

Role of Color Doppler in IUGR

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Abstract: Intra-uterine growth restriction (IUGR) is an important perinatal problem giving rise to increased morbidity and mortality in the growth restricted fetus. The aim of fetal medicine today, is to prevent the mere occurrence of IUGR in high risk pregnancies and to deliver the fetuses already afflicted with growth restriction, before they have suffered from the effects of hypoxia. The use of Doppler provides this information, which is not readily obtained from the other conventional tests of fetal wellbeing. The Doppler patterns follow a longitudinal trend in the arterial and venous circulation of the fetus as well as the placental vasculature guiding management decisions regarding the appropriate time of delivery. Progressive knowledge of the fetal circulation and its adaptation when the fetus is subjected to hypoxia has helped us recognize the early signs of IUGR thereby improving the prognosis of these complicated pregnancies. It has therefore become the gold standard in the management of the growth-restricted fetus.

Keywords: Intra-uterine, morbidity, growth restriction.

INTRODUCTION

Intrauterine growth restriction (IUGR) is a term used to describe the condition of a foetus whose size or growth is subnormal. The most common definition of intrauterine growth restriction is that "a foetus is growth restricted if its weight is less than the tenth percentile for its gestational age"[1].

IUGR is observed in about 24% of new-borns; approximately 30 million infants suffer from IUGR every year. The burden of IUGR is concentrated mainly in Asia which accounts for nearly 75% of all affected infants. In India, the prevalence of IUGR has been found to be 54%[2].

IUGR has many causes; maternal causes include hypertension, collagen vascular disease, renal disease, poor nutrition and drug or alcohol abuse which cause placental insufficiency. Foetal infections such as cytomegalovirus, toxoplasmosis and chromosomal anomalies such as triploidy and trisomies 13 and 18 also result in IUGR. Placental insufficiency in the absence of any maternal cause is called primary placental insufficiency and is common cause of IUGR [4].

Growth retarded foetuses have eight to ten fold increase in perinatal mortality and 50-75% morbidity compared to appropriately sized foetuses. Foetuses who have suffered from IUGR are prone to develop still birth, intrapartum foetal acidosis, perinatal asphyxia, meconium aspiration syndrome, hypoglycemia, hypocalcemia, hypothermia and hypoxic ischemic encephalopathy etc[3].

Accurate antenatal diagnosis of IUGR by ultrasound can reduce the complications and improve the foetal outcome. After the introduction of ultrasound the small for date foetuses could be identified, however it could not be determined which of these foetuses were at increased risk due to utero placental insufficiency and therefore needed special surveillance. Small foetuses were therefore monitored by non-stress test of foetal heart rate and the biophysical profile, but they were time consuming as well as operator dependant [4].

Doppler ultrasonography waveforms not only reflects blood velocity but also provides information on various aspects of blood flow like presence and direction of flow, velocity profile, flow volume and impedance. Essential pre-requisite for the assessment of true velocity depends on the angle between the ultrasound beam and direction of flow (also known as angle of insonation), which needs to be as close to zero degrees as possible. This can however lead to inter and

intra observer variability [4]. Therefore angle independent Doppler indices were developed for flow velocimetry and are in use today as mentioned below:

Pulsatility Index (PI) = (Peak Systolic Velocity – End Diastolic Velocity)/time – average maximum velocity (4)

Resistive Index (RI) = (Peak Systolic Velocity- End Diastolic Velocity)/ Peak Systolic Velocity [4].

Systolic: Diastolic ratio(S: D ratio) = Peak systolic velocity/ End diastolic Velocity [4].

The three most commonly assessed vessels in the Obstetric Doppler are Umbilical Artery (UA), foetal Middle Cerebral Artery (MCA) and maternal uterine arteries [5].

Alterations in the waveforms and Doppler indices of foetal middle cerebral artery (MCA), umbilical artery and bilateral uterine arteries have been extensively described in various studies in the literature.

Middle cerebral artery is a vessel of choice to assess foetal cerebral circulation because it is easy to identify, is highly reproducible and provides information on brain sparing effect. IUGR is associated with increased blood flow to foetal brain. This increase in blood flow during diastole can be demonstrated by a lower value of MCA PI [6].

