

Screening and Prediction of Preeclampsia with Uterine Artery Doppler

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Abstract: ***Introduction:** Hypertensive disorder of pregnancy (HDP) is among three leading causes of maternal mortality and morbidity. Pathophysiology of preeclampsia helps in understanding the use of ultrasonography doppler in its prediction when performed in first trimester during establishment of placental circulation. Resistance to the blood flow within uteroplacental circulation transmitted upstream to the uterine arteries can be measured with the help of different indices. Indices of uterine artery doppler such as Pulsatility Index (PI), Resistivity Index (RI), ratio of peak systolic and diastolic velocity (SD ratio), presence and absence of diastolic notch in first and second trimester are used as screening test for prediction of preeclampsia; as they indicate resistance in placental circulation. **Methodology:** In this prospective, comparative, observational study, doppler ultrasound of the uterine arteries was performed at 11 to 13+6 and 18 to 22 weeks of gestation and the average Pulsatility index (PI) of the blood flow through both uterine arteries was measured and mean PI was calculated. Subjects were followed up regularly with us by clinical examination, estimation of fundal height, Mean Arterial Pressure (MAP), urine examination for proteinuria and early signs for the development of preeclampsia or intrauterine growth restriction at regular intervals like between 19 - 25 weeks, 30 - 35 weeks, 35 to 38 weeks and upto delivery. **Result:** Comparison for predictive value of first trimester Doppler with second trimester Doppler in development of pre - eclampsia revealed that the positive Predictive values of First trimester Doppler was 41.67% and negative predictive value of first trimester uterine artery doppler was 88.06%, the p value being 0.8907, which was not significant. Positive Predictive values of second trimester doppler was 40.91% and negative predictive value of first trimester uterine artery doppler was 92.98%, the p value being 0.087, which was significant. **Conclusion:** Hypertensive disorders of pregnancy including preeclampsia if diagnosed earlier, may cause help to avoid further complications. Abnormal Uterine artery doppler changes have been associated with subsequent adverse pregnancy outcomes like hypertensive disorders of pregnancy, intrauterine growth restriction and perinatal mortality. Two staged doppler screening helps in prediction of preeclampsia, in earlier stages and helps to avoid complications.*

Keywords: Preeclampsia, Uterine Artery Doppler (UAD), Pulsatility index (PI), Mean Arterial Pressure (MAP)

1. Introduction

Hypertensive disorder of pregnancy (HDP) is among three leading causes of maternal mortality and morbidity. The incidence of Hypertensive disorders of pregnancy (HDP) range from 4 - 25%.¹ Among all the Hypertensive disorders in pregnancy, preeclampsia is a multisystem disorder which can culminate into end organ damage in various organs. It has been documented that Preeclampsia has caused 14% of maternal deaths per year worldwide; while in developing countries incidence is 5.6%.² Pathophysiology of preeclampsia helps in understanding the use of ultrasonography doppler in its prediction when performed in first trimester during establishment of placental circulation. Trophoblast normally invades decidual portion of myometrial arteries beginning by 8th week of gestation and invasion is complete by 13th week. After this time second stage of spiral artery invasion starts in where myometrial portion of spiral arteries are invaded by endovascular trophoblastic tissue. This is usually completed by 18 - 19 weeks but may be delayed up to 22 - 24 weeks. This process helps funnelling of spiral arteries, increasing their diameter and decreasing high resistance in placental vasculature. Uterine artery doppler waveforms indicate status of spiral arterial bed and gives idea about blood supply.³ Resistance to the blood flow within uteroplacental circulation transmitted upstream to the uterine arteries can be measured with the help of different indices. Indices of uterine artery doppler such as Pulsatility Index (PI), Resistivity Index (RI), ratio of peak systolic and diastolic velocity (SD ratio),

