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Radiodiagnosis

Assessment of Obstetric Doppler Ultrasound in High-Risk Pregnancy and Its Perinatal Outcome

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Abstract **Original Research Article**

Background: Intrauterine growth restriction (IUGR) is associated with an increased risk of perinatal mortality & morbidity. It accounts for a sizeable number of future unhealthy children, which is a significant burden to parents and society. IUGR can be minimized to some extent by timely & accurate detection of IUGR. ***Aims and objectives***: To evaluate various waveforms of the umbilical artery, middle cerebral artery, ductus venosus, and cerebroplacental ratio as a predictor of adverse pregnancy outcomes in high-risk pregnancies. ***Materials and Methods:*** Eightywomen with a gestational age of 24 to 36 weeks were studied in the department of Radiodiagnosis of SAMC & PGI, Indore, Madhya Pradesh, from April 2021 to September 2022. Subjects were divided into non-complicated pregnancy [Appropriate for gestational age (AGA); n=40) and high-risk pregnancy [Small for gestational age (SGA); n=40; ≥18 years of age, with or without risk factors]. All underwent Doppler interrogation of the uterine arteries, umbilical artery, middle cerebral artery, and ductus venosus between 24-36 weeks of gestation. ***Results:*** Elevated head circumference (HC)/ abdominal circumference (AC) ratio, elevated femur length (FL)/AC ratio, presence of oligohydramnios without ruptured membrane, and advanced placental grade was more frequently observed among SGA babies. In this series, among the various risk factors, hypertension was a significant risk factor for IUGR, which other workers also accepted. Pulsatility index (PI), resistive index (RI) and systolic/diastolic (SD) ratio of uterine & umbilical arteries was significantly raised in SGA babies compared to AGA babies. In contrast, middle cerebral artery (MCA)'s PI, RI, and SD ratios were significantly lower in SGA babies than in AGA babies. Uterine artery early Diastolic Notch was seen in 11 cases & all of them delivered SGA babies. Hypertension was present in 8 of these 11 cases. Absent Diastolic Flow was detected in only one case, and the foetus died in utero. High CS rate, lower gestational age at delivery, low birth weight, low Apgar score, and NICU admission were more frequently observed with SGA babies than AGA babies. CS in mothers with SGA babies was mainly done for acute Foetal Distress. ***Conclusion:*** Ultrasonography is the standard and simple way of detecting and confirming IUGR. Doppler imaging provides valuable information about the hemodynamic status of the fetus. The flow pattern of the uterine artery reflects the evidence of uteroplacental vascular ischemia. Umbilical artery Doppler waveforms reflect the status of the fetoplacental.

Keywords: Waveforms, Intrauterine growth restriction, pregnancy outcome.

INTRODUCTION

The incidence of intrauterine growth restriction (IUGR) is about 2-8% (Chew LC 2022). For normal placental function and foetal growth, adequate maternal and foetal blood flow in the uterus and fetoplacental circulation is required. The failure of a foetus to attain its expected growth may result from different complications; the final common pathway most often encountered is via uteroplacental insufficiency. Placental insufficiency promotes compensatory changes in the foetal circulation (Chew LC 2022). IUGR is associated with a four to eight-fold increased risk of perinatal mortality and morbidity. 50% of the survived IUGR children have significant morbidity (Chew LC 2022).

Accurate and timely detection of IUGR can prevent the adverse outcome of pregnancy to some extent (Robert Peter J 2015). The methods most often used for antenatal diagnosis of IUGR are clinical palpation and measurement of fundal height. With the advent of ultrasonography (USG), it has become the most widely used, standard, and simple way of detecting and confirming IUGR. Ultrasound is a high-frequency sound wave over 20,000 cycles per second

(20 kilohertz) which are inaudible to human ears. USG waves are generated by piezoelectric transducers, which change electric signals into USG waves (Bamfo JE 2011).

Once the diagnosis of IUGR is made, Doppler imaging is valuable for monitoring the pregnancy. Foetal arterial Doppler studies are primarily done in the umbilical artery and middle cerebral artery (Maged AM 2014). However, in specific indications, Doppler studies of the aorta, splenic artery, renal artery, coronary arteries, adrenal arteries, etc., are also done. Umbilical artery Doppler waveforms reflect the status of the fetoplacental circulation, and increased placental vascular resistance is strongly correlated with IUGR (Srikumar S 2017).

