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Role of Foetal Biometry and Doppler Studies in the Evaluation of Intrauterine Growth Restriction

Harkiran Kalsi MBBS[1], Parminder Kaur Sachdev MBBS, MD[2]

M.M. Institute of Medical Sciences and Research. Ambala, Haryana

Abstract: ***The term intrauterine growth restriction (IUGR) refers to a condition in which a fetus is unable to achieve its genetically determined potential size. IUGR is associated with four to eight fold increased risk of perinatal mortality and morbidity. 50% of the survived IUGR children have significant morbidity.Accurate and timely detection of IUGR can prevent adverse outcome of pregnancy to some extent. With the advent of ultrasonography (USG), it has become the most widely used, standard and simple way of detecting and confirming IUGR. Evaluation of IUGR fetuses by Doppler studies are done by studying uterine artery Doppler velocimetry waveforms, foetal arterial Doppler study and foetal envoisDoppler studies. Methods: This is a descriptive study is for a period of 14 months from May 2014 to July 2015. The population consisted of 100 pregnant women referred from the inpatient ward as well as outpatient department of Obstetrics and Gynecology Department of Maharishi Markandeshwar Hospital and Research Centre, 50 cases with clinically suspected intrauterine growth restriction (IUGR) and another 50 cases with clinically normal pregnancy are included. Results: Ultrasound biometry is the gold standard for assessment of foetal size. Foetal weight less than 10th percentile for gestational age is mostly used to diagnosis IUGR but other criteria like elevated HC/AC ratio, elevated FL/AC ratio, and presence of oligohydramnios without ruptured membranes, presence of advanced placental grade can also be used for improving the accuracy of diagnosis. Interpretation & Conclusion: The utero-placental insufficiency seen with IUGR is associated with a rise in vascular resistance in uterine & umbilical arteries which can be estimated by raised pulsatility index, resistance index, systolic/diastolic ratio in these arteries, and persistence of uterine artery diastolic notch, absent & reverse diastolic flow in umbilical artery. In the presence of foetal hypoxemia, central redistribution of blood flow occurs, known as the Brain – Sparing Reflex manifested by a fall in Pulsatility index, resistance indices, and systolic/diastolic ratio.***

Keywords: intrauterine growth restriction (IUGR),pregnancy, ultrasonography (USG)

1. Introduction

The term intrauterine growth restriction (IUGR) is defined by the American college of Obstetricians and Gynaecologists as estimated foetal weight less than that expected for gestational age.[1] Clinically this is applied when the expected foetal weight is less than 10th percentile for gestational age because perinatal mortality and morbidity is significantly increased in this group.

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. IUGR is associated with four to eight fold increased risk of perinatal mortality and morbidity. 50% of the survived IUGR children have significant morbidity.[2]

Accurate and timely detection of IUGR can prevent adverse outcome of pregnancy to some extent. 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.

Once diagnosis of IUGR is made Doppler imaging is valuable for monitoringthe pregnancy. The utero-placental insufficiency seenwith IUGR is associated with a rise in vascular resistance which can be estimated by pulsatility index, resistance index, systolic/diastolic ratio and persistence of uterine diastolic notch. Umbilical artery Doppler waveforms reflect the status of the feto-placental circulation and increased placental vascular resistance isstrongly correlated with IUGR.

This study was conducted to evaluate IUGR fetuses by ultrasonography using foetal biometry Doppler flow velocimetry waveform analysis in Maharishi Markandeshwar institute of medical sciences Ambala, India. We intended to study early detection of IUGR fetuses using real-time sonography and Doppler velocimetry and see how they vary in ultrasound morphometric measurements and Doppler vascular studies in normal and IUGR fetuseswith efficacy in detection of the same.

2. Material and Methods

This study was a longitudinal study done in Obstetrics and gynaecology departmentofMaharishi MarkandeshwarInstitute Of Medical Sciences Ambala, India in collaboration with the radio-diagnosis Department of the same Institute. The duration of the study was 14 months from May 2014 to July 2015. Thepopulation consisted of 100pregnant women referred from the inpatient ward as well as outpatient department. 50 cases with clinically suspectedintrauterine growth restriction (IUGR) and another 50 cases with clinically normalpregnancy were included. Patients excluded from the study were ones with multiple pregnancy,Intrauterine death (IUD),fetus with congenital anomalies,period of gestation less than 28 weeks,macrosomic babies.

After obtaining consent from the patients a detailed history were obtained with special reference to maternal age, parity, last menstrual and other obstetric history including previous pregnancy outcomes. Medical history including hypertension, diabetes, asthma, renal disease, heart disease was also noted. Gestational age was calculated from the last

menstrual period and/or early ultrasound examination. History taking was followed by physical examination.