Umbilical artery is best examined in segment of free floating umbilical cord. UA waveforms change with advancing gestation. End diastolic flow is often absent in the first trimester and the diastolic component increases with advancing gestation because of decrease placental vascular resistance. In pathologic conditions such as IUGR, the umbilical artery waveform change, with a decreased diastolic component, and the angle independent indices become abnormal. These changes reflect an increased placental vascular resistance. As the placenta insufficiency worsens, the diastolic velocity decreases then become absent and later reversed [7].

Uterine Artery Doppler velocimetry is a widely used non-invasive test for foetal wellbeing. It is an established primary investigation modality for monitoring and management of high risk pregnancies. Various Doppler indices are used in obstetric practice to identify those foetuses that are at a high risk of perinatal death and morbidity and therefore may benefit from closer surveillance or elective delivery. Amongst them UA PI, RI and S:D ratios are most commonly used[8].

MATERIALS AND METHOD

A prospective case control study was conducted over a period of two years on 25 patients with IUGR. The patients were evaluated with high resolution sonography and colour Doppler imaging.

INCLUSION CRITERIA

- 25 normal pregnancies (control group)
- 25 cases of pregnancy with IUGR on clinical examination and USG biometry.

EXCLUSION CRITERIA

- Those patients who are not giving consent
- Multiple Pregnancies
- Any pregnancy with foetal structural anomaly.

We used MEDISON ACCUVIX A30 machine with the transducer frequency of 35-5.0 MHZ.

Patients were allowed to rest for 5 min in a supine position prior to commencing the ultrasound investigation. Foetal biometry and color Doppler imaging was performed. Spectral waveform and results were tabulated. The findings were correlated with the clinical parameters and pregnancy outcome along with foetal birth weight and neonatal complications were statistically analysed. The waveforms were obtained during foetal inactivity.

Technique for measuring uterine artery

Trans abdominally, the probe is placed longitudinally in the lower lateral quadrant of the abdomen, angled medially. Color flow mapping is useful to identify the uterine artery as it is seen crossing the external iliac artery. The sample volume is placed 1cm downstream from the crossover point. In a small proportion of cases if the uterine artery branches before the intersection of the external iliac artery, the sample volume should be placed on the artery just before the uterine artery bifurcation. The sample process is repeated for the contra lateral uterine artery [9].

Transvaginal technique

Women should be asked to empty their bladder and should be placed in the dorsal lithotomy position. The probe should be placed into the lateral fornix and the uterine artery identified, using color Doppler, at the level of the internal cervical os. The same should then be repeated for the contralateral uterine artery [10].

Technique for measuring umbilical artery

There is a difference in Doppler indices measured at the fetal end, the free loop and the placental end of the umbilical cord. The impedance is highest at the fetal end, and absent/ reversed end-diastolic flow is likely to be seen first at this site. For the sake of simplicity and consistency, measurements should be made in free cord loop [11].

Technique for measuring middle cerebral artery

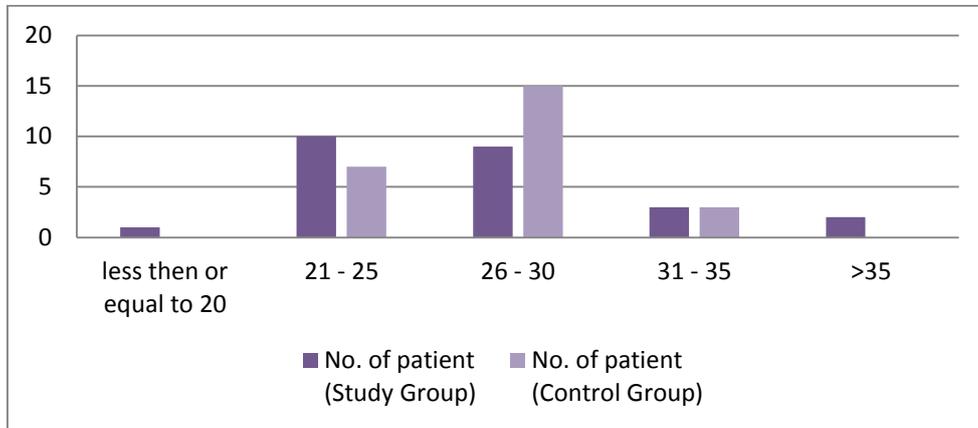
An axial section of the brain, including the thalami and the sphenoid bone wings, should be examined and magnified. Color flow mappings should be used to identify the circle of Willis and the proximal