High Pulsatility index (PI), high resistive index (RI), raised systolic/diastolic (SD)ratio, and absent diastolic flow is seen in IUGR (Srikumar S 2017). Reverse diastolic flow in the umbilical artery represents an advanced stage of placental compromise. It is associated with more than 70% of placental arterial obliteration and severe intrauterine growth restriction. Doppler study of middle cerebral artery (MCA) provides information regarding hemodynamic rearrangements in response to foetal hypoxia (Romero R 2015).

Previously foetal arterial Doppler studies were primarily done in the umbilical and middle cerebral arteries. In this series of the uterine artery, foetal Umbilical & MCA arterial Doppler velocimetry waveforms were studied. This study evaluated IUGR fetuses by ultrasonography using foetal biometry Doppler flow velocimetry waveform analysis. Since this study has not been carried out in this region previously, this work will provide further evidence.

Materials and Methods

The present analytical cross-sectional study was doneon 80 women with a gestational age of 24 to 36 weeksin the department of Radiodiagnosis of SAMC & PGI, Indore, Madhya Pradesh, between April 2021 to September 2022.

Women who did not give follow-up and consent and with documented congenital anomalous fetuses were excluded.

After obtaining consent from the patients, a detailed history was obtained from each patient with particular reference to maternal age, parity, last menstrual and other obstetric histories, including previous pregnancy outcomes. Medical history, including hypertension, diabetes, asthma, renal disease, heart disease, etc., was also noted. Gestational age was calculated from the last menstrual period and early ultrasound examination. A physical exam followed by history taking was performed. All the patients were subjected to ultrasound examination with an ultrasonography machine.

Subjects were divided into non-complicated pregnancy [Appropriate for gestational age (AGA); n=40) and high-risk pregnancy [Small for gestational age (SGA); n=40; ≥18 years of age, with or without risk factors]. All underwent Doppler interrogation of the uterine arteries, umbilical artery, middle cerebral artery, and ductus venosus between 24-36 weeks of gestation.

Those with an abnormal PI and abnormal fetal parameters [BPD, head circumference (HC), abdominal circumference (AC), femur length (FL)] were considered abnormal results and were evaluated and compared with those with normal results for adverse pregnancy outcomes, including small for gestational age and IUGR, etc. After the first examination mother was called for a follow-up accordingly. 2D SWE images were obtained with a general electric company LOGIQ E9 machine with the CL-6 MHz frequency probe

All the data analysis was performed using IBM SPSS ver. 25 software. Quantitative data were expressed as mean and standard deviation, whereas categorical data were expressed as percentages. Student t-test was used to compare the means, whereas the chi-square test was used to compare the proportions. A p-value of <0.05 was considered significant.

Results

The mean age of the pregnant women with SGA babies (29.56±2.15) was significantly higheras compared to those women who had AGA babies (26.34±4.48; p<0.001).

Of these 80 cases, 52 were primigravidae, and 28 were multigravidae. There was no significant statistical difference in the pregnancy outcome by Gravida of the patients (p=0.372).

Among the risk factors, those patients with hypertension were more likely to have SGA babies (79.2%) than other risk factors like urinary tract infection, respiratory tract infection, asthma, etc. (30% altogether; p=0.001).

The proportion of abnormal HC/AC ratio (>1) (84.8%; P<0.001) and abnormal FL/AC ratio (>23.5) (80.8%; p<0.001) was higher among the SGA babies.

SGA babies were significantly more likely to have oligohydramnios (80%) as compared to AGA babies (P<0.001). The proportion of Grade III placenta was higher among SGA babies (40.5%) than AGA babies (59.5%). Of the 80 cases studied, 29 cases had abnormal Doppler studies, and SGA foetuses were significantly more likely to give abnormal Doppler readings (79.3%) than AGA (20.7%; P<0.001).The mean of Uterine artery PI (1.536±0.57 vs. 1.006±0.35; p<0.001), Uterine artery RI (0.723±0.16 vs. 0.589±0.015; p<0.001), mean S/D ratio (2.95±1.004 vs. 2.4±0.558; P=0.001) and abnormal Uterine artery S/D ratio of >2.6 (72.4% vs. 27.6%; p<0.001) were higher in SGA babies than AGA babies respectively.

