Original Research Article

# Doppler study in second and third trimester in high risk pregnancy and perinatal outcome

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#### **Abstract**

**Background:** In order to screen for defective placentation and related consequences such pre-eclampsia, intrauterine growth restriction, and infant death, doppler examination of the placental circulation is crucial.

**Methods:** From August 2021 to July 2022, the study was carried out in the Department of Obstetrics & Gynecology, Owaisi Hospital and Research Centre, Hyderabad, Telangana, India. Prospective observational study conducted in a hospital involving 100 patients.

**Results:** Any gestational age after 32 weeks where REDV is detected should warrant consideration for an urgent delivery. Guidelines from the Society for Maternal-Fetal Medicine, which suggest intensive fetal monitoring of these fetuses and continuing expectant treatment until 32 weeks as long as fetal monitoring is still reassuring, support this.

**Conclusion:** Doppler velocimetry can be a valuable addition to standard antepartum surveillance procedures in patients with IUGR fetuses. If other antepartum surveillance tests are reassuring, an abnormal Doppler should not necessitate an obstetric intervention. When an aberrant Doppler finding is discovered, the obstetrician is made aware of the potential problems, and the delivery should be scheduled at a tertiary care center with good neonatal facilities.

**Keywords:** Doppler study, third trimester, high risk pregnancy, perinatal outcome

## Introduction

In order to screen for poor placentation and associated consequences such as pre-eclampsia, intrauterine growth restriction, and neonatal death, doppler monitoring of the placental circulation is crucial <sup>[1]</sup>. In order to better understand the pathophysiology of a variety of abnormal pregnancies and their therapeutic management, evaluation of the fetal circulation is crucial. Over the past ten years, doppler sonography has been incorporated into standard antenatal monitoring in obstetrics. Since the hemodynamic alterations in the uteroplacental and fetal arteries can be proven far before the clinical manifestation of obstetric problems, blood flow measurement has a substantial impact on the diagnosis of placental and fetal malfunction <sup>[2, 3]</sup>.

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Antenatal fetal surveillance's key objectives are to detect fetal compromise, confirm fetal well-being, and enhance perinatal outcomes in both normal and high-risk pregnancies so that prompt, effective action can be taken to lower perinatal death and morbidity. High risk pregnancy makes conditions that are prone to placental insufficiency worse <sup>[4]</sup>. By compromising the fetus, they lessen prenatal impairments and save newborn lives by being discovered early by antepartum surveillance. Numerous techniques, including NST, biophysical profile, and daily fetal moment, are used to evaluate the fetal health in high risk pregnancies <sup>[5]</sup>. Color Doppler flow velocimetry, a recent development in ultrasound technology, has revolutionized the identification of aberrant blood flow in the feto-placental bed. The ideal timing to deliver a baby is determined by early diagnosis of these aberrant patterns, which helps to reduce perinatal death. The early detection of IUGR, which can lower fetal morbidity and death, is another benefit of color Doppler flow velocimetry <sup>[6,7]</sup>. The blood flow in the fetus's umbilical artery and MCA is studied using this approach in

The blood flow in the fetus's umbilical artery and MCA is studied using this approach in high-risk pregnancies, particularly those with preeclampsia, twin gestation, gestational DM, and IUGR. This is a quick, safe, and repeatable non-invasive method for studying uteroplacental fetal inoculations. Color Repeated Doppler flow velocimetry has the ability to accurately forecast fetal events p [8]. Doppler ultrasound is one of the most crucial clinical tools for fetomaternal surveillance in high-risk pregnancies since it helps to better comprehend the hemodynamic changes. Perinatal mortality and morbidity have significantly decreased as a result [9].

