ROLE OF TRIPLE VESSEL DOPPLER ULTRASONOGRAPHY IN PREDICTION OF PERINATAL OUTCOME IN HIGH RISK PREGNANCY

Obstetrics & Gynecology

Manasa R*

Senior Resident, Department of OBG, BMCRI, Bengaluru. *Corresponding Author

Priyanka

Assistant Professor, Department of OBG, Gulbarga Institute of Medical Sciences, Kalaburgi.

ABSTRACT

BACKGROUND AND OBJECTIVES: To evaluate the role of Doppler ultrasonography in predicting the perinatal outcome in high-risk pregnancy and to establish its role in management of high-risk pregnancy. **MATERIALS AND METHODS:** The present study is a prospective study of Doppler ultrasound evaluation of uterine artery, umbilical artery and middle cerebral artery in 100 high-risk pregnant women, performed between 28 and 34 weeks of gestation. Doppler index Pulsatility index (PI) for each above mentioned artery and cerebro-placental ratio (CPR) will be calculated. Doppler Pulsatility index for the corresponding gestational age were compared with the reference values. The results of the Doppler ultrasound and AFI will be used for analysis of mode of delivery and perinatal outcome in the form of birth weight, APGAR score, NICU admission, perinatal mortality. **RESULTS:** Among newborns 46(46%) were admitted to NICU, 64(64%) of neonates had birth weight less than 2.5kg, there were 17 perinatal deaths. Of the 17 perinatal deaths, 2 cases had reverse end diastolic Flow (REDF) and 12 had absent end diastolic Flow (AEDF). Uterine artery PI was most sensitive(72.3%) than Umbilical artery PI(sensitivity 59.6%) and MCA PI(sensitivity 68.1%). Diagnostic accuracy of Cerebroplacental ratio (accuracy 71%) was better than Umbilical artery PI (accuracy 65%) and MCA PI(accuracy 70%) in predicting adverse outcomes. **CONCLUSION:** Triple vessel colour Doppler sonography is very useful in high-risk pregnancy diagnosis and in predicting perinatal outcome.

KEYWORDS

High-risk Pregnancy, Triple Vessel Colour Doppler, Pulsatility Index (PI), Cerebro-placental Ratio (CPR), Perinatal Outcome.

INTRODUCTION:

High risk pregnancy requires sophisticated maternal and fetal surveillance to help in its management decisions so as to ensure an optimal outcome for both mother and her newborn. A pregnancy at risk needs to be identified at an earlier state, in order to have an effective intervention strategy to deal with its complications. The two major conditions associated with placental dysfunction: Pre-eclampsia and IUGR (Intrauterine Growth Restriction).

Hypertensive disorders remains among the most significant unsolved problems in obstetrics. This complicates 5 to 10 percent of all pregnancies, and together they are one of the deadly triad-along with hemorrhage and infection-that contributes greatly to maternal morbidity and mortality rates. Defects in endovascular trophoblastic invasion with pre-eclampsia syndrome results in compromised uteroplacental perfusion is a major culprit in greater perinatal morbidity and mortality.¹

IUGR is defined as fetal growth less than the normal growth potential of a specific infant because of genetic, environmental, maternal and placental factors. World over, IUGR is observed in about 24% of newborns. In Asia it accounts for nearly 75% of affected infants. In India, incidence of IUGR reported to be 9.65% among hospital born live birth infants.²

Doppler ultrasound is a rapid non-invasive test that provides valuable information about hemodynamic situation of the fetus and is an efficient diagnostic test of fetal jeopardy that helps in management of high-risk pregnancy. Doppler ultrasound evaluates uteroplacental and fetoplacental circulation.³

Uterine artery Doppler has been used to estimate resistance in uteroplacental blood flow.³

Umbilical artery Doppler indicates extreme downstream resistance, placental dysfunction and fetal compromise.³

Middle cerebral artery Doppler evaluates altered cerebral circulation before there is hypoxemia significant enough to alter the fetal heart rate pater.³

Our study was an effort at establishing the role of Uterine artery(UtA), Umbilical artery(UA) and Middle Cerebral Artery(MCA) Doppler ultrasonography in prediction of perinatal outcome in high-risk pregnancy and to determine the role Doppler in management of high-risk pregnancy.