The mean of Umbilical artery PI (1.158±0.253 vs. 0.949±0.205; p<0.001), Umbilical artery RI (0.711±0.124 vs. 0.632±0.107; p=0.001), Umbilical artery S/D ratio (3.278±1.06 vs. 2.592±0.471; P=0.001) and abnormal Umbilical artery S/D ratio of >3 (81% vs. 19%; p<0.001) were higher in SGA babies than AGA babies respectively.

The mean of MCA PI (1.335±0.25 vs. 1.707±0.34; p<0.001), MCA RI (0.747±0.13 vs. 0.859±0.09; p<0.001) were significantly lower, and abnormal MCA S/D ratio of ≤ 4 (62.5% vs. 37.5%; p<0.001) were more in SGA babies than AGA babies respectively.

The proportion of CPI ≤ 1 indicative of brain sparing effect was significantly higher in the SGA foetus (81%) than AGA (19%) with P<0.001. The proportion CU index ≤ 1.08, indicative of brain sparing effect, was significantly higher in the SGA foetus (100%) than AGA (0%) with P<0.001.

Only 4 preterm cases, of which 3 were in the SGA group. Most of the SGA foetuses were of term size. There was no significant difference in the gestational outcome by the maturity of the babies, as shown in the table.

Out of 80 cases, 51 were delivered vaginally, of whom 2 required instrumental delivery. Cesarean sections were performed in 29 cases. Cesarean section rate was significantly higher in the SGA foetus group The mean gestational age at the time of delivery of the AGA babies was significantly higher than the mean gestational age at delivery of the SGA babies (P<0.000). SGA foetuses had lower birth weights as compared to AGA fetuses. SGA babies were significantly more likely to have an APGAR score<7 than AGA babies.

Table 1: Sensitivity, Specificity, PPV, and NPV in detecting SGA foetus

Variables	Sensitivity	Specificity	PPV	NPV
HC/ACRatio	84.8	92.3	84.8	89.5
FL/ACRatio	57.1	92.3	80	80
UtAS/D >2.6	60	87.6	72.4	80.2
Umbilical arteryS/D	48.5	93.8	80.9	77.2
MCAS/D	71.4	75.9	62.5	83.3
CPIorMCARI/UA RI	48.5	93.8	80.9	77.2
CUINDEX	45.7	100	100	77.3

Table 2: Perinatal outcome in IUGR babies (N=25) with abnormal & NormalDoppler findings

Events	AbnormalDoppler(18cases)	NormalDoppler(7cases)
NICUadmission	10	3
ApgarScore<7	11	0
Meanbirth wt.(kg).	2.05	2.21
No.ofCS	15	2

SGA babies with abnormal Doppler had lower birth weights, poor Apgar scores, Higher NICU admission, and higher CS rate. SGA babies were more likely to be admitted to the NICU than AGA babies, and the difference was statistically significant (P<0.001).

DISCUSSION

With the advent of USG, the diagnosis of IUGR has become more accessible and accurate. David *et al*., in 1998, remarked that ultrasound biometry is the gold standard for assessing foetal size (David P 1998) Botsis D *et al*., in 2006, with the help of USG, marked that 15% of all pregnancies constitute IUGR foetuses (Botsis D 2006).

In this study, no significant statistical differences were observed in the pregnancy outcome by Gravida of the patients, but the mean age of the mothers of SGA babies was higher. Madazli *et al*., (Madazli R 2001) and Devendra *et al*., (Devendra A 2005) observed no significant difference in mean maternal age and parity.

The failure of a foetus to attain its expected growth may result from different complications, but the final common pathway most often encountered is via uteroplacental insufficiency. In this series among the various risk factors hypertension was a very significant risk factor for IUGR which was in agreement with other workers (Kalsi H 2015).