MCA. The pulsed-wave Doppler gate should then be placed at the proximal third of the MCA, close to its origin in the internal carotid artery. The angle between the ultrasound beam and the direction of the blood flow should be kept as close as possible to 0 degree [11].

RESULTS

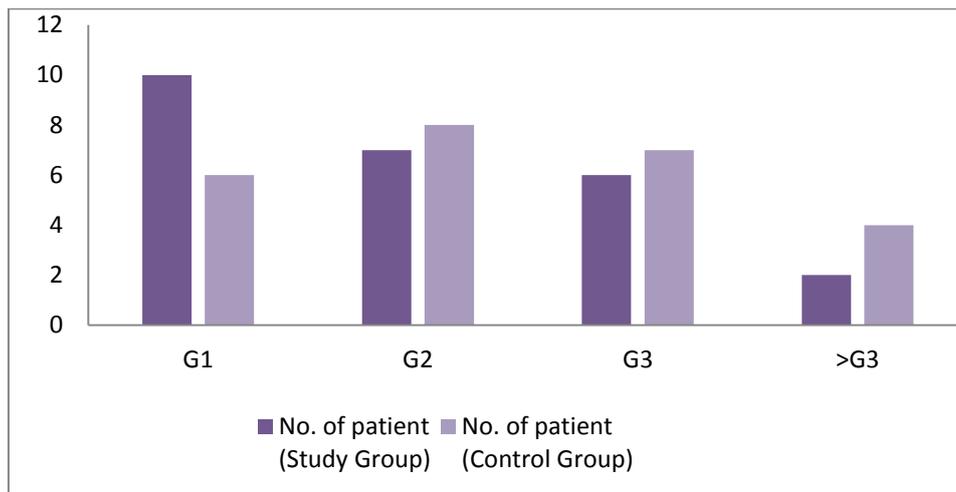
Age distribution

In our study group out of 25 cases, maximum number of cases was in age group of 31-35 years (40%). Second largest group was in 26-30 years (40%) of age.



Distribution of gravid status

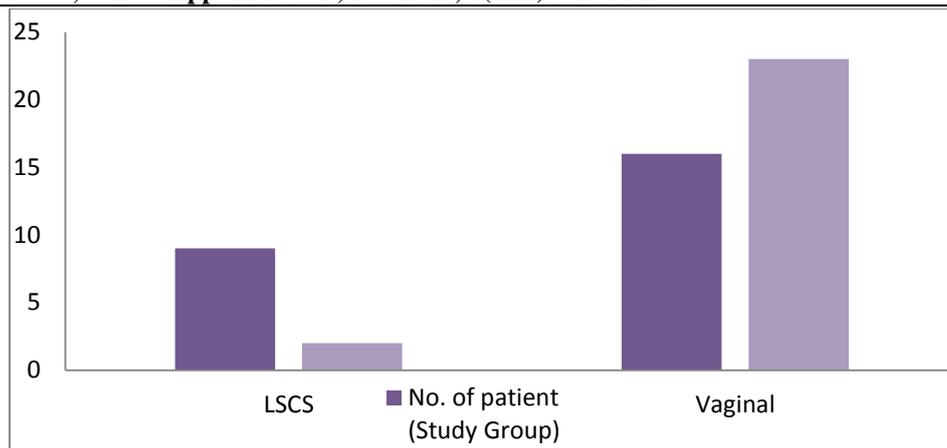
Majority cases in study population were primigravida, followed by 2nd gravida forming the second largest group.



Mode of delivery

In study group out of 25 patients 9(36%) were delivered by caesarian section and 16(64%) were

delivered vaginally whereas in control group 23(92%) patients delivered vaginally and 2(8%) patients by caesarian section.