METHODOLOGY

MATERIALS AND METHODS

Source of data:

data for the study was collected from all women with high risk pregnancy attending department of Obstetrics and Gynaecology in Chigateri hospital, Women and Children hospital and Bapuji hospital, attached to J.J.M medical college, Davangere

Duration of study: .

two years from November 2016 to September 2018

Inclusion criteria :

1. Singleton pregnancy with gestational age between 28 and 34 weeks.
2. Women with reliable dating of pregnancy confirmed by an early first trimester ultrasound examination using CRL or BPD or with known LMP will be selected.
3. High-risk pregnancy Pre-eclampsia, IUGR, BOH.

Exclusion criteria:

1. Rupture of membranes,
2. Multiple pregnancies
3. Fetuses with congenital anomalies,
4. Intrauterine Fetal Demise.

Sample size: 100

STATISTICAL ANALYSIS:

The data was compiled in Microsoft (MS) Excel work sheet and analysed using SPSS (Statistical Package for Social Sciences) software version 23.

Statistical analysis was done by using proportion. The sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy were determined for all Doppler measurements.

RESULTS

TABLE 1: Age distribution of study cases

Age (years)	No.of patients	Percentage %
18-25	62	62.0
26-30	30	30.0
31-35	6	6.0
>35	2	2.0
Total	100	100

62% of patients were between 18-25 age group

TABLE 2: Gravidity distribution of study cases

Gravida	No. of patients	Percentage
Primi	60	60.0
Multi	40	40.0

60% of patients were primigravida

TABLE 3: Amniotic fluid distribution in study cases

AFI	Doppler		Total	P value
	Abnormal	Normal		
Normal	2	36	38	0.000
	5.3%	94.7%	100.0%	
Oligo	32	30	62	
	51.6%	48.4%	100.0%	
Total	34	66	100	
	34.0%	66.0%	100.0%	

Among 34 patients with abnormal Doppler, 32(94.1%) patients had oligohydramnios.

TABLE 4: Distribution characteristics of placental maturity

Placental grading	No. of patients(%)
2	48(48.0%)
3	52(52.0%)
Total	100(100.0%)

52 patients had grade 3 placenta and 48 patients had grade 2 placenta
Association of Doppler Indices with Mode of delivery

TABLE 5: Doppler velocimetry and Mode of delivery

Doppler indices		Vaginal delivery n (%)	Cesarean delivery n (%)	Chi-square P- value	O.R
Umbilical artery Doppler PI	Normal	38 (67.9%)	18(32.1%)	9.84, P<0.002	1(ref. category)
	Abnormal	16 (36.4%)	28 (63.6%)		3.694 (1.61-8.49)
Uterine artery PI	Normal	28 (63.6%)	16 (36.4%)	2.937, P=0.087	1(ref. category)
	Abnormal	26 (46.4%)	30 (53.6%)		2.019 (0.9-4.53)
MCA PI	Normal	34(64.2%)	19(35.8%)	4.678, P=0.031	1(ref. category)
	Abnormal	20 (42.6%)	27 (57.4%)		2.416 (1.08-5.41)
CPR	Normal	40 (64.5%)	22 (35.5%)	7.26, P<0.007	1(ref. category)
	Abnormal	14 (36.2%)	24 (63.2%)		3.12 (1.35-7.22)

The cesarean delivery rate was high at 46% as this was a high-risk group and threshold for cesarean was low. As study included gestation age between 28-34 weeks and needed delivery for various obstetric and maternal indications, cesarean was restored to owing to the fact response to induction is poor in early preterm patients with unfavourable cervix. Prolonged induction and delivery would not be in the interest of compromised fetuses.

Caesarean delivery is more common in abnormal umbilical artery PI, MCA PI and CPR but no so with abnormal uterine artery PI.

TABLE 6: Mode of delivery

Mode of delivery	No. of cases(Percentage)
Preterm vaginal delivery	40(40.0%)
Preterm LSCS	34(34.0%)
Term vaginal delivery	18(18.0%)
Term LSCS	8(8.0%)
TOTAL	100(100.0%)

74% had preterm delivery and 36% had term delivery.