Benson and Dobuilet (Benson CB 1986) noted that the detection of IUGR with only weight estimation has some limitations because, in 95% of cases, the predicted weight falls up to 18% of the actual weight. Therefore, additional sonographic criteria like elevated HC/AC ratio, elevated FL/AC ratio, and presence of oligohydramnios without ruptured membranes and advanced placental grade are also used for improving the accuracy of diagnosis.

David P *et al*., (David P 1998) remarked that between 20-36 weeks of gestation, HC/AC ratio drops typically from 1.2 to 1. In asymmetric IUGR HC/AC ratio is elevated. In this study number of raised HC/AC ratio (>1) were higher among the SGA babies as compared to AGA babies, and the difference was clinically significant (P<0.001). In this study, 80% of SGA foetuses had an abnormal HC/AC ratio. Benson et al (Benson CB 1986) reported that an elevated HC/AC ratio has a sensitivity of 82%, specificity of 94%, a positive predictive value of 62%, and a negative predictive value of 98% for detecting IUGR and in this study sensitivity 84.8%, specificity 92.3%, PPV 84.8%, specificity 92.3%, PPV 84.8% and NPV 89.5% were noted.

FL/AC is another parameter used to detect IUGR. Dutta *et al*., (Dutta DC 2004) mentioned that FL/AC greater than 23.5 from 21 weeks onwards suggests IUGR. In this study abnormal FL/AC ratio (>23.5) was significantly higher among SGA babies as compared to AGA babies (p<0.000). Benson *et al*., (Benson CB 1986) noted elevated FL/AC ratio had a sensitivity of 34-49%, a specificity of 78-83%, a positive predictive value of 18- 20%, and a negative predictive value of 92-93%. This study noted a sensitivity of 57.1%, a specificity of 92.3%, a positive predictive value of 80%, and a negative predictive value of 80%.

Dutta *et al*., (Dutta DC 2004) noted that amniotic fluid volume can also indicate growth restriction. The vertical pocket of less than 2 cm & AFI of less than 5 cm suggests oligohydramnios. In 1980 Frank A manning *et al*., (Frank A Manning 1980) noted that this decreased amniotic fluid could be due to chronic intrauterine stress with a reduced foetal contribution to the amniotic fluid pool due to uteroplacental insufficiency. David *et al*., (David P 1998) remarked that a decreased amniotic fluid volume is closely associated with IUGR. In this study, SGA babies were significantly more likely to have oligohydramnios as compared to AGA babies. The proportion of advanced placental grade was also higher among SGA babies compared to AGA babies in this study.

Doppler ultrasonography has been in use since the 1980s for the evaluation of the foetal circulatory system. In this series of the uterine artery, foetal Umbilical & MCA arterial Doppler velocimetry waveforms were studied. Out of 100 cases, 29 had abnormal Doppler readings compared to AGA babies and 66% of SGA foetuses had abnormal Doppler readings. Trudinger *et al*., (Brain J Trudinger 1985) noted abnormal Doppler study in 74% of SGA foetuses.

Uterine arteries branch into arcuate arteries leading to spiral arteries within the myometrium. During the later part of the first trimester, the trophoblast invades the spiral arteries converting these vessels from high-resistance to low-resistance vessels and producing vasodilator peptides acting locally in deciduas and myometrium. In IUGR, a lack of trophoblastic invasion results in uteroplacental insufficiency. Doppler indices of the uterine artery can predict the onset of IUGR. But in 2005, Nagtegaal MJ *et al*., stated that uterine Doppler is not mainly in managing patients with a risk of developing uteroplacental insufficiency (Nagtegall MJ 2005).

Uterine artery means PI (1.5 vs.1), RI (.7 vs.0.5), and S/D (2.9 vs 2.4) ratio were all significantly raised in SGA foetuses in comparison to AGA foetuses in this study indicating raised impedance to blood flow. Bhushan and Shefeek (1999) also noted the same trend with a significant statistical difference (PI 1.3 vs. 0.6, RI 0.6 vs. 0.4, SD 2.9 vs. 1.8) (Bhushan N 1999).

Coleman MA *et al*., (2000) defined Ut A RI of > 0.58 as abnormal, and an RI of ≥ 0.7 was defined as very abnormal. They concluded that in high-risk women, uterine artery Doppler waveform analysis was better than clinical risk assessment in the prediction of pre-eclampsia and SGA babies (Coleman MA 2000).