In comparison to those with normal flow characteristics, fetuses with aberrant flow velocity waveforms have a higher rate of perinatal hypoxia and death. Doppler velocimetry determines the manner of birth, including whether to use conservative management or interventions to lower maternal and newborn morbidity [11, 12]. It also determines the frequency of prenatal testing and the ideal time for delivery. To improve prenatal outcomes and examine fetal welfare in high risk patients, every tertiary hospital should regularly use this service. The current study looked at Doppler indices to predict the perinatal outcome in high risk pregnancies [13]. Analyzing Doppler data in the second and third trimesters of high-risk pregnancies and predicting adverse pregnancy outcomes were among the study's objectives. To consider the potential advantages of Doppler ultrasound [14]. To forecast prenatal outcomes using the cerebroplacental ratio. To evaluate the efficacy of middle cerebral artery, umbilical artery, and uterine artery Doppler in the treatment of high risk pregnancy groups. Optimisation of delivery timing for better neonatal result and assessment of the perinatal outcome.

## Methods

August 2021 to July 2022, the study was carried out in the Department of Obstetrics & Gynecology, Owaisi Hospital and Research Centre, Hyderabad, Telangana, India. Prospective observational study conducted in a hospital involving 100 patients.

## **Inclusion criteria**

- All high risk pregnant females aged 19-35 years in second and third trimester between 2020 and 2021 at Obstetrics and Gynecology department of Deccan College of Medical Sciences.
- Women who are sure of their LMP (regular menstrual cycle prior to conception)
- Pregnant women with history and physical findings suggestive of Hypertensive disorders of pregnancy, diabetes mellitus diagnosed before conception or before 20 weeks of pregnancy, previous bad obstetric history with recurrent fetal losses and perinatal deaths, Small for gestational age and twin gestation.

## **Exclusion criteria**

- Patients who didn't give consent.
- Patients with congenital anomaly of fetus, renal diseases, cardiac diseases Patients who are not getting booked for delivery at our institution.
- Patients with unreliable LMP details not confirmed by first trimester scan.

Doppler ultrasound was used on all patients to evaluate their middle cerebral arteries, umbilical arteries, and uterine arteries. A VOLUSON E9 duplex Doppler scanner from GE Medical Systems will be used for the examinations, which will employ a 5 MHz transducer. This was established by a combination of direct ultrasound imaging observation and analysis of the uterine, umbilical, and middle cerebral arteries' Doppler waveform patterns. The same expert performed the Doppler analyses on all study participants, and consent was obtained in accordance with the PNDT Act's required format. In the absence of fetal respiratory movements, waveforms of acceptable quality were gathered and examined; on average, 3 independent measurements were carried out. The women underwent the evaluation with their heads and chests slightly lifted and in a semi-recumbent position.

#### Perinatal outcome assessment

The manner of delivery, surgical delivery for fetal distress, gestational age at delivery, newborn weight, Apgar scores at 5 and 10 minutes, NICU admissions, and any reported perinatal mortality were among the parameters evaluated.

## Statistical analysis and methods

The collection of data will be done utilizing a standardized proforma. Data entered in a Microsoft Excel spreadsheet and analyzed with IBM USA's SPSS 24.0 version Percentages will be used to express qualitative data. Mean and Standard deviation will be used to express quantitative data. Chi square test will be used to determine the relationship between two qualitative variables. Each variable's descriptive statistics will be shown in terms of the mean, standard deviation, and standard error of the mean. At a significance level of 5%, a p value of = or 0.05 will be regarded as statistically significant. Sensitivity, specificity, and predictive value will all be used to examine the study's findings.

# **Results and Observation**

113 women entered this prospective study over a period of August 2021 to July 2022.

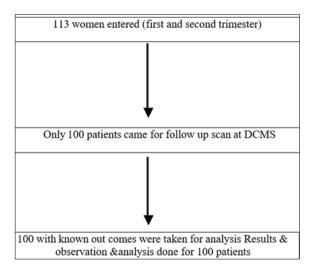


Fig 1: Flow chart for number of patients included Table 1: Age distribution in the study (yrs.)

Age (yrs.)	Frequency	Percentage
≤ 20	10	10.0
21-25	54	54.0
26-30	32	32.0
>31	4	4.0
Total	100	100.0

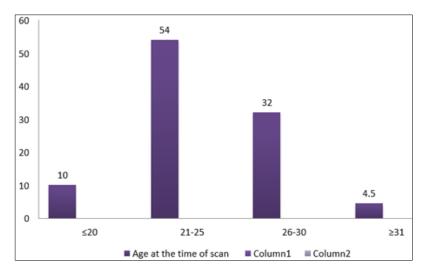


Fig 2: Bar diagram for age distribution

54% patients are in the age group 21-25 years only 4% are in the age group > 31 years.