Distribution of birth weight

In our study group out of 25 patients 23 patients had fetal birth weight less than 2.5kg and 2 patients had fetal birth weight more than 2.5kg whereas

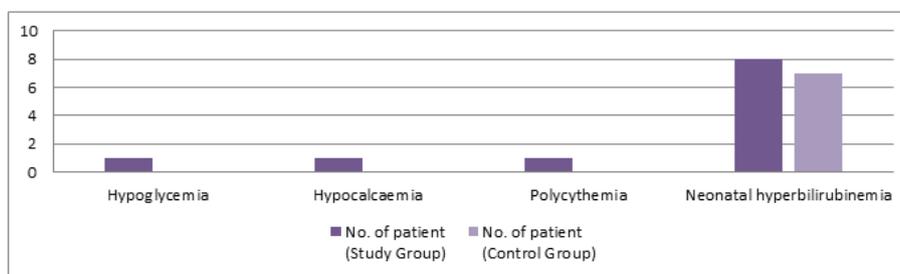
in control group maximum patients had fetal birth weight more than 2.5kg and only 2 patients had birth weight less than 2.5kg.

| SNO | BIRTH WEIGHT | |
|-----|--------------------------------------|--------------|
| 1 | STUDYGROUP MEAN STN.DEVIATION | 1.99 0.31 |
| 2 | CONTROL GROUP MEAN STN. DEVIATION | 2.82 0.42 |
| | P VALUE | <0.0001 |

There is statistically significant difference between the birth weight of control group and study group.

Out of 25 sonographically diagnosed IUGR babies eight had features of neonatal hyperbilirubinemia and out of rest 22 ,3 had hypoglycemia, hypocalcemia and polycythemia respectively.

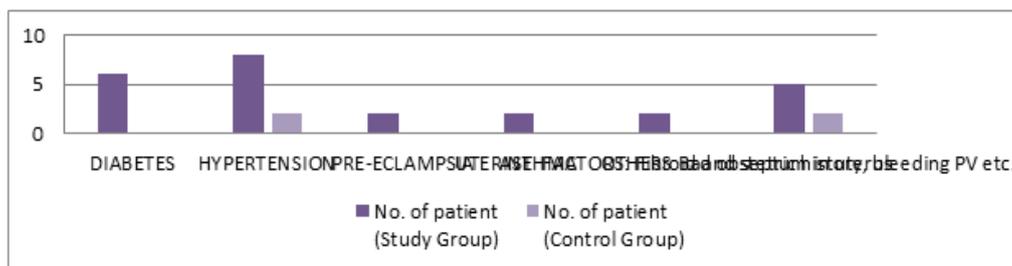
Neonatal complications



MATERNAL RISK FACTORS

In our study the risk factors of the mothers who had undergone Doppler studies were diabetes,

hypertension, Pre-eclampsia, and some of the uterine factors such as fibroid and septum in uterus. Maximum mothers in our study were diabetic



Comparison of mean value of HC/AC between study and control group

| SNO | FETAL BIOMETRY | HC/AC |
|---|------------------------------------|-----------------|
| 1. | STUDY GRP MEAN STN. DEVIATION | 1.2007 0.07 |
| 2. | CONTROL GRP MEAN STN. DEVIATION | 1.0745 0.077 |
| TEST OF SIGNIFICANCE (P VALUE) P value <.05 taken as significant | | <0.0001 |

There is statistically significant difference between **AFI** the HC/AC ratio of study group and control group

| | AFI |
|------------------|-----------|
| STUDYGROUPMEAN | 8.76 |
| STN. DEVIATION | 2.04 |
| CONTROLGROUPMEAN | 13.48 |
| STN. DEVIATION | 2.4 |
| P VALUE | P< 0.0001 |

There is statistically significant difference between AFI values of study group and control group.