Association of Doppler Indices with NICU Admission

TABLE 7: Doppler velocimetry and NICU Admission

Doppler indices	Absent n (%)	Present n (%)	Chi-square P- value	O.R
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Umbilical artery Doppler PI	Normal	38 (67.9%)	18 (32.1%)	9.839, P=0.002	1(ref. category)
	Abnormal	0 (0.0%)	44 (100.0%)		3.694 (1.6-8.5)
Uterine artery PI	Normal	32 (72.7%)	12 (27.3%)	11.09, P=0.001	1(ref. category)
	Abnormal	0 (0.0%)	34 (60.7%)		4.121 (1.76-9.67)
MCA PI	normal	37 (69.8%)	16(30.2%)	11.35, P=0.001	1(ref. category)
	Abnormal	17(36.2%)	30(63.8%)		4.081 (1.7-9.4)
CPR	Normal	44 (71%)	18(29%)	18.91, P<0.000	1(ref. category)
	Abnormal	10 (26.3%)	28(73.7%)		6.844 (2.8-16.9)

CPR is significantly associated with NICU admission ($\chi^2=18.9, p<0.000$). Women who had lower CPR had 6.844 times higher risk of NICU admission of their baby.

Association of Doppler Indices with APGAR score

TABLE 8: Doppler velocimetry and APGAR Score

Doppler indices		Normal APGAR n (%)	Low APGAR n (%)	Chi-square P- value	O.R
Umbilical artery Doppler PI	Normal	42(75%)	14(25%)	15.1, P<0.000	1(ref. category)
	High	16(36.4%)	28(63.6%)		5.25 (2.22-12.4)
Uterine artery PI	Normal	30 (72.7%)	12 (27.3%)	6.99, P=0.008	1(ref. category)
	Abnormal	26 (46.4%)	30 (53.6%)		3.07 (1.3-7.17)
MCA PI	Normal	41 (77.4%)	12 (22.6%)	17.35, P<0.000	1(ref. category)
	Abnormal	17 (36.2%)	30 (63.8%)		6.03 (2.5-14.5)
CPR	Normal	48 (77.4%)	14 (22.6%)	25.26, P<0.000	1(ref. category)
	Abnormal	10 (26.3%)	28(73.7%)		9.6 (3.76-24.5)

CPR is significantly associated with low APGAR score ($\chi^2=25.26, p<0.000$).

Women who had abnormal CPR are 9.6 times increased risk of having baby with Low APGAR score.

Association of Doppler indices with Perinatal mortality

TABLE 9: Doppler velocimetry and perinatal mortality

Doppler indices		absent n (%)	present n (%)	Chi-square P- value	O.R
Umbilical artery Doppler PI	Normal	53 (94.6%)	3 (5.4%)	12.23, P<0.000	1(ref. category)
	Abnormal	30 (68.2%)	14 (31.8%)		8.2 (2.2-31.02)
Uterine artery PI	Normal	43 (97.7%)	1 (2.3%)	12.08, P=0.001	1(ref. category)
	Abnormal	40 (71.4%)	16 (28.6%)		17.2 (2.2-135.7)
MCA PI	Normal	52 (98.1%)	1(1.9%)	18.25, P<0.000	1(ref. category)
	Abnormal	31 (66.6%)	16 (34%)		26.839 (3.4-212.4)
CPR	Normal	59 (95.2%)	3 (4.8%)	17.1, P<0.000	1(ref. category)
	Abnormal	24 (63.2%)	14 (36.8%)		11.5 (3.02-43.6)

MCA PI is significantly associated with perinatal mortality($\chi^2=18.25$, $p<0.000$). Women with abnormal MCA PI is 11.5 times increased risk with perinatal mortality.

Association of Doppler Indices with overall Perinatal outcome

TABLE 10: Doppler velocimetry and overall Perinatal outcome

Doppler indices		Uneventful n (%)	Eventful n (%)	Chi-square P- value	O.R
Umbilical artery Doppler PI	Normal	37 (66.1%)	19 (33.9%)	8.73, P=0.003	1(ref. category)
	Abnormal	16(36.4%)	28 (63.6%)		3.407 (1.49-7.71)
Uterine artery PI	Normal	31 (70.5%)	13(29.5%)	9.6, P=0.002	1(ref. category)
	Abnormal	22 (39.3%)	34 (60.7%)		3.685 (1.59-8.54)
MCA PI	High	38(71.7%)	15 (28.3%)	15.83, P<0.000	1(ref. category)
	Low	15 (31.9%)	32 (68.1%)		5.404 (2.3-12.8)
CPR	Normal	43 (69.4%)	19 (30.6%)	17.52, P<0.000	1(ref. category)
	Abnormal	10 (26.3%)	28 (73.7%)		6.337 (2.57-16.27)

CRP is significantly associated with adverse perinatal outcome($\chi^2=17.52$, $p<0.000$). women with abnormal CPR is 17.52 times increased risk of adverse perinatal outcome like low APGAR score, NICU Admission and Perinatal mortality.