presence and absence of diastolic notch in first and second trimester are used as screening test for prediction of preeclampsia; as they indicate resistance in placental circulation.⁴ In a nonpregnant state uterine artery has low peak velocity, at 18 weeks there is high flow with no diastolic notch. Impaired uterine artery flow is considered when there is high resistance uterine artery waveforms and presence of diastolic notch which represents arterial vessel tone and elasticity of vessels.⁵ A high resistance pattern is associated with higher rate of pregnancy complications with a 70% chance of developing proteinuria and hypertension and 30% chance of a coexisting small for gestational age fetus.⁶ Varying sensitivities are obtained depending on type of doppler used, the sampling site, the definition of abnormal uterine artery resistance, gestational age of assessment and different end points. Multiparametric predictive models combining first trimester uterine artery doppler Pulsatility index with maternal characteristics and biochemical markers, can achieve a detection rate for early onset preeclampsia of over 90%. (Study by Su Lynn Khong et al) thereby allowing early commencement of management strategies to minimize risk of adverse outcome, including facilitation of appropriate level of pregnancy monitoring. Application of antiplatelet agent like Aspirin 150mg daily dosage at night initiated before 16 weeks reduces incidence of preeclampsia by 62% as given by Evidence based Preeclampsia Prevention Data.⁷ Application of predictive tests for preeclampsia is important as, preventive measures can be started in early stages to prevent further complications caused by preeclampsia like Eclampsia, Acute

renal failure, Abruption Placentae, Preterm Births, etc leading to increase in maternal mortality and morbidity. In this study sequential uterine artery Doppler study at 11 - 14 weeks and repeated at 19 - 22 weeks are used to predict pregnancy outcome in the form of preeclampsia and small for gestational age babies.

2. Aims and Objectives of the Study:

Aim

To predict development of preeclampsia by uterine artery Pulsatility Index in first trimester.

Secondary Objectives:

- 1) To study incidence of preeclampsia based on changes in uterine artery doppler in first trimester.
- 2) To know the sensitivity and specificity, positive and negative predictive value of uterine artery doppler in first and second trimester.
- 3) To study association of preeclampsia with first and second trimester uterine artery doppler changes.

Study Design- Observational Prospective

Time of Study- May 2019 to July 2021

Place of Study- All early ANC attending OPD of a tertiary care center during 11 to 14 weeks

Ethical clearance- information was obtained from institutional ethical committee

Sample Size - Sample size based on - diagnostic test

- Tests available
- diagnostic test studies based upon positive likelihood ratio
- Diagnostic test

Sensitivity of new test 0.42

Specificity of new test 0.74

Anticipated positive likelihood ratio 1.65

Desired confidence level 95

Required sample size in each group (diseased/non diseased) 26

Loss of follow up (almost 1/3rd) $26+7=35*2$ groups =Total 70

Data Analysis

Data was entered in Ms Excel sheet, coded and analysed in statistical software STATA version 10.1, 2011. Data analysis included both descriptive n inferential statistics. Descriptive statistics is used to summarize clinical characteristics with mean n standard deviation for quantitative variables while frequency n percentage is used to summarize categorical (qualitative) variables. Inferential statistics includes chi square test for assessing significance of difference between incidence of preeclampsia between early ANCs with normal uterine artery doppler and abnormal uterine artery doppler. A p - value of <0.05 is considered statistically significant for all the comparisons.

Inclusion Criteria

- 1) Singleton pregnancy

- 2) All the pregnant registered cases
- 3) Patients willing to participate in study
- 4) Patients willing for follow up throughout pregnancy

Exclusion Criteria

- 1) Congenital anomalies
- 2) Multiple pregnancy
- 3) Antenatal cases of chronic hypertension
- 4) Antenatal cases of diabetes mellitus, chronic renal failure

