ROLE OF UTERINE ARTERY DOPPLER AT 11 TO 16 WEEKS OF GESTATION IN PREDICTION OF PREECLAMPSIA : AN OBSERVATIONAL STUDY

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ABSTRACT

Background: Pre-eclampsia is a major cause of perinatal and maternal morbidity and mortality. Doppler is a non-invasive method for evaluation of feto-placental circulation without affecting pregnancy. A high resistance index in uterine artery Doppler waveform has been shown to be the best non-invasive screening test.

Aims: The aim of the study is early prediction of pre-eclampsia and its obstetrical outcome by transvaginal uterine artery Doppler at 11-16 weeks of gestation.

Materials and methods: It is a Observational study in 100 Pregnant Women between 11-16weeks of gestational age . After an informed consent women were subjected to transvaginal ultrasound for dating scan during which uterine artery Doppler waveforms were taken. These women were further followed up clinically for development of preeclampsia. Uterine artery Doppler were studied in all 100 cases.

Results: About 17 women developed preeclampsia among 100 women. Uterine artery notch is seen in 38% of women at 11-16 weeks and about 28.94% of women with notch at 11-16weeks developed preeclampsia. In preeclamptic women mean PI at 11-16 week is 2.6241 which is statistically highly significant as compared to normotensives ($p<0.0001$) and hence this will help in prediction preeclampsia. Uterine artery notching at 11- 16 weeks gestation had 64.70% sensitivity and 90.32% NPV. PI > 95^{th} centile at 11-16 weeks has sensitivity of 82.35% and NPV by 96.05%. When maternal risk factors are considered along with PI> 95^{th} centile sensitivity increased to 88.23% and NPV increased to 97.56%. Mean gestation age at delivery is 33+6 week in preeclamptics and 38+5 week in normotensives ,47% had full term vaginal delivery, 9% had preterm vaginal delivery and 15% had preterm caesarean delivery

and 29% had term caesarean delivery. Mean birth weight is 2.04kg in preeclamptics and 3.08kg in normotensives, mean Apgar at 1 min is 7.44 and at 5 min is 9.31. In preeclamptic women 7 babies were associated with IUGR and 1 IUFD. Mean duration of NICU stay is 36hrs.

Conclusion: Uterine artery Doppler studies between 11-16 weeks has high NPV, they help us to categorize our patients into low risk and high risk so that proper vigilance may be done in high risk women along with prophylactic aspirin therapy for improving maternal morbidity and mortality.

Keywords: Uterine artery notching, Pulsatility Index, Diastolic notch

INTRODUCTION

Hypertensive disorders of pregnancy remain among the most significant and intriguing unsolved problems in obstetrics. Preeclampsia syndrome is one of the leading cause of maternal morbidity and mortality. It is estimated that preeclampsia complicates 2- 8% of pregnancies globally·According to National Health Portal of India, incidence of Preeclampsia was identified in 8-10% in India.[1] Hypertension in pregnancy is also responsible for fetal growth restriction and its incidence is 33.37% in mild to moderate PE and 62% in severe PE, leading to substantiative perinatal morbidity and mortality. Due to iatrogenic prematurity, respiratory distress syndrome and NICU admission there is 5 fold increase in perinatal morbidity in preeclampsia. In nulliparous woman, who conceive with Assisted Reproductive technology the incidence of preeclampsia ranges from 2% to 7% which accounts for 29,000 maternal deaths per year world wide.[2]

Early screening for PE may allow vigilant antenatal surveillance and appropriate timing of fetal delivery in order to avoid serious sequelae. Various haemodynamic and biochemical measures have been found to have limited accuracy as a screening measures for this condition. Preeclampsia is characterised by an imbalance between prostacycline and thrombaxane A2 production as well as failure of second wave of trophoblastic invasion of the endometrio -myometrial vasculature. The result is abnormal uteroplacental blood flow which leads to an idea of using Doppler assessment of uterine artery velocimetry waveforms as the method of screening. In recent years, ultrasonography is commonly used in measurement of fetal biometry and diagnosis of congenital anomalies and IUGR. Problem which still exists is identification of those pregnancies which are at risk of increased maternal and fetal morbidity and mortality as in PE. Various biochemical tests used in screening of high risk population for PE have lower positive predictive values, high cost and less patient compliance. Doppler is a non-invasive method for evaluation of feto-placental circulation without any disturbance to human pregnancy. A high Pulsatility Index , resistance index and persistent uterine artery notching in uterine artery doppler wave form has shown as a better screening test. [3]

Even though several studies used uterine artery Doppler method as a screening indices for preeclampsia and fetal growth restriction, a debate continues as to its value. Varying

sensitivities are acquired depending on the category of Doppler employed, the sampling size, the description of abnormal uterine artery resistance, gestational age at evaluation and dissimilar end points. Thus, we have conducted this study to find out the predictive value of transvaginal Uterine artery Doppler in early pregnancy at 11-16 week of gestation for the prediction of preeclampsia and subsequent pregnancy outcome.