Doppler to Delivery interval

TABLE 11: Doppler velocimetry and the duration between doppler and delivery

Doppler to Delivery Interval	Doppler	
	Normal n (%)	Abnormal n (%)
<24hrs	1 (3.57%)	27 (96.43%)
1 to 2 weeks	0 (0.0%)	30 (100.0%)
3 to 4 weeks	2 (33.3%)	4 (66.7%)
5 to 6 weeks	28 (100%)	0 (0.0%)
7 to 8 weeks	8 (100.0%)	0 (0.0%)

Patients with abnormal Doppler has less Doppler to delivery interval like majority delivered within 2 weeks of Doppler examination.

Performance characteristics of Doppler Indices

TABLE 12: Performance characteristics of Doppler Indices

Outcome	Parameters	Sensitivity (%)	Specificity (%)	PPV	NPV	Diagnostic accuracy
Perinatal mortality	U.A PI	82.4	63.9	31.8	63.9	67
	Ut. A PI	94.1	51.8	28.6	97.7	59
	Diastolic notch	94.1	66.3	36.4	98.2	71
	MCA.PI	94.1	62.7	34	98.1	68
	CPR	82.4	71.1	36.8	95.2	73
Low APGAR	U.A PI	66.7	72.4	63.6	75	70
	Ut. A PI	71.4	55.2	53.6	72.7	62
	Diastolic notch	61.9	69	59.1	71.4	66
	MCA.PI	71.4	70.7	63.8	77.4	71
	CPR	66.7	82.8	73.7	77.4	76
NICU admission	U.A PI	60.9	70.4	63.6	67.9	66
	Ut. A PI	73.9	59.3	60.7	72.7	66
	Diastolic notch	65.2	74.1	68.2	71.4	70
	MCA.PI	65.2	68.5	63.8	69.8	67
	CPR	60.9	81.5	73.7	71	72

Total eventful Outcome	U.A PI	59.6	69.8	63.6	66.1	65
	Ut. A PI	72.3	58.5	60.7	70.5	65
	Diastolic notch	63.8	73.6	68.2	69.6	69
	MCA.PI	68.1	71.7	68.1	71.7	70
	CPR	59.6	81.1	73.7	69.4	71

Performance characteristics of Doppler indices

FIGURE 1: Graph showing Performance characteristics of Doppler Indices

Most sensitive was uterine artery PI(72.3%), most specific was CPR(81.1%) , high PPV was CPR(73.7%), High NPV was MCA PI(71.7%) and most diagnostically accurate is CPR(71%).

DISCUSSION

High risk pregnancy are known to cause maternal and fetal morbidity and mortality. Adverse Fetal outcomes can be assessed by clinical examination as well as Doppler ultrasonography. Doppler velocimetry is a rapid non invasive test that provides information about hemodynamic status of the fetus at an early period of gestation when compared to clinical examination and is an efficient diagnostic test of fetal jeopardy that helps in management of high risk pregnancy. Doppler is been used to assess adverse perinatal outcome.^{5,6,7}

In our study majority of the women were found below 25 years and primigravida similar to Gupta P et al. In our study majority of the women had PE and IUGR compared to B.O.H and majority of them had combination of both PE and IUGR similar to Gupta et al.⁸

Majority of the Indian studies conducted have only used 3 indices namely Um A PI, MCA PI and CPR..⁹ Doppler velocimetry of the Uterine arteries reflects vascular impedance on the maternal side of the placental circulation. Increasing impedance, due to anomalous invasion of cytotrophoblastic cells into the decidual tissue of the placental bed, and defect remodelling of the spiral arteries, is reflected in decreasing diastolic blood flow velocities and/or persistent early diastolic notch in the uterine artery blood flow waveform. In pregnancies complicated by pre-eclampsia, increased uterine artery vascular impedance in the third trimester has been correlated with adverse perinatal outcomes such as small.for.gestational.age (SGA) newborns, delivery by caesarean section, premature delivery and admission to a neonatal intensive care unit (NICU).^{10,11}

TABLE 13: Performance characteristics of umbilical artery PI in present study with reference range.