 Table 2: Parity distribution

Gravida	Frequency	Percentage
Primi (singleton)	47	47.0
Gravida 2	32	32.0
Gravida 3	14	14.0
Gravida 4	4	4.0
Twins	3	3.0
Total	100	100.0

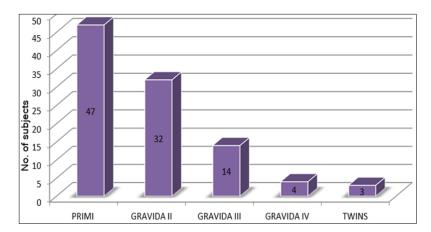


Fig 3: Bar diagram for parity distribution

Among 100 study population, 47 were primigravida, the incidence being 47%, G2P1L1 32%, third Gravida 14%; most of the study population were primigravida

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Table 3: Placental position

Placenta Position	Frequency	Percentage
Left	21	21.0
Right	21	21.0
Centre	58	58.0
Total	100	100.0

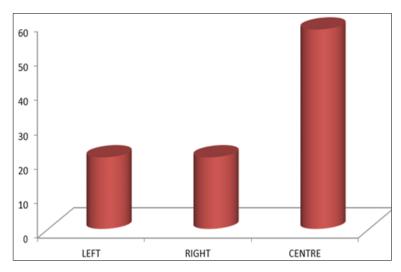
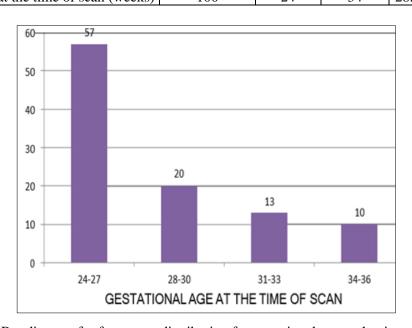


Fig 4: Bar diagram for placental location

58% of placentas are centrally located.

Table 4: Descriptive Statistics for age and gestational age at the time of scan

Study variable	No. of subjects	Minimum	Maximum	Mean	SD	Std. Error
Age (yrs)	100	18	35	24.75	3.6	0.36
Gestational age at the time of scan (weeks)	100	24	34	28.5	2.9	0.29



 $\textbf{Fig 5:} \ \textbf{Bar diagram for frequency distribution for gestational age at the time of scan}$ 

Table 5: Pregnancy outcome in the study

Pregnancy Events	No. of subjects	Percent
Normal	64	64.0
Pre-eclampsia (Proteinuric PIH)	12	12.0

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PIH (Non-proteinuric PIH)	18	18.0
IUGR	8	8.0
Intrauterine Death	5	5.0
Stillborn	3	3.0
Abruption	2	2.0
Severe Oligohydramnios	7	7.0
Any of the above requiring Del<34 weeks	10	10.0

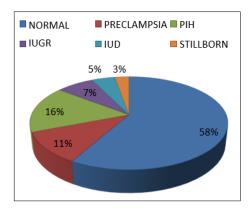


Fig 6: Pregnancy outcome

36% patients' had abnormal outcome. 64% of patients had normal outcome.

**Table 6:** Type of delivery

Type of delivery	No. of subjects	Percent
Vaginal Delivery	60	60.0
Emergency LSCS	24	24.0
Elective LSCS	16	16.0
Total	100	100.0

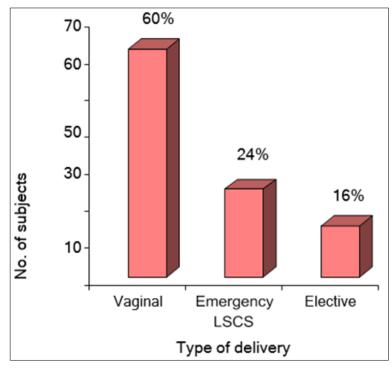


Fig 7: Bar diagram for type of delivery

60% of patient's had vaginal delivery, 24% of Patients had emergency LSCS & 16% of Patients had Elective LSCS.