MATERILAS AND METHODS

It is a Observational study in 100 Pregnant Women between 11-16weeks of gestational age attending the outpatient department for antenatal care at Government Maternity Hospital, Hanmakonda from November 2019 to June 2021.

Incluison Criteria: All pregnant women between 11-16 weeks of gestational age, singleton pregnancy and maternal age between 15 -35yrs

Exclusion Criteria: multiple gestation, maternal comorbidities like thyroid disorders, diabetes mellitus , chronic hypertension, congenital heart disease, SLE and APLA, congenital uterine anomalies , habits like smoking , alcohol consumption and substance abuse.

PROCEDURE:

After assessment of inclusion and exclusion criteria, 100 antenatal women of 11 to 16 weeks of singleton pregnancy were selected for the study. Women booking for antenatal care were examined and investigated. After an written informed consent, the women were subjected to transvaginal ultrasound. Women were placed in the dorsal position with knee flexed, a trans-vaginal ultrasound scan was done and doppler assessment of uterine circulation for uterine artery indices using Philips USG machine with 7.5 Mhz transvaginal curvilinear transducer. After initial assessment, the cervix was identified. Uterine artery is located on one side by placement of probe in that fornix and colour flow mapping was done as it crosses over hypogastric artery and vein just before it enters the uterus at utero-cervical junction[13]. The utero placental circulation was measured by uterine artery doppler indices like Pulsatility Index (PI). Increased resistance to flow in the uterine artery is associated with the appearance of diastolic notch and increase in all these indices. Same procedure was repeated on the opposite side. The flow velocity waveforms on the right and left uterine arteries were taken when 3 or 4 waves of equal height were seen, the image was frozen and measurements were taken either by trace method/ manually/automatic trace . Then Doppler indices were obtained directly from the machine and patients are further followed up clinically for development of pre-eclampsia. The utero placental circulation were measured by uterine artery pulsatility index (PI). Increased resistance to flow in the uterine artery is associated with the appearance of diastolic notch and increase in pulsatality index. These patients were followed up till delivery and details of pregnancy events, delivery and neonatal outcome were noted. The abnormal pregnancy outcomes considered are preeclampsia. Perinatal outcomes are considered are IUFD, Apgar at 1and 5 minutes, birth weight and NICU admission.

Statistical analysis

Statistical analysis was done using descriptive statistical methods like mean, percentages and proportions. Chi-square test was used to find the association between two attributes and unpaired t-test was used to find the association between two variables. A p-value of less than 0.05 was considered to be statistically significant.

RESULTS

After assessment of inclusion and exclusion criteria, 100 singleton antenatal women of 11 to 16 weeks of singleton pregnancy were selected for the study in the OPD of Obstetrics and Gynaecology at Government Maternity Hospital, Hanamkonda. After an informed consent, the women were subjected to transvaginal ultrasound for doppler assessment of uterine circulation and uterine artery indices were noted. These women were further followed up clinically for development of preeclampsia. The following results are obtained in our study.

Table 1: Demographic distribution in our study

Age in years	**Frequency**	**Percent**
Less than 20	6	6.0
20-24	42	42.0
25-29	36	36.0
30-34	14	14.0
More than 34	2	2.0
Total	100	100.0
Schooling		
Primary	12	12.0
Secondary	48	48.0
Intermediate	35	35.0
Graduate	5	5.0
Class		
Upper middle	5	5.0
Lower middle	21	21.0
Upper lower	36	36.0
Lower	38	38.0
Marital life		
< 6 mnth	10	10.0
6mnth – 1yr	21	21.0
1-2 yr	17	17.0
>2yr	52	52.0
Gravida		
Primi	51	51.0

G2	32	32.0
> G2	17	17.0
SBP in mmHg		
<130	80	80.0
130-139	3	3.0
140-149	9	9.0
>149	8	8.0
DBP in mmHg		
< 80	78	78.0
80-89	5	5.0
90-99	10	10.0
> 99	7	7.0

About 78 % of women are in the age group 20-29 years and 6% belong to teenage group. About 48%of women got secondary education, 35% got intermediate and 12% studied till primary and 5% were graduates. About 21%, 36%, 38% of women belong to lower middle, upper lower and lower socioeconomic status respectively, as per Updated Modified Kuppuswamy classification – 2021. In our study, 31% are married for less than 1yr and 52% were married for more than 2yrs About 51% of women were primigravida. Mean gestation age at transvaginal USG is 13+6 wks

About 83% are normotensive and 17% are associated with hypertensive disorders of pregnancy. About 83% are normotensive and 17% are associated with hypertensive disorders of pregnancy.