3. Methodology

All pregnant women attending antenatal outpatient Department of Obstetrics and Gynaecology in the first trimester were screened according to inclusion criteria. Informed written consent was taken in local language of the subjects selected for study. Maternal characteristics were noted with respect to height, weight, body mass index (BMI), obstetric history, parity, gestational age, past history of preeclampsia, past h/o intrauterine growth restriction, history of smoking, diabetes or chronic hypertension. Baseline mean arterial pressure was measured and gestational age estimation was done from menstrual history and ultrasound examination. Baseline blood and urine investigations were done like complete blood count, liver function tests, kidney function tests, blood sugar, urine for proteinuria. Doppler ultrasound of the uterine arteries was performed at 11 to 13+6 weeks gestation and the average pulsatility index (PI) of the blood flow through both uterine arteries was measured and mean PI was calculated. A second ultrasound examination was performed at 18–22 weeks for measurement of fetal growth and examination for fetal defects. In the cases where no major fetal defect was detected, women was offered the option of Second trimester uterine artery doppler in the same manner as that of in first trimester and average pulsatility index (PI) of the blood flow through both uterine arteries measured and mean PI was calculated. Subjects were followed up regularly with us by clinical examination, estimation of fundal height, Mean Arterial Pressure (MAP), urine examination for proteinuria and early signs for the development of preeclampsia or intrauterine growth restriction at regular intervals like between 19 - 25 weeks, 30 - 35 weeks, 35 to 38 weeks and upto delivery. • Delivery outcome was noted in terms of manner of onset of labour, mode of delivery, baby outcome like Livebirth, weight and APGAR score and NICU admission, condition of baby at the time if discharge, etc. • Demographic characteristics, ultrasound findings and the results of biochemical testing were entered into a computer database at the time of assessment. Data on pregnancy outcome were obtained from examination of individual patient notes and labor ward records. • Blood pressure was measured in both upper arms in sitting position with electronic BP apparatus twice and a mean of all four readings was calculated. • Uterine artery doppler was done by Ultrasound machine in the Department of OBGY. Each uterine artery was identified using color flow mapping, and pulsed wave Doppler was then used to obtain three similar consecutive waveforms. The PI was measured of each uterine artery and the mean PI of the two uterine arteries was calculated. • Demographic characteristics, Ultrasound and doppler findings and the results of maternal serum markers

were entered into a computer database at the time of assessment

4. Observations and Results

A total 79 of 130 pregnant women were recruited, however 51 participants excluded from the final analysis of this prospective study due to following reasons: • Pregnancy outcomes were not available • Did not return for follow up scans Due to a small sample size regression models could not be applied, instead cross tabulations were employed. All 79 women included in study were selected according to inclusion criteria.

Doppler study was done and values of Pulsatility index, Resistivity Index and S/D Ratio in right and left uterine arteries were noted.

Diastolic notch was present in 27.85% cases and absent in 72.15% of study population.

First trimester uterine artery doppler changes were present in 12 subjects out of 79 i. e.15.19% of study population. Second trimester uterine artery doppler changes were present in 22 subjects out of 79 i. e.27.85 % of study population. Uterine artery doppler changes involving pulsatility index mainly were considered since it is an indicator that showed strong association with development of preeclampsia.

In the given study population overall incidence of preeclampsia, as assessed by mean arterial blood pressure as well as clinical signs was found out to be 16.46% i. e. with confidence interval of 95%; minimum 9.06% to maximum 26.49%. Incidence of early preeclampsia was 12.66% (more) and Incidence of late preeclampsia was 3.80%.

In the given study population 16.46% subjects showed changes in uterine artery doppler indicating positive predictive value of study. In whole study population 83.54% subjects did not show changes in uterine artery doppler indicating negative predictive value of study.

In the given study population, 38.46% showing changes in first trimester doppler developed preeclampsia.89.39% not showing changes in first trimester doppler did not develop disease.

Among the given study population 69.23% subjects showing changes in second trimester uterine artery doppler develop preeclampsia.80.30% population not showing changes in second trimester uterine artery doppler changes did not develop disease.

Sensitivity (true positives) of the first trimester uterine artery doppler to in prediction of preeclampsia was 38.46%; while there was 10.61% probability of subject being predicted positive when he is actually negative i. e. false positives.

Specificity (true negatives) of the first trimester uterine artery doppler to in prediction of preeclampsia was 89.39%; while there was 61.54% probability of subject being predicted negative when it was actually positive i. e. false

negatives. From above table P value of the given study is 0.07 which was significant.

Cohen Kappa of the test was 0.28 indicating fairly strong correlation between first trimester uterine artery doppler and preeclampsia.