	Fong K W et al	Gramellini et al	Present study
Sensitivity	44.7%	64%	59.6%
Specificity	86.6%	90.7%	69.8%
PPV	54%	72.7%	63.6%
NPV	81.7%	86.7%	66.1%

Umbilical artery was found to have low sensitivity of 59.6% when compared with uterine artery PI and MCA PI. This sensitivity was comparable with that of Fong KW et al¹⁸ and Gramellini et al¹⁹. The specificity of Umbilical artery PI 69.8% more than uterine artery PI but less compared to MCA PI and CPR. The PPV of Umbilical artery PI 63.6% more than uterine artery PI but less compared to MCA PI and CPR. The PPV of Umbilical artery PI is comparable with that of Fong KW et al and Gramellini et al. The NPV of Umbilical artery PI 66.1% less compared to any other variables.

Patients with absent end diastolic volume (AEDV) and reverse end

diastolic volume (REDV) have the gravest outcome. Fetuses with AEDV require intensive surveillance as fetal wellbeing may deteriorate very fast. Fetuses with REDV are most severely compromised. REDV indicate preterminal fetal state similar to Mishra D et al.¹⁴

Our findings confirms the result of Fong K W et al, Gramellini et al that abnormal Umbilical artery PI is associated with adverse perinatal outcome like low APGAR score, NICU Admission and perinatal mortality. Our findings agree with Harrington et al¹⁵ that umbilical artery can be normal in term and late term with abnormal MCA.

TABLE 14: Perinatal outcomes in absent and reverse umbilical artery doppler in hypertensive groups.

Spectral characteristic	No. of patients	Perinatal Mortality (%)
AEDF	18	12(66.66%)
REDF	2	2(100%)

TABLE 15: Different studies showing high perinatal mortality in AEDF and REDF.

Author	Mortality in % (AEDF)	Mortality in % (REDF)
Bhatt et al ¹⁶	50%	50%
Lakhar et al ⁴	100%	100%
Smitha et al ¹⁷	27.78%	100%
Srilakhshmi et al ¹⁸	100%	100%
Present study	66.66%	100%

AEDF and REDF flow in the umbilical artery significantly influenced the risk of cerebral haemorrhage, anemia or hypoglycaemia. A caesarean section is recommended in all pregnancies complicated by AEDF and REDF if the gestational age and predicted neonatal weight can be handled by the NICU.¹⁹

TABLE 16: Performance characteristics of MCA PI in present study with reference range.

	Fong K W et al	Gramellini et al	Present study
Sensitivity	72.4%	24%	68.1%
Specificity	58.1%	100%	71.7%
PPV	37.7%	100%	68.1%
NPV	85.7%	77.3%	71.7%

MCA was found to have sensitivity 68.1% more than umbilical artery PI, CPR and less than uterine artery PI. The values were compared with reference range as showed above.

It showed sensitivity of 68.1% similar to Fong K W et al. Specificity of 71.7% almost similar to Fong K W et al. study agrees with Fong K W et al that MCA PI is less specific than CPR. There are several possible explanation for low specificity of the MCA PI for adverse perinatal outcome. Among several published normogram for MCA PI the cut off values for an abnormal MCA PI are similar up to about 30 weeks gestation age but differ after 32 weeks. The normograms we choose to use for analysis are from the largest published cross-sectional study by Harrington K et al.

MCA PI PPV 68.1% in predicting adverse perinatal outcome is also less than that of CPR, which can be attributed to the more false positive values.

The NPV of 71.7 % is comparable to Fong K W et al, more compared with umbilical artery PI, uterine artery PI and CPR. Thus indicating the usefulness of MCA PI in ruling out possibility of adverse perinatal outcome.

TABLE 17: Performance characteristics of CPR in present study with reference range.

	Fong K W et al	Gramellini et al	Present study
Sensitivity	51.3%	68%	59.6%
Specificity	80.6%	98.4%	81.1%
PPV	48.1%	94.4%	73.7%
NPV	82.5%	88.8%	69.4%

CPR has highest specificity of 81.1% was found to be better than any other variable. The specificity was comparable with above mentioned studies. The CPR is effective to rule in the possibility of adverse perinatal outcome when it is abnormal.