All the patients were subjected to ultrasound examination with ultrasonography machine PHILIPS X 30 with the facility of colour Doppler imaging. Carrier frequency of3.5 MHz and 7.5 MHz were used. The foetal biometry included assessment of biparietal diameter (BPD), head circumference (HC), abdominal circumference (AC),and femoral length (FL). Head Circumference/Abdominal Circumference ratio, Femur Length/Abdominal Circumference Ratio, foetal heart rate, placentalmaturity and amount of liquor were noted. Amniotic fluid index was calculated byadding the vertical depths of the largest pocket in each of the four uterine quadrants.

Foetal weight was estimated according to the Hadlock formulae that uses Femur Length, Abdominal Circumference andBi-parietal Diameter. Foetal weight less than 10th percentile based on the chart given by Doubilet et alin 1997 were taken as small for gestational age (SGA) babies and foetal weight between 10th percentile to 90th percentile were taken as appropriate for gestational age(AGA) babies. [3]

Pulse wave Doppler ultrasound examination were then performed.Uterine artery was studied by first identifying the placental site. If the placentawas central, bilateral uterine arteries were studied and the mean were taken.

Sampling point for the uterine artery was the point where it crossed the external iliacartery near the cervico-uterine junction. For the umbilical artery flow velocitywaveforms were obtained from a free floating loop of cord. The sampling point forthe middle cerebral artery (MCA) was taken near its origin from the internal carotidartery. Flow velocity waveforms obtained from the arteries were computed automatically. The programme identified individual cardiac cycles and computedpeak systolic velocity (S), end diastolic velocity (D), mean velocity and the indicespulsatility index (PI), resistance index (RI) and systolic/diastolic (S/D) ratios.

S/D=S/D ratio.
S – D/S= RI ratio.
S – D/mean = PI ratio

Parameters observed were pulsatility Index (PI), resistance index (RI),systolic/diastolic (S/D) ratio, uterine notch, absent or reversed end diastolic flow in Umbilical Artery, Cerebro-placental index (CPI) and cerebro-umblical indexes (CU). Umbilical Artery& Uterine ArteryPulsalitiltyIndex&Resistance Index values were based on chart given by Merz E in 2005.[4] 95th percentile was taken asthe cutoff point. Umbilical Artery S/D >3, Uterine artery S/D>2.6 and Middle Cerebral Artery S/D<4 were consideredabnormal (Bhatt et al 2003). Middle Cerebral Artery Resistance Index values were based on chart given by Bahimannet al in 2002. [5]

Middle Cerebral ArteryPulsalitityIndex >1.45 in pre term & 1 for term were considered normal (Fawazet al 2005). [6] CerebroplacentalIndex (Middle Cerebral Artery Resistance Index/Umbilical Artery RI) < 1 considered abnormal (Alaa E et al 2005).[7]

Data regarding pregnancy outcome in terms of period of gestation at birth,mode of delivery, indication of caesarean section, birth weight, Apgar score andNICU admissions were retrieved from the delivery records of the Obstetrics andGynaecology Department of Maharishi Markandeshwar Institute of Medical Sciences And Research,Ambala, India.

3. Results and Observations

A total of 100 cases were included in the study, 50 clinically suspected IUGR cases and another 50 with normal uncomplicated singleton pregnancies were included in this study. Of 50 IUGR suspected cases, 35 cases (about 2/3rd) were actually small for gestational age (SGA) and 15 cases had foetuses appropriate for gestational age (AGA) and were included in the control group as shown in the pie chart (figure1).

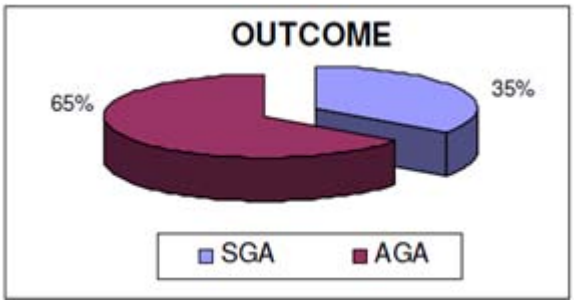


Figure 1:

Table 1: t-test showing Mean Difference in Age of Pregnant Women by Outcomes

Outcome	Age of pregnant women (Yr) Meam (SD)	Mean difference	T	P-value
SGA	29.69(3.6)	2.09	2.025	0.046
SGA	27.54(4.5)			

The mean age of the pregnant women with SGA babies were significantly
higher as compared to those women who had AGA babies (P<0.000).

Table 2: Comparison of outcome by Gravida (N=100)

Gravida	Outcome,N(%)		P-value
	SGA	AGA	
Primi	19(30.6%)	43(69.4%)	0.244
Multi	16(42.1%)	22(67.9%)	

Of these 100 cases, 62 were primigravidae and 38 were multigravidae. There was no significant statistical difference in the pregnancy outcome by Gravida of thepatients.