Table-2: Diastolic notch Pulsatality index in preeclamptic and normotensive women at 11-16 week

Diastolic notch	**Preeclampsia (n=17)**		**Normotensive (n=83)**	
	No	**%**	**No**	**%**
Present(n=38)	11	64.70	27	32.53
Absent (n=62)	6	35.29	56	67.46
X^2 =6.200, df= 1, p= 0.0128				
Pulsatility Index				
At 11-16 Weeks	2.6241	0.26149	1.8322	0.20751
t = 13.6928 , df = 98 , p <0.0001				
Uterine artery Doppler pulsatility index				
PI > 2.35 (n=24)	14	82.35	10	12.04
Normal PI (n=76)	3	17.64	73	87.95
X^2 =38.236 , df= 1, p <0.0001				

Uterine artery Doppler notching at 11-16 weeks is seen in 38% of women. Uterine artery Doppler notching at 11-16 weeks is seen in 64.70% of preeclamptic women

At 11-16 weeks, mean PI of both uterine arteries is more than 2.35 in 24% study population.

Mean pulsatality index at 11-16 weeks of gestation in preeclamptic women is 2.6241 and in normotensive is 1.8322. Preeclamptic women ,uterine artery doppler pulsatality index is more than 2.35 (i.e 95^{th} centile) at 11-16 weeks

Table-3: Comparision between uterine artery diastolic notch detection of preeclampsia at 11-16weeks

PI >2.35 in	**Preeclampsia (n=17)**	
	Number	**Percentage**
Diastolic notch (n= 38)	11	28.94%
PI > 2.35 (n= 24)	14	58.33%
PI > 2.35 in high-risk group		
PI >2.35 (n=24)	14	58.33%
PI >2.35 + Risk factors (n=18)	15	83.33%

In abnormal uterine artery doppler at 11-16 wks , diastolic notch detected 28.94% of preeclampsia. But PI >2.35 detected 58.33% of preeclampsia. In high risk group, PI >2.35 detects about 83.33% of preeclampsia women compared to general population.

Table-4: Role of uterine artery Doppler in predicting preeclampsia at 11-16 weeks

Study variables	**Sensitivity**	**Specificity**	**PPV**	**NPV**
Diastolic notch	64.70%	67.46%	28.94%	90.32%
PI> 2.35 (> 95^{th}centile)	82.35%	87.95%	58.33%	96.05%
PI >2.35 + Risk factors	88.23%	96.38%	83.33%	97.56%

Pulsatality index of more than 95^{th} centile is better predictor of preeclampsia at 11-16 weeks and detection rate increases to 83.33% when maternal risk factors are included.

Table-5: Gestation age and mode of delivery in preeclamptic women

Gestation age in weeks at delivery	**Frequency (n=17)**	**Percentage**
>38	5	29.41
36- 38	3	17.64
34- 36	3	17.64
32- 34	6	35.29
Mode of delivery		
FTND	47	47.0
PTVD	9	9.0
LSCS (PT)	15	15.0
LSCS	29	29.0

In preeclampsia 52.93% women delivered at less than 36 weeks of gestation , 17.64% delivered between 36-38 weeks and 29.41% delivered at more than 38 weeks of gestation. About 47% had FTVD, 9% had PTVD and 44 % had LSCS.

