

During first trimester of pregnancy, 50% pulsatile index, 29% diastolic notching

Notching and preeclampsia:

37.1% of patients who had notching in 1st trimester had significantly higher preeclampsia while 85.9% of them who did not have notching had no preeclampsia ($\chi^2=7.97$, $p=0.007$) Sensitivity of notching was only 52% (95% CI between 31.8% and 71.7%) while specificity was 76.8% (95% CI between 66.8% and 84.6%). The positive predictive value was 37.1% and negative predictive value was 85.9%.

Pulsatile index and preeclampsia:

20% of patients who had pulsatile index in 1st trimester had not significantly higher preeclampsia while 78.3% of them who did not have pulsatile index had no preeclampsia ($\chi^2=0.00$, $p=1.000$). Sensitivity of pulsatile index was only 48% (95% CI between 28.3% and 68.2%) while specificity was 49.5% (95% CI between 39.1% and 59.9%). The positive predictive value was 20% and negative predictive value was 78.3%.

Second Trimester:

During second trimester of pregnancy, 43.33% pulsatile index, 23% diastolic notching

Notching and preeclampsia:

63% of patients who had notching in 2nd trimester had significantly higher preeclampsia while 91.4% of them who did not have notching had no preeclampsia ($\chi^2=37.49$, $p<0.001$). Sensitivity of notching was only 68% (95% CI between 46.4% and 84.3%) while specificity was 89.5% (95% CI between 81.1% and 94.6%). The positive predictive value was 63% and negative predictive value was 91.4%.

Pulsatile index and preeclampsia:

19.2% of patients who had pulsatile index in Second trimester had not significantly higher preeclampsia while 77.9% of them who did not have pulsatile index had no preeclampsia ($\chi^2=0.143$, $p=0.822$) Sensitivity of pulsatile index was only 40% (95% CI between 21.8% and 61.1%) while specificity was 55.8% (95% CI between 45.3% and 65.9%).The positive predictive value was 19.2% and negative predictive value was 77.9%.

IUGR**First trimester:****Notching and preeclampsia:**

20% of patients who had notching in 1st trimester had significantly notching while 64.7% of them who did not have notching had no IUGR ($\chi^2=2.72$, $p=0.129$). Sensitivity of notching was only 18.9% (95% CI between 8.6% and 35.7%) while specificity was 66.3% (95% CI between 55% and 76%).The positive predictive value was 20% and negative predictive value was 64.7%.

Pulsatile index and preeclampsia:

21.7% of patients who had pulsatile index in 1st trimester had significantly IUGR while 60% of them who did not have pulsatile index had no IUGR ($\chi^2=4.728$, $p=0.047$). Sensitivity of pulsatile index was only 35% (95% CI between 21% and 53%) while specificity was 65% (95% CI between 54% and 75%).The positive predictive value was 31% and negative predictive value was 69%.

Second Trimester:**Notching and preeclampsia:**

37% of patients who had notching in Second trimester had not significantly notching while 71% of them who did not have notching had no IUGR ($\chi^2=0.629$, $p=0.481$) Sensitivity of notching was only 27% (95% CI between 14.4% and 44.4%) while specificity was 79.5% (95% CI between 69% and 87.3%).The positive predictive value was 37% and negative predictive value was 71%.

Pulsatile index and preeclampsia:

21.2% of patients who had pulsatile index in second trimester had not significantly IUGR while 61.8% of them who did not have pulsatile index had no IUGR ($\chi^2=4.031$, $p=0.049$) Sensitivity of pulsatile index was only 29.7% (95% CI between 16.4% and 47.2%) while specificity was 50.6% (95% CI between 39.5% and 61.7%).The positive predictive value was 21.2% and negative predictive value was 61.8%.

4. DISCUSSION (SATRT 15)

Preeclampsia is a change in blood pressure that happens during pregnancy. It is marked by less blood flow to organs after severe vascular vasospasm (15). The World Health Organization says that preeclampsia and its complications kill more than a million women around the world every year. Most of these deaths happen in developing countries (16,17). Preeclampsia usually happens to young women who have never given birth before. Race, ethnicity, and genetics also play a big role in how often it happens (18,19). Doppler ultrasonography is a non-invasive way to measure blood flow between the uterus and the placenta (20). Some studies show that a Doppler that isn't working right in the first and

second trimesters of pregnancy can help find women who are likely to get preeclampsia (21,22).

The current study sought to determine the predictive value of uterine artery Doppler ultrasonography in the prevalence of preeclampsia and IUGR in pregnant women admitted at our tertiary care centre between 2021 and 2022.

In the prospective cohort study, uterine artery Doppler ultrasonography was done on 120 pregnant women, with a mean age of 27.86 years. This was done in the first and mid trimesters of pregnancy. In the study by Barzin et al. (23), transabdominal uterine artery Doppler ultrasonography was done on 100 pregnant women with an average age of 23.2 years and gestational weeks between 11 and 14 and 21 and 24. In another study by Dehghani-Firouzabadi (24), a Doppler ultrasound of the uterine artery was done between 14 and 16 weeks of pregnancy. In the same way, Papageorghiou et al. (25) used transvaginal uterine artery Doppler ultrasonography to predict how often preeclampsia would happen in patients.