**Table 7:** Descriptive statistics for Gestational age at the time of delivery, Birth Weight, Apgar and Stay in NICU

Study variable	No. of Subjects	Minimum	Maximum	Mean	Std. Deviation	Std. Error
Gestational age at the time of delivery (weeks)	100	28	41	34.5	1.962	0.196
Birth Weight (Kgs)	100	1	4.2	2.811	0.5627	0.056
Apgar at 1 minute	100	0	8	7.56	1.610	0.16
Apgar at 5 minute	100	0	10	8.61	1.8	0.18
Stay in NICU (days)	22	1	45	6.36	10.7	2.281

Due to preterm delivery at 24 weeks, the minimum and maximum NICU stays were 1 day and 45 days, respectively. A newborn could weigh as little as 1 kilogram and as much as 4200 gms. Mean gestational age was 28 weeks at the time of the scan.

**Table 8:** Types of Uterine artery abnormality and associated perinatal outcome

Donnloy flow nottown	Perinat	tal outcome
Doppler flow pattern	Normal	Abnormal
Normal (64)	55	9
Abnormal (36)	12	24
U/L high resistance	10	7
B/L High resistance	6	5
U/L notch	5	10
B/L notch	0	3

Standard uterine artery Doppler flow was related to a favourable perinatal outcome in 85.9% of cases and a bad outcome in 14.06% of cases. Neonatal morbidity was 10%, with a death rate of 4.6%. When the uterine artery was aberrant, perinatal mortality was 30.5% in 33.3% of instances, while it was abnormal in 66.67% of cases. In 41.1% of instances, adverse outcomes were linked to high impedance flow in a single uterine artery, with mortality being 5%. In 41.6% of cases, a high resistance flow in both uterine arteries led to an adverse outcome, and 16% of patients died. One uterine artery being notched resulted in a 66.6% unsatisfactory prenatal outcome and a 26.6% perinatal mortality. A bilateral notch had a 100% death rate.

Given that death is 100% with bilateral notch, this demonstrates that bilateral uterine artery abnormality is more relevant than unilateral abnormality in predicting unsatisfactory fetal outcome.

 Table 9: Umbilical artery Doppler value distribution and perinatal outcome

Ilmbilical outous Donnlon	Perinatal Outcome			
Umbilical artery Doppler	Normal	Abnormal		
Normal (76)	65	11		
Abnormal (24)	3	21		

In 76% of cases, the pattern of blood flow in the umbilical arteries was normal; 14% of these patients had adverse perinatal outcomes. In 24% of cases, there was aberrant umbilical artery flow, and in 87% of those cases, the perinatal outcome was abnormal.

**Table 10:** Types of Umbilical artery abnormality and associated perinatal outcome

Ilmbilical autous		Peri	natal outcome	
Umbilical artery	Nammal	Abnormal		al
Doppler	Normal	Total	Mortality	Morbidity

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Normal (76)	65	11	3	4
Abnormal (24)	3	21	10	4
High resistance (17)	5	12	6	6
AEDF (6)	0	6	1	5
RDF (8)	0	8	2	6

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When umbilical artery flow was normal, 85.5% of pregnancies ended well, whereas just 13.1% of them did not, with death and morbidity being roughly equal. Mortality was 58.3%, and aberrant umbilical artery flow was associated with 87.5% bad perinatal outcomes. High resistance flow in the umbilical artery revealed that the rates of morbidity and mortality were identical, with 70.5% having poor perinatal outcomes. Umbilical arteries in AEDF and RDF are linked to death rates of 20% and 25%, respectively.

Table 11: Middle cerebral artery Doppler value distribution and perinatal outcome

MCA Donnlor	Perinatal Outcome			
MCA Doppler	Normal	Abnormal		
Normal (86)	78	8		
Abnormal (14)	0	14		

In 86% of cases, the MCA Doppler flow pattern was normal, and 90.6% of those cases had successful pregnancies. 14% of cases had abnormal MCA Doppler flow patterns, and 100% of those cases had adverse perinatal outcomes.