Doppler parameters

Comparison of mean value of Umbilical Artery Doppler indices between study and control group.

| SNO | TYPE OF WAVEFORM | UMBILICAL ARTERY | | |
|--------------------------------|------------------------|------------------|-------------|-------------|
| | | PI | RI | SDR |
| 1 | STUDY GRP MEAN SD | 1.2 0.6 | 1.6 0.18 | 3.4 0.6 |
| 2 | CONTROL GRP MEAN SD | 0.9 0.4 | 0.6 0.14 | 2.9 0.57 |
| TEST OF SIGNIFICANCE (P VALUE) | | 0.0429 | <0.0001 | 0.0040 |

There is statistically significant difference between the RI and PI values as well as S/D ratio of Umbilical Artery in the study group vs control group.

| UMBILICAL ARTERY | SENSITIVITY | SPECIFICITY | PPV | NPV |
|------------------|-------------|-------------|--------|--------|
| RI | 56% | 80% | 73.68% | 64.52% |
| PI | 44% | 52% | 47.8% | 48.15% |

Comparison of mean value of MCA between study group and control group

| | SNO | TYPE OF WAVEFORM | |
|--------------------------------|----------------------|------------------|--------------|
| | | PI | RI |
| 1 | STUDY GRP MEAN SD | 1.7 0.14 | 0.77 0.10 |
| 2 | CONTROL GRP MEAN SD | 1.86 0.17 | 0.8 0.15 |
| TEST OF SIGNIFICANCE (P VALUE) | | 0.0007 | 0.4095 |

There are statistically significant difference PI values of Middle Cerebral Artery in study group as well as control group.

| MCA | SENSITIVITY | SPECIFICITY | PPV | NPV |
|-----|-------------|-------------|-------|--------|
| RI | 36% | 48% | 40.9% | 42.86% |
| PI | 44% | 48% | 45.8% | 46.15% |

Comparison of mean value of Uterine Artery (left and right) between study group and control group

| SNO | TYPE OF WAVEFORM | UTERINE ARTERY | | | |
|--------------------------------|------------------|----------------|-------|--------|---------|
| | | PI (L) | RI(L) | PI (R) | RI(R) |
| 1 | STUDY GRP MEAN | 1.7 | 1.0 | 1.3 | 0.9 |
| | SD | 0.6 | 1.30 | 1 | 0.17 |
| 2 | CONTROL GRP MEAN | 1.02 | 0.43 | 0.7 | 0.49 |
| | SD | 0.44 | 0.17 | 0.3 | 0.17 |
| TEST OF SIGNIFICANCE (P VALUE) | | <0.0001 | 0.034 | 0.0060 | <0.0001 |

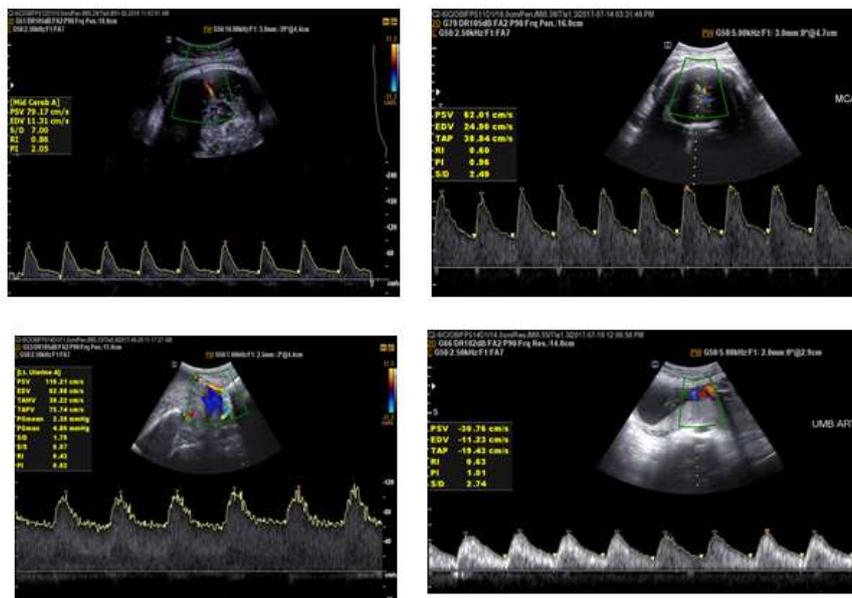
There is significant correlation between PI and RI values of bilateral Uterine Artery between study group and control group