This study looked at how the Doppler pattern of the uterine artery changes between the first and mid trimesters. In line with the research,²⁶ our data show that the blood flow in the uterus changes significantly during the first half of pregnancy. Surprisingly, the changes between 11 and 14 weeks were bigger than those between 20 and 26 weeks, showing a decrease in uterine artery PI and a decreasing the number of women with a bilateral notch. One could guess that these changes in blood flow become more noticeable early in the second trimester of pregnancy. This is likely because of the big changes that happen during placentation. Between 8 and 12 weeks of pregnancy, the trophoblast moves into the dead cell part of the spiral arteries.²⁷ Changes in steroid hormones and protein hormones may also be important in this vascular change. At this early stage of pregnancy, the intervillous circulation is also set up, and the umbilical and foetal circulations go through major changes. Based on the follow-up investigation of 120 pregnant women of the current study, 2 (1.67%), 5 (4.17%) and 3 (2.5%) patients were diagnosed with mild and severe hypertension and gestational hypertension.

Out of 120 pregnant women, 25(20.83%) developed pre-eclampsia, including 8 (6.67%) who had previous pre-eclampsia, 3 (2.5%), and 37 (30.83%) gave birth to infants with IUGR. This resulted in a somewhat lower incidence of IUGR associated with aberrant Doppler results and a much greater rate in the high-risk group than the findings of the other investigations. Incidence of IUGR was 36.54% in Bhattacharya et al. study of²⁸ patients. Preeclampsia prevalence in other research ranged from 18.8% to 39.2%.

The tests used to predict preeclampsia include clinical history, examination findings, laboratory and hemodynamic tests. Since alpha fetoprotein, fibronectin, and uterine artery Doppler (bilateral notching) all have specificities within a range, it is safe to say that early pregnancy tests for predicting the later onset of preeclampsia have better specificity than sensitivity. Only the Doppler pulsatility index of the uterine artery, and combinations of indices, are more sensitive. In other such similar studies, various demographic factors were studied and the predictive value of the uterine artery Doppler was also studied.

BIRTH WEIGHT

Our study sample of average birth weight was 2.522 ± 0.655 kg. In the study by Bhattacharya et al., the average birth weight was 2.25 ± 0.58 kg. Many studies show a lower birth weight in high-risk patients with abnormal uterine artery Doppler studies. In our study, since a higher number of high-risk patients had abnormal uterine artery Doppler and subsequently intrauterine growth restriction, the birth weight had a statistically significant p value.

BLOOD PRESSURE

We observed that systolic and diastolic blood pressure were highly significant in preeclampsia patients compared to non-preeclampsia patients. ($p = <0.0001$). We also observed that systolic and diastolic blood pressure were highly significant in IUGR patients compared to non-IUGR patients. ($p = <0.0001$).

Waveform Analysis of Uterine Artery Doppler

Uterine artery All subjects had their uteroplacental circulation evaluated using Doppler waveforms in the first and mid trimesters. The potential utility of doppler assessment in detecting pregnancies at risk of difficulties due to poor placentation has been investigated in a number of screening studies using assessment of flow in the uterine arteries.

The sensitivity of PI and diastole notching as a diagnostic tool to anticipate pre-eclampsia and IUGR was evaluated in the existing study. Doppler waveform deviations were present in 17 of the 25 individuals who developed pre-eclampsia and were visible as early as the first trimester. Accordingly, the study showed that an aberrant uterine artery waveform with early diastolic notching could accurately predict 68% of cases that went on to develop preeclampsia from as early as the first trimester. What is significant, though, is that patients who presented with the disease's earliest symptoms and had the worst pregnancy outcomes were able to have the most severe cases of preeclampsia predicted using uterine artery waveform analysis.

Uterine Artery Doppler of Predictive Value

The sensitivity and specificity in our study's evaluation of the predictive value of PI in the first trimester were 48% and 49.5%, respectively, which was greater than studies with Coleman et al. [29] as well as Caforio et al. [30]. The study by Cnossens et al.'s [31] findings were identical in terms of the PPV and NPV value. Our study had a negative likelihood ratio of 1.05 and a positive likelihood ratio of 0.95, $P = 1.000$, which was similar to prior studies by Chien et al. [32] in terms of both the positive and negative likelihood ratios. In comparison to prior research, our study also offers higher sensitivity and specificity.

Doppler imaging of the uterine artery with PI has been shown to have predictive value in early pregnancy by a number of studies.