Sensitivity (true positives) of the second trimester uterine artery doppler in prediction of preeclampsia was 69.23%; while there was 19.70% probability of subject being predicted positive when it is actually negative i. e. false positives. Specificity (true positives) of the second trimester uterine artery doppler in prediction of preeclampsia was 80.30%; while there is 30% probability of subject being predicted negative when it is actually positive i. e. false negatives. From above table P value of the given study was 0.02 which was significant.

Cohen Kappa of the test was 0.38 indicating fairly strong correlation between second trimester uterine artery doppler and preeclampsia.

Comparison for predictive value of first trimester Doppler with second trimester Doppler in development of pre - eclampsia revealed that the positive Predictive values of First trimester Doppler was 41.67% and negative predictive value of first trimester uterine artery doppler was 88.06%, the p value being 0.8907, which was not significant. Positive Predictive values of second trimester doppler was 40.91% and negative predictive value of first trimester uterine artery doppler was 92.98%, the p value being 0.087, which was significant.

5. Discussion

Preeclampsia is the most common pregnancy complication associated with serious maternal - fetal morbidity and mortality. At present the only effective treatment is delivery of placenta. Uterine artery Doppler waveforms can identify women with obstetric complications related to abnormal placentation, since doppler ultrasonography is a useful method to assess the velocity of uterine artery blood flow. An abnormal velocity waveform is characterised by high resistance to flow and or an early diastolic notch. Early screening of preeclampsia by uterine artery doppler has been suggested based on the concept that pathogenic mechanisms of preeclampsia may be modified if prophylactic therapies are initiated early in pregnancy. Abnormal uterine artery doppler waveforms are also able to identify foetuses at the high risk of preterm delivery and low birth weight. The purpose of this study was to assess the sensitivity of uterine artery doppler screening in predicting pre - eclampsia and FGR before the onset of disease. The results of this study could be used to evaluate whether it is worthwhile implementing a routine screening programme for preeclampsia. In this prospective study first and second trimester doppler screening was carried out in 79 consecutive singleton pregnancies at 11 to 14 weeks of gestation and 19 to 26 weeks of gestation. Out of total 79 pregnant women under study 13 developed preeclampsia, 6 subjects delivered before 36 weeks of gestation and 4 aborted before period of viability.11 developed early onset preeclampsia while 2 developed late onset preeclampsia. In

the various other studies the incidence of preeclampsia ranged from 8.18% to 39.2%. Various tests used to predict preeclampsia include clinical history, examination findings, Laboratory and hemodynamic tests. Only uterine artery doppler pulsatility index and combination of indices have a sensitivity over 60 %. In general, biochemical tests in early pregnancy; for predicting later development of preeclampsia have better specificity than sensitivity. For example alpha fetoprotein, fibronectin and uterine artery doppler (bilateral notching) all have higher specificities when combined with the patient characteristics and uterine artery doppler changes i. e. upto 90%.⁸

Maternal Age- Preeclampsia is more common in extremes of ages. Pregnant women below 20 years and above 35 years are at an increased risk, and in later group preeclampsia superimposed on chronic hypertension is seen. In our study majority 3 of the patients who developed preeclampsia were above age of 30 years. Total 2 patients were below 20 years of age and 10 patients were above 30 years of age.

Parity- Preeclampsia is twice common in primigravid women as compared to women for whom it is their second or more pregnancy. Women with preeclampsia are therefore twice as likely to be nulliparous as women without preeclampsia. In our study 9 patients out of total 13 who developed preeclampsia are primigravida, thus indicating that gravidity can be taken as strong predicting factor for the disease.

Blood pressure- The mean systolic blood pressure in the third trimester of pregnancy was 127.72+/- 8.71mmHg. The diastolic blood pressure was 80.03+/- 6.64mmHg. All 13 patients who developed preeclampsia, showed rise in blood pressure. The raised blood pressure in case of preeclampsia is due to release of placental antiangiogenic factors and other factors which causes maternal endothelial cell activation/ endothelial dysfunction.