CPR

| SNO | | CPR |
|---------|--------------------|-------|
| 1 | STUDY GROUP MEAN | 1.08 |
| | STN.DEVIATION | 0.32 |
| 2 | CONTROL GROUP MEAN | 1.27 |
| | STN.DEVIATION | 0.36 |
| P VALUE | | 0.054 |

There is statistically significant difference between CPR values of control group as well as study group

Middle cerebral artery



Uterine artery

Umbilical artery

DISCUSSION

Doppler velocimetry of uteroplacental, umbilical and fetal vessels have become an established method for fetal monitoring in day to day obstetric practice. Circulatory changes, reflected in fetal Doppler adverse perinatal outcome. Several investigations have highlighted the utility of Doppler Ultrasonography

(DU) of umbilical and fetal vessels for monitoring fetal well-being, IUGR, fetal anaemia and perinatal outcomes [9]. One of the prime goals of obstetric care is to detect fetal distress at the earliest and intervene in appropriate cases to prevent any adverse perinatal outcome. In addition to traditional Non Stress Test (NST) and Contraction Stress test (CST). Doppler

indices of uteroplacental and fetoplacental circulation are well known as a non-invasive, reliable and reproducible technique for predicting adverse perinatal outcomes in high risk pregnancies. This has led to its routine obstetrics application.

In our study, we undertook those patients who were suspected to have IUGR by clinical examination as well as by ultrasound. Our was case- control study in 25 patients. Comparison of Doppler indices in group of 25 normal pregnancies and 25 IUGR clinically suspected pregnancies and correlation of Doppler findings with the birth weight of the baby.

DEMOGRAPHIC DATA

Age group

Mothers in age group of 21-25 years comprised the largest number of total (40%) and only 3 belong to age group of 30-35 years. This observation leads us to believe that most of the high risk mothers were of reproductive age group which is an agreement to the study done by Kuber R *et al.* [11] who evaluated the role of Doppler ultrasound in the evaluation of biometrically suspected IUGR pregnancies and stated that the maximum number of pregnant women were in the age group of 21-30 years (>50%).

Basumatary J *et al.* [12] did a prospective study in 100 opd patients who were suspected to have IUGR and found that 43% of the women were of age group 26-30years followed by 34% of women in age group 21-25years.

Filho FL *et al.* [13] did a cross –sectional study using 5,063 samples to verify the existence of maternal age and perinatal outcome and they found that 75% of the patients were in age group 20-35 years.

Birth weight

In present study 88% cases in control group had BW>2.5kg and the mean birth weight is 2800 gm. In study group the mean birth weight is 1900 gm and 93 % shows birth weight <2.5kg , this is an agreement with the study done by Ranjan K Sahoo *et al.* [12] In which 90% cases in control group had BW> 2.5 kg and the mean birth weight is 2749 gm., which is normal according to Indian standards. In study group the mean birth weight is 1806 gm and 96% shows birth weight < 2.5kg.

Rekha BR *et al.*[13] did prospective study in 72 women with singleton pregnancies with gestational age above 28 weeks who were diagnosed with IUGR and detected that 66 out of 72 neonates had birth weight ranging from 1.5-2.5 kg i.e approximately 91% had BW

<2.5kg and rest 9% had BW>2.5kg which is again in agreement with our study.

Sonographic parameter

In our study HC/AC ratio have been found to have a statistically different mean value or frequency of occurrence in growth retarded (mean 1.2007) as compared with normal fetuses (mean 1.0745) in present study.

Crane JP, Kopta MM. Prediction of intrauterine growth retarding via ultrasonically measured head/abdominal circumference ratios. *Obstet Gynaecol* [14] has similar statistical significant different mean in IUGR and normal pregnancy.

Afi

In our study there is statistically significant correlation between the AFI of study group(mean=8.76) as well as control group(mean=13.48) with p value<0.0001.

Kuber R *et al.* [11] stated that all growth restricted pregnancies showed oligohydromnios as another common association. 76% had a lower amniotic fluid index against 24% had a normal amniotic fluid index?

In a study by Arora *et al.* they highlighted the increased risk of oligohydroamnios in growth restricted fetuses with abnormal Doppler indices, as an associated finding in their study group 6.