**Table 12:** Correlation of uterine artery Doppler with pregnancy outcome (%)

Uterine artery doppler	Preeclampsia	PIH (Non protein uric)	IUGR	IUD	Still birth	NICU admission
S/D Ratio (n=15)	32%	10%	31%	22%	11%	22%
RI (n=7)	29%	14%	29%	29%	14%	14%
Early diastolic notch (n=8)	40%	13%	30%	29%	13%	25%

This indicates notch in uterine artery is associated with poor pregnancy outcome

**Table 13:** Correlation of umbilical artery Doppler with pregnancy outcomes

Umbilical artery Doppler	Preeclampsia	PIH (Non protein uric)	IUGR	IUD	Still birth	NICU admission
SD Ratio (n=5)	60%	20%	40%	20%	20%	40%
RI (n=8)	13%	25%	25%	-	-	12%
Absent diastolic flow (n=6)	100%	80%	100%	20%	20%	100%

This indicates umbilical artery Doppler is associated with abnormal pregnancy outcome. Six patients had absent diastolic flow which were associated with pre- eclampsia and IUGR. All babies required NICU stay indicating that absent diastolic flow is associated with poor pregnancy outcome.

**Table 14:** Statistical significance of Doppler studies- Uterine Artery studies

Litanina Antony	Perinatal Outcome			
Uterine Artery	Abnormal	Normal		
Abnormal (36)	24	12		
Normal (64)	9	55		

According to the study mentioned above, uterine artery Doppler analysis plays a statistically significant impact in forecasting worse neonatal outcomes.

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**Table 15:** Umbilical Artery studies

Ilmbiliaal Autour	Perinatal Outcome			
Umbilical Artery	Abnormal	Normal		
Abnormal (24)	21 (a)	3 (b)		
Normal (76)	11(c)	65 (d)		

The chi square value is 44.70, p 'value is < 0.00001 Significant at p<.05. The above study shows umbilical artery study has a statistically significant role in predicting abnormal perinatal outcome

**Table 16:** Evaluation of cerebroplacental ratio (CPR)

APGAR	Cases with abnormal CPR @ 1 min	Cases with abnormal CPR @ 5 min	Cases with normal CPR @ 1 min	Cases with normal CPR @ 5 min
2/10	5	3	-	-
4/10	10	9	-	-
6/10	8	11	10	8
8/10	2	2	63	67

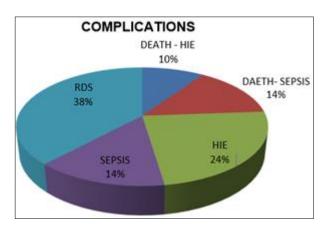


Fig 8: Pie diagram for perinatal complications in those with abnormal CPR

#### Discussion

The prognostic values of numerous Doppler indices have been assessed in this prospective study in a setting of tertiary level care center, whose inflow includes Indian women from rural and urban sectors. The current study's objectives were to examine the perinatal outcome between normal and aberrant Doppler waveforms, as well as to analyze blood flow in the uterine umbilical and middle cerebral arteries using Doppler ultrasound. Doppler is a special instrument for non-invasively assessing uteroplacental and fetal placental circulations, and as such, it serves as the foundation for an organized antenatal surveillance program that includes prompt intervention. We looked at the maternal factors, including age, parity, and gestational age at the latest Doppler scan.

## Gravida

47 of the 100 study participants were primi gravida, representing a 47% incidence, followed by 32% for G2P1L1 and 14% for third gravida. The majority of the patients had low socioeconomic status.

## Risk factors associated

The most frequent risk factor in the high-risk group is preeclampsia. Preeclampsia was

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present in a large number of the prime gravida in the high risk group, either as the only problem or in conjunction with fetal growth restriction and other risk factors. The second most frequent risk factor is fetal growth restriction.