The PPV of CPR is 73.7% was more than that of other variables. It indicates the likelihood of adverse perinatal outcome in growth restricted fetus with abnormal CPR. The PPV of CPR was not much comparable to above mentioned studies.

The sensitivity of CPR 59.6% comparable with above mentioned studies. The NPV of CPR 69.4% was less than Uterine artery PI and MCA PI.

Our findings confirms the results of Fong K W et al that abnormal CPR is associated with adverse perinatal outcome like Low APGAR score, NICU Admission and perinatal mortality.

Uterine artery Doppler

Sensitivity of uterine artery PI 72.3%, more compared to any other variable. Examination of both Uterine arteriosis an indispensable element of doppler examination to assess placental performance and risk to the fetus.²⁰

Rai L et al suggested Uterine artery is a better predictor of Perinatal adverse outcome in third trimester, hence should be included in determination of adverse perinatal outcomes.

It showed specificity 58.5%. the PPV 60.7% similar to Umbilical artery PI and NPV of 70.5% more than Umbilical artery PI.

Diastolic notch of uterine artery specificity 73.6% ,more compared to specificity of umbilical artery PI and MCA PI. This was different compared to Swapnali C. Kshirsagar et al observed that presence of notch has got maximum sensitivity and negative predictive value for adverse perinatal outcome.

Including uterine artery Doppler in the surveillance of growth-restricted fetuses might detect a group of pregnancies at high risk, even though the umbilical artery Doppler was normal.

In our study when we compare the overall diagnostic accuracy in prediction of adverse outcome in high-risk pregnancy, CPR has the diagnostic accuracy of 71% which is more than Umbilical artery PI(65%), uterine artery PI(65%) and MCA PI(70%) similar to Gramellini et al.

TABLE 18: Diagnostic accuracy in Gramellini et al and present study

	Gramellini et al	Present study
CPR	90%	71%
Umbilical artery PI	83.3%	65%
MCA PI	78.8%	70%

MCA PI and CPR are strong predictors of adverse perinatal outcome.

Our study assesses four parameters of Doppler, multiple outcome of high risk pregnancy and was a Prospective study. The study was conducted both in private and government set up hence had population distribution from low as well as high economic status.

On assessing for association between adverse perinatal outcome we found that all the indices were significantly associated as demonstrated by previous studies. Ut A PI had higher sensitivity (72.3%) compared to rest of the doppler indices but lower specificity (58.5%). CPR had higher specificity (81.1%). Diagnostic accuracy of CPR was higher (87%) than other Doppler indices. Mishra D et.al and Singh M et.al claim that CPR is better indices than MCA PI and Um. A PI, as it measures both the indices together. Most of the studies show varied results and suggest all indices have to be considered together for prediction of perinatal outcome. Most of these studies didn't evaluate the importance of Uterine artery PI index. Earlier studies have shown that fetal redistribution may exist in the presence of normal umbilical artery Doppler in late pregnancy. Hence fetal middle cerebral artery was included in evaluation of late gestational perinatal morbidity

CONCLUSION

Our study has succeeded in demonstrating the efficacy of Doppler in predicting the fetal outcome in high-risk pregnancy.

Doppler ultrasonography is the best noninvasive investigation to assess changes in fetal hemodynamics in pre-eclampsia and IUGR.

- Doppler of multiple vessels will give more information, hence useful than single vessel changes.
- Doppler helps to differentiate the fetus with pathological growth restriction from that of other small for gestational age fetus.
- Raised uterine artery PI as in pre-eclampsia indicates reduced placental perfusion with maternal blood and consequent decrease in fetal arterial oxygen content.
- Raised umbilical artery PI- occurs when at least 60% of the placental vascular bed is obliterated and is the first pathological finding in growth restricted fetus.
- Absent and reversed end diastolic flow in umbilical artery is an ominous finding, associated with increased perinatal morbidity and mortality.
- Umbilical artery Doppler is an integral part of monitoring high-risk pregnancies.
- Adverse pregnancy outcome in third trimester is better predicted with uterine artery Doppler.
- Normal uterine artery Doppler in third trimester predicts good perinatal outcome and hence reassuring.
- Hence Doppler ultrasonography is essential for management of high-risk pregnancies.

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