Similar to the investigations by Cnossens et al. [31], the sensitivity and specificity for the uterine artery pulsatility index in the mid trimester were 43.33% and 56.67% utilising PI is greater than to 1.6 as the abnormal Doppler study criteria. In contrast to the current study, several studies by Papageorghiou et al [25] and Ratanasiri et al [33] have better sensitivity and specificity. The current study is similar to studies by Ratanasiri et al. [33] and Bhattacharya et al. [28] in terms of its positive and negative predictive value. Similar to studies by Cnossens et al. [31], Jimmy Espinoza et al. [34], and Chien et al. [35], the positive and negative likelihood ratios of the current study were 0.90 and 1.08, respectively. However, Ratanasiri et al. [33] showed a higher positive likelihood ratio, indicating a better predictive value of the test as shown in below Table.

Various studies showing predictive value of the uterine artery Doppler using PI in 2nd trimester.

When the pulsatility index was employed with higher sensitivity, specificity, and predictive value, as well as a larger positive likelihood ratio and a lower negative likelihood ratio, the predictive value of the uterine artery was higher. Additionally, when the pulsatility index was

utilised, the relative risk was greater. As indicated in the current study, other investigations have demonstrated that using the pulsatility index increases the uterine artery Doppler study's predictive value for preeclampsia and other unfavourable pregnancy outcomes.

Swanepoel et al., (37) suggested that In contrast to the pulsatility index, the presence of a notch is an excellent predictor of a negative pregnancy outcome. On the other hand, other research has linked the presence of notching in the mid trimester to an increased risk of FGR and preeclampsia in a low-risk group. The danger can rise as much as 60% in high-risk pregnancies (Hernandez-Andrade et al., [38]). It has been proven that uterine artery notching that continues after 26 weeks of gestation is considered a risk factor for poor pregnancy outcomes (Andrarle et al., [39]). (Andrarle et al., [39]). 25-40% of instances with an early diastolic after 26 weeks of gestation were found to have a persistent pattern (37).

In our study, the presence of notching in the mid trimester was the best forecaster for the growth of pre-eclampsia.

Our findings corroborate those of Pilalis et al.(40) and Andrarle et al. [39]), who shown that Doppler screening of the uterine artery during the mid-trimester is an effective method for identifying women at high risk for developing pre-eclampsia and foetal growth restriction.

Uterine artery diastolic notch detection in the first trimester had a sensitivity of 52 and a specificity of 76.8 percent, respectively. To a lesser extent than in the studies by Cnossens et al., as determined by the criteria for abnormal Doppler scans (31) In comparison to previous research by Cnossens et al (31) and Jimmy Espinoza et al. (34), the present study's positive and negative probability ratios were greater at 2.25 and 0.62, respectively.

The sensitivity and specificity of the diastolic notch in the uterine artery were 68% and 89.5%, respectively, in the mid trimester. It was consistent with the findings of the experiments conducted by Cnossens et al (31) This study's positive and negative probability ratios of 6.46 and 0.36 were comparable to those of Cnossens et al. (31), Jimmy Espinoza et al. (34), and Chien et al. (35).

Our results are consistent with those of Kurdi [42], who also found that an early diastolic notch is linked to poor pregnancy outcomes. Our results corroborate those of other researchers who have establish that women with notches are more likely to experience complications during pregnancy, including preterm labour and delivery.

PREGNANCY OUTCOMES IN THE STUDY POPULATION

In the current study 70% of the population delivered at term, and 71.67% of the population delivered babies weighing more than 2500g.

CROSS TABULATIONS IN LOW BIRTHWEIGHT BABIES

Infants born with low birth weights were cross-tabulated with respect to the presence or absence of notching during the first and mid trimesters as a predictor of FGR. Once again, the best predictor was a notch in the mid trimester. It has been found that mothers who experience notching in the mid trimester are 2.5 times more likely to give birth to a baby with a low birth weight than those who do not.

ASSOCIATION BETWEEN PREECLAMPSIA AND IUGR

Both the current study and prior research have established beyond a reasonable doubt that preeclampsia is strongly linked to IUGR. Preeclampsia has been linked to IUGR with a sensitivity of 66.67 percent and a specificity of 95.12 percent, as reported by Mittal N. et al. (2016) [43]. The current study had a sensitivity of 35.1% for detecting IUGR in patients with preeclampsia, and a specificity of 85.5%. This demonstrates that the known pathophysiology of both preeclampsia and IUGR early defective placentation shared by both entities.

5. CONCLUSION

There is evidence that suggests preterm and term pre-eclampsia may have different causes, as higher Doppler indices are linked to the development of preterm rather than term pre-eclampsia. Defective invasion of the spiral arteries is linked to preterm conditions, but it plays much less of a role, if any at all, in the cases closer to full term. Both high-risk and low-risk patients had an increased pulsatility index with notching in the mid trimester, which was predictive of preeclampsia overall. Severe preeclampsia was predicted by an raised pulsatility index or by bilateral notching. However, this prediction is largely useless because there is currently no safe and effective pharmacological treatment for preventing preeclampsia and other complications. Doppler ultrasonography, we have concluded, is the most reliable non-invasive method for monitoring uteroplacental blood flow.

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