## Maternal age

Only 4% of patients are older than 31 years, with 54% of patients between the ages of 21 and 25. The high risk patients' advanced mother age may also be a factor in the pregnancy's problems. Preeclampsia was prevalent at 5%, which is comparable to the figure given. Similar to the 8% prevalence of SGA below the 10 percentile reported by North et al. [15, 16], 64% of patients had normal outcomes, compared to 36% who had adverse outcomes, 60% of patients gave birth naturally, 24% underwent emergency LSCS, and 16% underwent elective LSCS. A normal vaginal birth occurred in 60 patients, of whom 30 experienced spontaneous labor onset. The remaining 35 patients required inductions due to conditions such PROM, FGR, gestational diabetes mellitus, pregnancy-induced hypertension, postdated pregnancy, etc. Due to abnormal Doppler changes, including the brain sparing effect, reverse and absent EDF, decreased fetal movements, severe oligohydramnios, intrapartum events, including abnormal CTG, meconium-stained alcohol, failed induction, fetal distress, antepartum eclampsia, and imminent eclampsia with unfavorable cervix, twenty-four cases were delivered by emergency LSCS. Due to indications such CPD, Big Baby, placenta previa, malpresentations, prior classical C-sections, and other maternal co-morbidities, 16 more cases were planned for elective LSCS [17].

The average gestational age at which the pregnancy ended was 34 weeks, indicating early termination in IUGR cases and matching the results of a 2012 study by Tumbal PS; *et al.* (61.46% of cases received termination at 34 weeks of gestation). Due to preterm delivery at 30 weeks, the minimum and maximum lengths of stay in the NICU were 1 day and 45 days, respectively. A newborn could weigh as little as 1 kilogram and as much as 4200g [18].

2.81 kg + 0.356 SD is the average birth weight. The PI of the umbilical artery decreases significantly as birth weight rises; birth weight is highest in the group with a normal doppler study and lowest in the group with absent or reversed end diastolic flow. This is consistent with research by Fleischer *et al.*, who found that placental vascular resistance was higher in fetuses with lower birth weights (25<sup>th</sup> percentile) than higher birth weights (>25th percentile) [19, 20]. Uterine artery Doppler was employed in the current investigation to screen high risk pregnancy groups in the second and third trimester. The benefit of employing uterine arteries over small arcuate or radial arteries is that uterine arteries accurately reflect the overall amount of blood flow resistance in the distal uteroplacental vasculature, in contrast to these smaller arteries that do not. Pre-eclampsia was found in 5% of the population under study, which is comparable to the percentage described by Walker *et al.* [21, 22].

In our study, 76% of cases had normal umbilical artery flow patterns; 14% of these individuals had aberrant perinatal outcomes. In 24% of cases, there was aberrant umbilical artery flow, and in 87% of those cases, the perinatal outcome was abnormal. When umbilical artery flow was normal, 85.5% of pregnancies ended well, whereas just 13.1% of them did not, with death and morbidity being roughly equal. Mortality was 58.3%, and aberrant umbilical artery flow was associated with 87.5% bad perinatal outcomes. High resistance flow in the umbilical artery revealed that the rates of morbidity and mortality were identical, with 70.5% having poor perinatal outcomes. RDF and AEDF in the umbilical arteries are linked to a 100% mortality rate. The umbilical artery was found to have a positive predictive value of 87.5%, a specificity of 95.58 percent, a sensitivity of 65.62 percent, and a negative predictive value of 85.5 percent in identifying adverse fetal outcomes [23].



Fig 9: REDF in umbilical artery in a primigravida at 31 weeks period of gestation

In this study, there were eight patients with reverse end diastolic flow (REDF) and six individuals with absent end diastolic flow (AEDF). In the umbilical artery, reverse end diastolic flow was observed in four patients with severe preeclampsia and three individuals with severe IUGR. Two patients with extreme preeclampsia had inductions and gave birth to newborn stillborn babies. At roughly 32–33 weeks, four patients with severe pre-eclampsia and absent end-diastolic flow required emergency cesarean sections. Although newborns were maintained in neonatal intensive care units due to low birth weight, the neonatal outcome in absent end-diastolic flow patients was good [24].