In this series, abnormal S/D ratios of > 2.6 in the uterine artery were significantly more in SGA foetuses. Fleicher *et al*., (Fleicher A 1986) noted that if the S/D ratio of the uterine artery exceeds 2.6, the situation is predictive of adverse perinatal outcomes. Here S/D ratio of >2.6 had a sensitivity of 60%, specificity of 87.6%, PPV of 72.4%, and NPV of 80.2%. Bhushan and Shefeek (Bhushan N 1999) reported that sensitivity, specificity, PPV, and NPV of uterine artery S/D ratio for detecting SGA babies are 67%, 90.3%, 80%, and 82.6%.

In this study, uterine artery notching was found in 11 cases, all of whom had SGA babies. Eight of them were associated with hypertension. Thaler *et al*., (Thaler I 1992) also noted the higher association of uterine notching with hypertension.

Umbilical Artery Doppler waveforms reflect the status of the fetoplacental circulation. Increased placental vascular resistance is strongly correlated with IUGR. Gadelha Da Costa et al. (Gadelha Da Costa A2005) observed that umbilical artery resistance decreases progressively during the second half of pregnancy, with the resistance index being 0.69 in the 22nd week and 0.56 in the 38th week of pregnancy. In this study, mean UA PI, RI, and S/D ratio were raised in SGA babies compared to AGA foetuses (1.2 vs. 0.94, 0.7 vs. 0.63, and 3.3 vs. 2.6). Bhushan and Shefeek (Bhushan N 1999) also found raised UA PI, RI, and S/D ratio in IUGR babies compared to normal babies (PI 1.9 vs. 1; RI0.78 vs. 0.65 and 5.9 vs. 3.15). TA Mills *et al*., (TA Mills 2005) found that umbilical artery (UA) Doppler PI and RI were significantly higher in IUGR compared with normal (PI 1.02 vs. 89, RI 0.70 vs.58).

Abnormal UA S/D ratio (>3) was significantly higher in the SGA group in this study & had a sensitivity of 48.5%, specificity of 93.8%, PPV of 80.9%, and NPV of 77.2%, respectively. Bhatt *et al*., (Bhatt KR 1996) reported a sensitivity of 100%, a specificity of 66.66%, a positive predictive value of 100%, and a negative predictive value of 50% for UA S/D. Bhushan and Shefeek (Bhushan N 1999) reported US S/D ratio had a sensitivity of 50%, specificity of 50-90%, PPV of 75%, and NPV of 66.7%.

Here absent Diastolic Flow in the umbilical artery was found in only 1 case, which died in utero after 14 days of diagnosis. Riza Madazli *et al*., (Madazli R 2001) noted the time interval between the detection of AEDF in UA to antepartum foetal death ranged from 3 to 18 days with a median of 7 days. Neena Malhotra *et al*., (Malhotra N 2001) noted that delivery could be delayed by 1-2 weeks if desired, with very intensive foetal surveillance in cases of AEDF. Still, immediate delivery is advocated when REDF sets in.

Riza Madazli *et al*., (Madazli R 2001) noted that in growth restriction the main and primary pathology is inadequate uteroplacental perfusion which is reflected as increased umbilical artery impedance, changes in the MCA are a secondary phenomenon. This study significantly decreased the mean MCA PI, RI, and S/D ratio in SGA fetuses. Ravi Chandran and co-workers (Ravi Chandran 1993), Manabe *et al*., (Manabe A 1995) noted that MCA PI values in growth retarded foetuses were consistently lower than those in the normal foetuses, Malhotra *et al*., (Malhotra N 2001) noted that PI of the middle cerebral artery can identify those foetuses at high risk for growth retardation. In this study, mean MCA PI was significantly lower in SGA foetuses (1.3 vs. 1.7). Mean MCA RI and S/D ratios were also lower in SGA foetuses as compared to AGA foetuses in this series (0.75 vs. 0.86 and 3.3 vs. 4.4). Bhatt *et al*., (Bhatt KR 1996) remarked that the S/D ratio of less than 4 in MCA suggests a brain-sparing effect.