Uterine artery doppler waveform analysis

The current study assessed the sensitivity of PI and diastolic notching as a diagnostic tool to predict preeclampsia and FGR.5 out of 13 patients who developed preeclampsia had abnormal doppler waveforms which were evident from as early as the first trimester. While 22 subjects had showed changes in second trimester uterine artery Doppler, 9 out of them subsequently developed preeclampsia. The study therefore demonstrated that an abnormal uterine artery waveform with early diastolic notching and could predict 38.46% of cases that developed preeclampsia from as early as first trimester. What is however significant is that uterine artery waveform, analysis was able to predict preeclampsia in most severe cases; who later on presented with early manifestations of the disease and had worst pregnancy outcomes.

PI Values

A study done by Melchoirre 2008 reported that uterine artery doppler indices were significantly higher in women who developed preterm preeclampsia. In a current studies PI values upto the 95th percentile of PI chart was considered as normal.⁹The following table was populated with data

obtained from a study done by Gomez and coworkers 2000: 130.¹⁰

Uterine Artery Doppler Indices

Gomez et al	1 st trimester	2 nd trimester
5 th percentile	1.1	0.7
50 th percentile	1.7	1.0
95 th percentile	2.7	1.5

These values represent the 50th centile for each of the trimester of pregnancy at 12 weeks and 22 weeks and are also used as cut off values by the Fetal Medicine Unit at Cris Hani Baragwnath Hospital in Johannesburg. (Nicolau, 2011)

Uterine Artery Doppler Indices (Current Study)

Current study	1 st trimester	2 nd trimester
50 th percentile	1.7	1

Comparing the mean values in our study to that done by Gomez and colleagues, a difference in mean (50th centile) in the 1st trimester was noted. The second trimester mean values in this study were similar to values obtained by Gomez et al. In both studies it can be seen that mean PI values decreased as gestation increased as is to be expected in normal pregnancy. In our study the first trimester PI values in patients who developed preeclampsia was not a strong predictor of preeclampsia. None of the values recorded were above the 95th centile when compared to the values by Gomez and co - workers. However, in clinical practice a first trimester PI value of >1.5 is seemed as elevated and warrants monitoring. (Nicolaidis, 2017) In the group that developed preeclampsia, first trimester PI values ranged between 0.9 to 1.75 respectively.¹¹ It is thus evident that only in selected cases an increased resistance to the flow is recorded in first trimester. In the second trimester most of preeclampsia had PI value above 50th centile signifying that PI proved as better predictor of preeclampsia in second trimester. Comparing the mean PI values in the patients who developed preeclampsia to the mean PI values developed by Gomez et al., only 4 out of 13 were above 50th centile in first trimester and only 8 out of 13 were above 50th centile in second trimester. Doppler PI values obtained in this study were above the 50th centile, a few patients had increased PI values of who most were marginally elevated.

Predictive values of uterine artery doppler

In our study when predictive value of PI in first trimester was elevated, the sensitivity and specificity were 38.46% and 69.23% respectively in first trimester which was similar to the studies by Velauthor and M N Plana.¹² The positive and negative predictive value was similar to the studies by Cnossen et al, the positive and negative likelihood ratios of 3.515 and 0.3832 and 0.8 value.¹³ It was found that PI in the first trimester had reduced statistical significance in detecting preeclampsia. This is consistent with findings of other study by Su Lynn Khong et al, who have shown an unchanged PI throughout 11 - 14 weeks interval, but Gomez et al demonstrated the lower impedance in the uterine artery of a normal uteroplacental circulation at this early stage of pregnancy may predict the later development of some pregnancy complications.¹⁴ The existing data suggest that increased impedance to flow in uterine arteries identifies