Scifres *et al.* found that oligohydramnios (amniotic fluid index < 5) and abnormal umbilical artery Dopplers (absent or reverse end-diastolic flow) had modest predictive value for perinatal mortality [15].

Mode of delivery

In study group out of 25 patients 9(36%) were delivered by caesarian section and 16(64%) were delivered vaginally whereas in control group 23 patients delivered vaginally and 2 patients by caesarian section.

Rekha BR *et al.* [13] did prospective study in 72 women with singleton pregnancies with gestational age above 28 weeks who were diagnosed with IUGR and found that out of 72 patients, 62(86%) delivered by LSCS and 10 vaginally(14%).

Monika G *et al.* did case control study in 140 subjects who were diagnosed as IUGR clinically and found that caesarian delivery was significantly more frequent in IUGR group (66.9%) as compared with control (46.5%).

| SNO | STUDY | VAGINAL DELIVERY | CAESARIN DELIVERY |
|-----|----------------|------------------|-------------------|
| 1. | PRESENT STUDY | 64% | 36% |
| .2 | REKHA BR ET OL | 14% | 86% |
| 3 | MONIKA G ET OL | 46.5% | 66.9% |

Maternal risk factors

In present study the risk factors of the mothers who had undergone Doppler studies were diabetes (n=7), hypertension (n=6), Pre-eclampsia (n=3), and some of the uterine factors such as fibroid and septum in uterus (n=5).

Study done by Kuber R *et al.* [11] on 50 patients who were biometrically suspected to have growth restricted babies, majority (n=21) presented with maternal hypertensive disorder, followed by anaemia (n= 7), Diabetes mellitus (n= 3) and bad obstetric history (n=4). Only IUGR with no other associated risk factor was observed in 16.

Filho FL *et al.* [11] did a cross –sectional study using 5,063 sample, they found approximately 47% (n=2377) were anaemic followed by hypertension (n=827) and diabetes (n=106).

Neonatal outcome

In present study out of 25 sonographically diagnosed IUGR babies eight had features of neonatal hyperbilirubinemia and out of rest 22(88%), 3(12%) had hypoglycemia, hypocalcemia and polycythemia respectively and in normal pregnancies seven had features of hyperbilirubinemia and rest were normal.

Monika G *et al.* studied neonatal short-term outcome in infants with IUGR, subjects were studied and found patients with IUGR had higher percentage of hypoglycaemia or interventricular haemorrhage (p<0.05)

Doppler waveforms

Middle cerebral artery

In our study there is statistically significant difference in PI and RI values of study group as well as control group. Study group(PI =1.7+/-0.14, RI=0.77+/-0.10) and control group (PI=1.86+/- 0.17, RI= 0.8+/-0.15).There is significant decrease in PI and RI values of study group as compared to control group.

Ranjan K Sahoo *et al.* [12] did case control study. 30 cases were in study group with the risk factors of hypertension, diabetes or heart disease and rest 20 cases were in control group. He stated that RI of IUGR fetuses in middle cerebral artery was significantly lower than that of normal fetuses.(0.059+/-0.12 vs 0.0742+/-0.129; p <0.01).

Wijngaard JW *et al.* in [20], studied flow velocity waveforms in the middle cerebral artery. In growth retarded fetuses pulsatility in MCA was significantly reduced compared with normal pregnancy suggesting participation of MCA in a brain sparing effect in presence of clinical fetal hypoxia.

Umbilical artery waveform

In our study there is statistically significant difference between the RI and PI values as well as S/D ratio of Umbilical Artery in the study group vs control group which correlates with the study done by Ranjan K Sahoo *et al.* [12] who stated that in umbilical artery S/D ratio, PI and RI of IUGR fetuses were significantly higher than that of normal fetuses (4.03+/-0.15 vs 1.99+/-0.493 ; p<0.01, 1.334+/-0.37 vs 0.736+/-0.17; p<0.01, 0.753 +/-0.151 vs 0.482+/-0.109; p<0.01).

In a study by Wladimiroff *et al.* he stated that there is a linear decline in PI and RI values according to advancing gestational age, whereas elevated PI and RI values are observed in IUGR which also corresponds to our study.