Table-6:Gestational age, birth weight and neonatal paramethers after birth

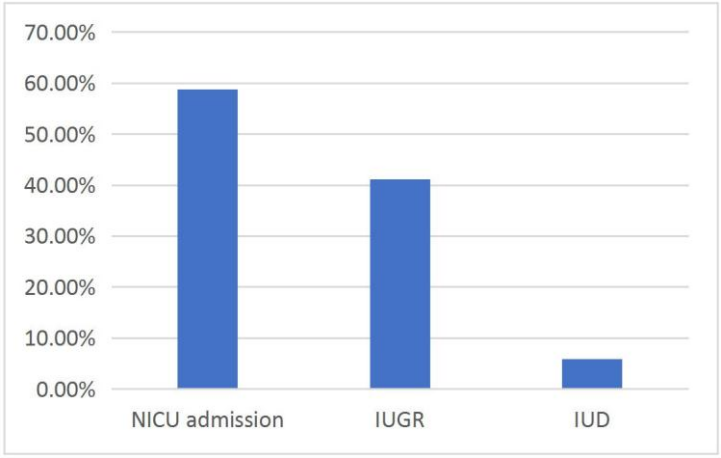
Gestational age at delivery	**Minimum**	**Maximum**	**Mean**
Preeclamptics	32+3	39+4	33+6
Normotensives	33+1	41+2	38+5
Birth weight			
Preeclamptics	1kg	2.8kg	2.04kg
Normotensives	2.1kg	3.9kg	3.08kg
APGAR score, NICU stay			
Ap1	0	8	7.44
Ap5	0	10	9.31
NICU Stay in days	0	30	1.47

Mean gestational age of delivery in preeclamptics is 33+6 weeks compared to 38+5 weeks in normotensives.

Mean birth weight among preeclamptics is 2.04kg compared to 3.08 kg in normotensives.

Mean APGAR at 1min is 7.44. Mean APGAR at 5min is 9.31. Mean NICU stay is 1.47day i.e 36 hours.

Figure-1:Neonatal outcome in preeclampsia



In Preeclampsia 41.17% IUGR, 5.88% IUFD noted and 58.82% of neonate required NICU admission.

DISCUSSION

In our observational study done over a period of one year, 100 women attending the outpatient department for antenatal care at Government Maternity Hospital, analyzed for Doppler changes of uterine artery at 11-16 weeks by transvaginal ultrasound were followed up till delivery and details of pregnancy events, delivery and neonatal outcome were noted. In our study population, mean age is 25.39 yr with range 17-36 yr which is similar to Varapong Phupong et al[4] (27.4yr). 31% has marital life of less than 1year and 52% has marital life of more than 2years. Nulliparous women constitute 51% of study population similar to Albaiges et al[5] (52.6%). Past history of preeclampsia present in 7% population. Mean gestational age for uterine artery doppler study was 13+6 weeks with range being 11+2 weeks to 16 weeks.

Uterine artery Doppler assessment for presence of diastolic notch and PI values at 11-16 weeks are studied. Out of 100 women studied 17% women developed preeclampsia thus prevalence is similar to Gupta Shashi et al[6] (18.1%) and Neela Arun et al[7] (16%) and high prevalence compared to that quoted by Plasencia et al[8] (3%) and O Gomez et al[10] (6.7%).

Among 100 women 38% had notching at 11-16 weeks which is similar when compared to Naimisha et al[10] where 32% had notching at 13-16 weeks and Asha neravi et al[11] where 35% had notching at 12-16 weeks.

In our study when uterine artery notch at 11-16 weeks is considered, 28.94% of women developed preeclampsia . 64.70% preeclamptic women had diastolic notching at 11-16 weeks when compared to normotensive women where 32.53% had diastolic notching which is statistically significant (p= 0.0128)

Out of 100 women, 38 patients had diastolic notching at 11-16 weeks and 11 women developed preeclampsia. Hence sensitivity of uterine artery diastolic notching is 64.70%, specificity is 67.46% positive predictive value is 28.94%, and negative predictive value is 90.32% in prediction of preeclampsia similar to Gupta Shashi et al[6] and Neela Arun et al[7].

In our study, PI more than 95th centile is considered to be cut-off value. So for 11- 16 weeks gestational age mean PI value of both uterine arteries more than 2.35 is taken as cut off according to O Gomez[12]. Out of 100 women, 24 women had PI more than 2.35 and 14 of them developed preeclampsia.

In our study, mean PI in preeclamptic women is 2.6241 at 11-16 weeks which is statistically highly significant ($p<0.0001$) as compared to normotensive women whose mean PI is 1.8322. Hence this will help in prediction preeclampsia similar to AM. Martin et al[13] and O Gomez et al[12].

In our study out of 100 women 24 had mean PI more than 2.35 at 11- 16 weeks and 14 women developed preeclampsia. Hence sensitivity of mean PI more than 95th centile is 82.35%, specificity is 87.95%, positive predictive value is 58.33% and negative predictive value is 96.05% in prediction of preeclampsia similar to S Chakraborthy et al[14].