The proportion of CPI (MCA RI/UA RI) ≤ 1 indicative of brain sparing effect was significantly higher in the SGA foetus group. Its sensitivity was 48.5%, specificity 93.8%, PPV 80.9%, and NPV 77.2%. Alaa *et al*., (Alaa E 2005) considered MCA RI/UA RI < 1.0 abnormal. It had a sensitivity of 64.1%, specificity of 72.7%, PPV of 89.2%, and NPV of 36.3%, respectively. There was a strong correlation between the MCA RI/UA RI and neonatal outcome. They concluded that MCA RI/UA RI< 1.0 may be helpful in the identification of newborns at risk of morbidity, irrespective of whether they are small or appropriate for the gestational age.

Malhotra *et al*., (Malhotra N 2001) remarked that the PI ratio of MCA/ UA (CU index) is valuable for monitoring growth retarded and small for gestational age foetuses, particularly those whose umbilical artery PI is high. In this study, the proportion CU index (MCA PI/UA PI) ≤ 1.08, indicative of brain sparing effect, was significantly higher in the SGA foetus group. It was associated with a sensitivity of 45.7%, specificity of 100%, PPV of 100%, and NPV of 77.3%.

In 2001, Takahashi Y *et al*., (Takahashi Y 2001) observed three patterns depending on the severity of growth restriction. Phase I, UA PI < MCA PI (no brain sparing effect); Phase II, UA PI > MCA PI (brain sparing effect); Phase III, both Pls elevated with the absence of end-diastolic flow or presence of reverse end diastolic flow, which was designated as the 'breakdown of the brain sparing effect. 'The change from decreased to increased MCA PI along with increasing UA PI may predict a severe growth-restricted infant. Hecher *et al*., (Hecher K 2001) described the sequence of changes in growth-restricted foetuses. Amniotic fluid index and umbilical artery pulsatility index were the first variables to become abnormal, followed by the middle cerebral artery, aorta, and variation of fetal heart rate, ductus venosus, and inferior vena cava.

The mean gestational age at delivery (38w) and birth weight of SGA babies (2.1kg) in this study were lower than AGA babies (gestational age 39w andbirth weight 3.1Kg). Patrizia *et al*., (Patrizia Vergani 2002) also observed lower gestational age at delivery (37.7 ± 20 vs. 38.8 ± 1.6) and lower birth weight (2193 ± 446 vs. 2524 ± 379) in growth-restricted foetuses near term.

Cesarean section rates noted in this study were significantly higher in the SGA foetus group. In the SGA group CS rate was 51%, and in the AGA group, 32%. Peter Holmqvist *et al*., (Peter Holmqvist 1986) also noted a similar trend.

Low APGAR score of < 7 and NICU admissions in this study were significantly more in SGA babies than in AGA babies. Arora Devendra *et al*., (Devendra A 2005) and Francesc Figueras *et al*., (Figueras F 2008) also had similar findings.

In 2000, Ott WJ observed that Umbilical artery Doppler blood flow studies were a better predictor of neonatal outcome than estimated foetal weight. SGA foetuses with normal Doppler studies most likely represent constitutionally small, not pathologically, growth-restricted foetuses. In this study, SGA foetuses with abnormal Doppler study had a poor outcome compared to those with normal Doppler study. SGA babies with abnormal Doppler had lower fetal weight, poor Apgar scores, NICU admissions, and higher CS rates. Arora Devendra *et al.*, (Devendra A 2005), and Francesc Figueras *et al.*, (Figueras F 2008) also found the same.

Conclusion

Ultrasonography (USG) is the standard and simple way of detecting and confirming IUGR. Elevated HC/AC ratio, elevated FL/AC ratio, presence of oligohydramnios without ruptured membranes, and advanced placental grade can also be used to improve the accuracy of diagnosis. Hypertension was more frequent in SGA babies. Once the diagnosis of IUGR is made, Doppler imaging is valuable for monitoring the pregnancy; it provides valuable information about the hemodynamic status of the foetus. The flow pattern of the uterine artery reflects the evidence of uteroplacental vascular ischemia. Umbilical artery Doppler waveforms reflect the status of the fetoplacental.

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