Elevation of the umbilical artery systolic/diastolic ratio or of the pulsatility index is a moderately accurate predictor of adverse outcome in growth-retarded foetuses [17].

Uterine artery waveform (left and right)

In present study there is significant difference between PI and RI values of bilateral Uterine Artery between study group and control group. PI (L)(1.7 vs 1.02;P<0.0001) PI (R) (1.3 vs 0.7;P=0.006), RI(L) (1 vs 0.43; P=0.03), RI (R)(0.9 vs 0.4;P<0.0001).

Cnossen *et al.* identified 61 studies with >41,000 women and noted increased PI and increased RI (>0.58) for IUGR which was in agreement with our study.

Fleischer *et al.* have found that in IUGR complicated by PIH, there is inadequate trophoblastic invasion, leading to increased resistance in spiral arteries and decreased blood flow in uterine artery, thereby resulting in increased PI which is again in agreement with our study.

CPR

In present study there is statistically significant difference between the CPR values of study group as well as control group (1.08 vs 1.27;p<0.05).

Study done by Ranjan K Sahoo *et al.* [12] stated that CPR of IUGR fetuses were significantly lower than that of normal fetuses (0.814+/-0.20 vs 1.59+/-0.361;p<0.01)

Giancarlo M *et al.* [17] did study to determine whether the Doppler CPR predicts perinatal outcome in fetuses at risk for IUGR and stated that there as statistically significant increase in perinatal morbidity and mortality inn cases with abnormal CPR. For birth weight <10th percentile P<0.001(significant).

Demographic data

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NEONATAL OUTCOME

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Doppler waveforms

Middle cerebral artery

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Comparison of pi values of mca

| SNO | STUDY | YEAR | SENSITIVITY | SPECIFICITY | PPV | NPV |
|-----|------------------|------|-------------|-------------|-------|--------|
| 1. | PRESENT STUDY | 2017 | 44% | 48% | 45.8% | 46.15% |
| 3. | GRAMELLINI ET OL | 1992 | 24% | 100% | 100% | 77.3% |
| 4. | FONG KW ET OL | 1999 | 72.4% | 58.1% | 60% | 80% |

Umbilical artery waveform

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Pi values of umbilical artery

| SNO | STUDY | YEAR | SENSITIVITY | SPECIFICITY | PPV | NPV |
|-----|------------------|------|-------------|-------------|-------|--------|
| 1. | PRESENT STUDY | 2017 | 44% | 52% | 47.8% | 48.15% |
| 2. | GRAMELLINI ET OL | 1992 | 64% | 90.7% | 72.7% | 86.7% |
| 3. | FONG KW ET OL | 1999 | 44.7% | 86.6% | 84% | 91% |

Uterine artery waveform (left and right)

In present study there is significant difference between PI and RI values of bilateral Uterine Artery between study group and control group. PI (L)(1.7 vs 1.02;P<0.0001) PI (R) (1.3 vs 0.7;P=0.006), RI(L) (1 vs 0.43; P=0.03), RI (R)(0.9 vs 0.4;P<0.0001).

Crossen *et al.* identified 61 studies with >41,000 women and noted increased PI and increased RI (>0.58) for IUGR which was in agreement with our study [19].

CPR

In present study there is statistically significant difference between the CPR values of study group as well as control group (1.08 vs 1.27;p<0.05).

Study done by Ranjan K Sahoo *et al.* stated that CPR of IUGR fetuses were significantly lower than that of normal fetuses (0.814+/-0.20 vs 1.59+/-0.361;p<0.01)[13].

CONCLUSION

The study was conducted to assess the Doppler sonographic evaluation of umbilical, middle cerebral and uterine arteries of the patients who were clinically and ultrasonographically diagnosed as IUGR.

We found that RI value of Umbilical artery is most specific (80%) for diagnosing IUGR followed by the PI value of MCA which shows specificity of approx. 48%.

Fetal Doppler indices provide information that is not readily obtained from more conventional tests of fetal wellbeing. Fetal Doppler velocimetry helps in the recognition of the compromised growth retarded fetus thus allowing for timely interventions. It is therefore an important role to play in management of growth retarded fetus.

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