about 25% of those who subsequently develop preeclampsia. In First trimester, the sensitivity and specificity for the uterine artery pulsatility index were 38.46% and 89.39%, with P value 0.8 (not significant). The positive predictive value of first trimester uterine artery doppler was 41.67% when pulsatility index was used with a higher sensitivity, specificity, predictive value, higher positive likelihood ratio, while negative predictive value was 88.06%, which is matching with other studies of reference, also the relative risk washigher when pulsatility index was used, with diagnostic odds of 5.268 (1.346 - 20.62). In Second trimester, the sensitivity and specificity for the uterine artery pulsatility index were 69.23% and 80.30%, with PI value >0.8. The positive predictive value of second trimester uterine artery doppler was 40.91% when pulsatility index was used with a higher sensitivity, specificity, predictive value, higher positive likelihood ratio, while negative predictive value was 92.98%, which is statistically significant and matching with other studies of reference, also the relative risk was higher when pulsatility index was used, with diagnostic odds of 9.173 (2.439 - 34.51). Various studies have proved a higher predictive value of uterine artery doppler study for preeclampsia and other adverse pregnancy outcomes when pulsatility index is used as seen in the present study also. In our study presence of notching in second trimester was good predictor for the development of low birth weight than preeclampsia. As 3 (3.81% of study population) subjects with diastolic notching who has resulted in low birth weight but did not develop preeclampsia, proving it independent marker for small for gestational age. In 1st trimester, the sensitivity and specificity for uterine artery diastolic notch were 38.46% and 89.39% as the abnormal doppler criteria which was lower to the studies by Cnossens et al. The positive and negative likelihood ratio of the present study were 3.626 (1.464 - 8.984) and 0.6884 (0.5367 - 0.883) which was lower to the study by Cnossens et al. In the second trimester sensitivity and specificity of uterine artery diastolic notch were 69.23% and 8.30% as the abnormal doppler study criteria which was similar to the studies by Cnossens et al, Jimmy Espinoza et al and Chien et al.^{5,16} We found that 1st trimester notching persisted into the second trimester in 3 patients who developed preeclampsia. The presence of notching, even with a normal PI Index, places the patient at higher risk for adverse fetal outcomes. The findings of our study thus concur with the findings by Melchoirre at al who states that presence of an early diastolic notch is associated with adverse pregnancy outcomes.¹⁷ Our study also supports the findings of Kurdi (1998: 344) who found that women with notching represent a group with an increased risk of developing complications, in particular that require early delivery.

6. Summary

Incidence of Preeclampsia in study population is 16.46%. Reaching to aim and objectives of study, sensitivity of uterine artery doppler in first trimester based on PI value is 38.46%. Specificity is 89.39%. Positive and negative likelihood ratio is 3.26 and 0.6884, respectively. Apart from Hypertension other complications include fetal growth restriction.

7. Conclusions

Early diagnosis of the Preeclampsia is the desirable goal. Hypertensive disorders of pregnancy including preeclampsia if diagnosed earlier, may cause help to avoid further complications. Abnormal Uterine artery doppler changes have been associated with subsequent adverse pregnancy outcomes like hypertensive disorders of pregnancy, intrauterine growth restriction and perinatal mortality. Two staged doppler screening helps in prediction of preeclampsia, in earlier stages and helps to avoid complications. Though, prediction is not of much use, as there is no effective pharmacological treatment to absolutely revert the pathophysiology of the disease, predictive measures help early recognition of the disease and prevent further dreadful complications, leading to achieve desired goal of safe motherhood.

8. Limitations

- The present study is conducted in a tertiary care centre, where the sample is selected from the population attending the out - patient department, hence this population is not a representative of general population and the estimated sensitivity and specificity may not be achievable.
- This study has given statistical results from study population of 79 subjects, which is low sample size to apply on the larger population norm.
- As this is prospective study and includes observation till termination of pregnancy, increased drop - out rate may hinder observational results.

Conflict of Interest: Authors declare no conflict of interest.

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Table 1: Distribution of study subjects according to PI values in Uterine Artery Doppler

UAD (PI value)	Yes		No	
	Number	%	Number	%
1 st trimester UAD	12	15.19	67	84.81
2 nd trimester UAD	22	27.85	57	72.15
McNemars' Schi2 (1) = 22.75 Prob<chi 2 = 0.0001				

Table 2: Frequency of preeclampsia predicted by Doppler and confirmed clinically

Preeclampsia	yes		no	
	Number	%	number	%
Confirmed	13	16.46	66	83.54
Predicted by Doppler parameters				
Right Uterine Artery Pulsatility Index	10	12.66	69	87.34
Left Uterine Artery Pulsatility Index	10	12.66	69	87.34
Frequency of mean PI for 1 st Trimester Uterine Artery Doppler		12.66		87.34
Right Uterine Artery Resistivity Index	13	16.46	66	83.54
Left Uterine Artery Resistivity Index	11	13.92	8	86.08
Frequency of mean PI for 2 nd Trimester Uterine Artery Doppler		15.19		84.81
Total Subjects - 79				