Fig 10: AEDF in umbilical artery in a patient at 36 weeks period of gestation with severe IUGR

AEDF/REDF in umbilical velocimetry was linked to catastrophic prenatal outcomes, and intensive perinatal care was indicated in these patient groups, according to a study by Rochelson B *et al.* and Brar HS *et al.* The current study supports their recommendation. Higher mortality rates were noted in fetuses with absent or reversed end diastolic flow, according to Ley D. *et al.* and Kurkinen M. *et al.* [25, 26].

Doppler results can identify abnormalities in cardiotocographic tracings up to days or more in advance. Evaluation of end diastolic flow (EDF) is important because when it is reduced, it can detect 30% severe hypoxia, when AEDF is present, it can detect 50% severe hypoxia, and when REDF is present, it may detect 70% severe hypoxia, which can result in fetal death within seven days. With intensive fetal monitoring, the pregnancy might be carried on even in the presence of AEDF for one to two weeks [27]. Additionally, the additional days may increase the fetal weight. This may give time for the introduction of steroids to improve fetal lung maturation. This period also allows for the patient to be sent to a tertiary facility where appropriate neonatal care can be given. A very high perinatal mortality rate is linked to

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REDF, a fatal event. When REDF manifests, usually within 24 hours of diagnosis, immediate delivery is advised, and cesarean birth is typically the method used in these pregnancies. In fetuses with pre-existing defective umbilical artery velocimetry, it is plausible to predict that decreased uteroplacental perfusion during uterine contractions is likely to further imperil gaseous exchange. According to our study, perinatal morbidity and mortality were considerably higher in fetuses with aberrant umbilical artery Doppler tests than in fetuses with normal Doppler exams. The findings of our study demonstrate that fetuses with aberrant umbilical artery velocimetry are more likely to be born early, require more admission to the neonatal intensive care unit (NICU), and have lower Apgar scores [27, 28].

Thus an higher requirement for an operation to deliver the baby because of suspected fetal compromise and admission to the NICU were linked to abnormal CPR at term. The CPR can be used to identify pregnancies that are at risk for unfavorable outcomes and has been found to be a reliable predictor of the fetal oxygenation status at birth. Compared to the biophysical profile, CPR found more fetuses that would have a negative outcome. Portable ultrasound devices can be acquired since ultrasound equipment is becoming more affordable. These devices enable the doctor to identify the UA and MCA using color Doppler. However, this study had certain limitations, including biases of selective evaluation of a group referred for scan assessment at risk, thus there were a little more at-risk fetuses than anticipated. Because the ultrasound and Doppler evaluation results were not blinded, there was a chance for later therapeutic intervention and the likelihood of a "treatment effect" in terms of fetal safety. Changes in personnel and attitudes toward intrapartum management are also likely to have had an impact on the threshold for the identification of fetal compromise [29]. The fact that the study was conducted in a single location could have also impacted the findings. Another drawback is that the study methodology omitted other Doppler measures that would have been useful, like ductus venous or myocardial performance index. The study's strength was the single operator who used established methods and identical machine scans to reduce interobserver variation.

## Conclusion

Fetuses at much higher risk than those with normal studies include those with aberrant umbilical, middle cerebral, and uterine flow velocity. Predicting pre-eclampsia is more accurate with the diastolic notch in the uterine artery as a single metric than it is using the uterine artery's various Doppler indices. Doppler abnormalities in the umbilicus (AEDF or RDF) and MCA (increased diastolic flow) are better indicators of uteroplacental insufficiency and perinatal prognosis. On patients with IUGR fetuses, doppler velocimetry may be a significant addition to routine antepartum surveillance exams. If other antepartum surveillance tests are positive, an abnormal Doppler alone shouldn't necessitate obstetric intervention. The obstetrician is informed of the potential difficulties that may arise as soon as an abnormal Doppler finding is discovered, and the delivery should be scheduled at a tertiary care facility with excellent newborn facilities.

# **Conflict of Interest**

None

## **Funding Support**

Nil

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