Our study shows , when only abnormal uterine artery doppler is considered, mean PI more than 95th centile is better predictor of preeclampsia at 11-16 weeks of gestation when compared to diastolic notch as notching is physiological in early gestational age. Similar results are seen in study by Adekanmi et al[15]

Out of 17 women who developed preeclampsia in our study, 64.60% are nulliparous with mean age being 25 years . 58.82% have marital life less than 1year and 35.29% have marital life more than 2years. 57.14% had past history of preeclampsia and 5.88% women conceived on ART. Of 17 preeclampsia patients, early onset preeclampsia requiring delivery at less than 34 weeks are 58.82% and late onset preeclampsia requiring delivery at more than 34 weeks is 41.17%. Abruption occurred in 2 patients. Hence abnormal uterine artery doppler at 11-16 weeks is useful for prediction of early onset preeclampsia similar to Demers S et al[16].

Our study shows that when maternal risk factors like age less than 20yrs , nulliparity, past history of preeclampsia and conceived on ART are taken into consideration along with mean PI more than 95th centile , 15 out of 18 women developed preeclampsia. Hence sensitivity of PI > 95th centile along with maternal risk factors is 88.23%, specificity is 96.38% , positive predictive value is 83.33% and negative predictive value is 97.56%.

From our study, we observed that in uterine artery doppler PI > 95th centile is a better predictor pf preeclampsia compared to diastolic notching at 11-16 weeks of gestation. But

when we include maternal risk factors along with PI> 95th centile, detection rate increased to 83.33% from 58.33% and sensitivity increased from 82.35% to 88.23%. Hence PI> 95th centile is a better predictor of preeclampsia in high risk group when compared to general population.

Mean gestation age at delivery is 33+ 6 week in preeclamptic women and 38+ 5 week in normotensive women , 47% had full term vaginal delivery and 9% had preterm vaginal delivery and 44% had Caesarean delivery of which 34.09% were preterm LSCS. Minimum and maximum birth weight are 1kg and 3.9kg respectively. Mean birth weight is 2.04 kg in preeclamptic women and 3.08kg in normotensives. Mean Apgar at 1 min is 7.44 and at 5 min is 9.31. In preeclamptic women 7 babies were associated with IUGR ,10 babies required NICU admission and there is one IUFD. Mean duration of NICU stay is 36hrs.

Table-6: Comparison of our study with previous studies for preeclampsia with uterine artery doppler with respective to diastolic notch

Author	**Gestation age (weeks)**	**Incidence Of PE (%)**	**Sensitivity (%)**	**Specificity (%)**	**PPV (%)**	**NPV (%)**
Albaiges [5]	23 weeks	3.7	32.3	96.7	27.3	97.4
Gupta shashi [6]	12-16	18.18	68.75	66.6	31.42	90.5
Sharma.S. Singh [17]	16-28	32	15.63	98.53	83.33	71.28
Asha Neravi [11]	12-16	22	34.29	84.62	54.55	70.51
Neela Arun [7]	13-16	16	71.42	74.41	31.25	94.11
Naimisha [10]	13-16	24	83.7	84.9	64.5	94
Our Study	11-16	17	64.70	67.46	28.94	90.32

Table-7: Comparison of our study with previous studies, for preeclampsia with uterine artery Doppler with PI more than 95th centile

Author	**Gestation age (weeks)**	**Incidence of PE (%)**	**Sensitivity (%)**	**Specificity (%)**	**PPV (%)**	**NPV (%)**
Albaiges [5]	23	3.7	35.3	96	25.8	97.5
AM Martin [13]	11-14	2.1	27	95.4	11	98.4
O Gomez [12]	11-14	6.7	24	95.1	11.3	97.9
Leelavathi [18]	11-13	37	81.46	92.5	91.6	-

Chakraborty [14]	16-29	28	85.71	91.67	80	94.29
Mihaela Oancea [19]	11-14	21.6	61.5	63.8	-	-
Our study	11-16	17	82.35	87.95	58.33	96.05

CONCLUSION

Hypertensive disorders of pregnancy are the foremost cause of maternal mortality and morbidity worldwide, predominantly in developing countries. In view of the fact that its aetiology stands unknown and preeclampsia being a complex clinical syndrome involving multiorgan systems and perinatal mortality and morbidity. The research for ideal predictive test and preventive measure remains challenging.

In our study, uterine artery indices showing impedance to uteroplacental circulation (PI, notching) are statistically significant. Infact, pulsatality index is statistically more significant than diastolic notching. Uterine artery Doppler studies between 11-16 weeks has high NPV, they help us to categorize our patients into low risk and high risk so that proper vigilance may be done in high risk women along with prophylactic aspirin therapy for improving maternal morbidity and mortality.

Additional research necessitates to appraise the generalizability with special resource settings among the multiparametric models, besides evaluating the bang of screening on clinical outcomes.

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