Table 3

Incidence of Preeclampsia in Study samples (n=79)			
Incidence	Number	%	95% CI
Overall	13	16.46	9.06 - 26.49
Early	10	12.66	6.24 - 22.05
Late	3	3.80	0.79 - 10.70

Table 4

Agreement between Preeclampsia confirmed and changes in Doppler (First Trimester UAD)				
1 st Trimester UAD	Yes		No	
	Number	%	Number	%
Yes	5	38.46	7	10.61
No	8	61.54	59	89.39
Total	13	100	66	100
Total subjects - 79				
McNemar'schi2 (1) = 0.07, chi2 = 0.7963				

Table 5

Agreement between Preeclampsia confirmed and changes in Doppler (Second Trimester UAD)				
Second Trimester UAD	Yes		No	
	Number	%	Number	%
Yes	9	69.23	13	19.70
No	4	30.77	53	80.30
Total	13	100	66	100
Total subjects - 79				
McNemar'schi2 (1) = 4.76, chi2 = 0.0290				

Table 6

Validity of First Trimester Doppler in Predicting Preeclampsia						
PE	Positive		Negative		Total	
	Number	%	Number	%	Number	%
Positive	5	38.46	7	10.61	12	15.19
Negative	8	61.54	59	89.39	67	84.81
Total	13	100	66	100	79	100
McNemar'schi2 (1) = 0.07, Prob> chi2 = 0.7963, Not Significant						

Table 7

Estimation of Different Parameters For First Trimester Uterine Artery Doppler		
Parameters	Estimate	95% confidence intervals
Sensitivity	38.46%	(17.71, 64.48 ¹)
Specificity	89.39%	(79.69, 94.77 ¹)
Positive Predictive Value	41.67%	(19.33, 68.05 ¹)
Negative Predictive Value	88.06%	(78.17.93.82 ¹)
Diagnostic accuracy	81.01%	(71.01, 88.14 ¹)
Likelihood Ratio of a Positive Test	3.626	(1.464 - 8.984)
Likelihood Ratio of a Negative Test	0.6884	(0.5367 - 0.883)
Diagnostic Odds	5.268	(1.346 - 20.62)
Cohen's kappa (unweighted)	0.2874	(0.06716 - 0.5077)

Table 8

Validity of Second Trimester Doppler in Predicting Preeclampsia						
PE	Positive		Negative		Total	
	Number	%	Number	%	Number	%
Positive	9	69.23	13	19.70	22	27.85
Negative	4	30.77	53	80.30	57	72.15
Total	13	100	66	100	79	100
McNemar'schi2 (1) = 4.76, Prob> chi2 = 0.0290, Significant						

Table 9

Estimation of Different Parameters For Second Trimester Uterine Artery Doppler		
Parameters	Estimate	95% confidence intervals
Sensitivity	69.23%	(42.37, 87.32 ¹)
Specificity	80.30%	(69.16, 88.11 ¹)
Positive Predictive Value	40.91%	(23.26, 61.27 ¹)
Negative Predictive Value	92.98%	(83.3, 97.24 ¹)
Diagnostic accuracy	78.48%	(68.21.86.11 ¹)
Likelihood Ratio of a Positive Test	3.515	(2.744 - 4.502)
Likelihood Ratio of a Negative Test	0.3832	(0.2326 - 0.6311)

Diagnostic Odds	9.173	(2.439 - 34.51)
Cohen's kappa (unweighted)	0.3876	(0.179 - 0.5962)

Table 10

Comparison for Predictive Value of First Trimester Doppler with Second Trimester Doppler in Development of Preeclampsia			
Predictive Values	First Trimester Doppler	Second Trimester Doppler	p value
Positive Predictive Value	41.67%	40.91%	0.8907, not significant
Negative Predictive Value	88.06%	92.98%	0.087, significant