Table 3: Comparison of Gestational outcome by presence of risk factors (N=44)

Risk factors	Outcome,N(%)		P-value
	SGA	AGA	
Hypertension	19(79.2)	5(20.8)	0.001
Others	6(30.0)	14(70.0)	

Among the risk factors, those patients with hypertension were more more likely to have SGA babies as compared with other risk factors like urinary tract infection, respiratory tract infection, asthma etc. And the difference was found to be statistically significant as shown in this table.

Table 4: Comparison of Gestational Outcome by HC/AC ratio (N=100)

HC/AC	Outcome,N(%)		P-value
	SGA	AGA	
≤ 1	7(10.4)	60(69.4%)	0.000
> 1	28(84.8)	5(15.2)	

The proportion of abnormal HC/AC ratio (>1) is higher among the SGA babies as comparted to AGA babies and the difference was clinically significant (P<0.000).

Table 5: Sensitivity, Specificity, PPV & NPV of HC/ AC ratio in detecting SGA foetus

HC/AC Ratio	SGA	AGA	TOTAL
>1	28	5	33
≤ 1	7	60	67
Total	35	65	100

SENSITIVITY 84.8%
SPECIFICITY 92.3%
Positive Predictive Value 84.8%
Negative Prodictive Value 89.5%

Table 6: Comparison of Gestational outome by FL/AC Ratio (N=100)

FL/AC Ratio	Outcome,N(%)		P-value
	SGA	AGA	
≤ 2.6	15(20.4)	60(80.0)	
> 2.6	20(80.8)	5(20.0)	0.000

Abnormal FL/AC ratio (>23.5) was significantly higher among SGA babies as compared to AGA babies (p <0.000) as seen in table.

Table 7: Comparison of Gestational outome by Placental Grade (N=100)

Placental Grade	Outcome,N(%)		P-value
	SGA	AGA	
Grade II	5(19.2)	21(80.0)	0.050
Grade III	30(40.5)	44(59.5)	

The proportion of Grade III placenta was higher among SGA babies as
compared to AGA babies as seen in table 7.

Table 8: Comparison of Gestational outcome by Doppler study outcome (N=100)

Doppler study	Outcome,N(%)		P-value
	SGA	AGA	
Normal	12(16.9%)	59(83.1%)	0.000
Abnormal	23(79.3%)	6(20.7%)	

Of 100 cases studied, 29 cases had abnormal Doppler studies and SGA
foetuses were significantly more likely to give abnormal Doppler readings as shown in table 8.

Table 9: 't-test' showing mean difference in Uterine artery PI among the two groups

Outcome	Uterine artery PI Mean (SD)	Mean difference	T	P-value
SGA	1.536(0.57)			
AGA	1.006(0.35)	0.5306	5.699	0.000

The mean (SD) of Uterine Artery PI were higher in SGA babies than AGA babies and the difference was statistically significant.

Table 10: Comparison of Gestational outcome by Uterine artery S/D (N=100)

Uterine artery S/D	Outcome, N (%)		P-value
	SGA	AGA	
≤2.6	14(19.7%)	57(80.3%)	
>2.6	21(72.4%)	8(27.6%)	0.000

Abnormal S/D ratio of >2.6 in uterine artery were significantly more in SGAfoetus' as seen in this table.

Table11: Sensitivity, Specificity, PPV & NPV of Uterine artery SD Ratio indetecting SGA.

Ut A S/D	SGA	AGA	TOTAL
>2.6	21	8	29
≤2.6	14	57	71
TOTAL	35	65	100

SENSITIVITY 60%, SPECIFICITY 87.6%, PPV 72.4%, NPV 80.2%. Uterine artery diastolic notching was seen in 11 SGA foetuses, 8 of them hadunilateral notching and 3 bilateral notching.And 8 of them had hypertension.

Table 12:'t-test' Showing mean difference in Umbilical artery RI among the twogroups

Outcome	Umbillical artery RI Mean (SD)	Mean difference	T	P-value
SGA	0.7115(0.124)	0.0822	3.445	0.001
AGA	0.6329(0.107)			

The mean (SD) of UA RI were higher in SGA babies than AGA babies andthe difference was statistically significant.

Table13: Comparison of Gestational outcome by Umbilical artery S/D (N=100)

Umbilical artery S/D	Outcome, N (%)		P-value
	SGA	AGA	
≤ 3	18(22.8)	61(77.2)	0.000
> 3	17(81.0)	4(19.0)	

Table 14: Comparsion of Gestational outcome by Cerebro-placental index(CPI=MCA RI/UA RI) (N=100)

CPI MCA RI/UA RI	Outcome, N(%)		P-value
	SGA	AGA	
>1	18(22.8%)	61(77.2%)	0.000
≤ 1	17(81.0%)	4(19.0%)	

The proportion of CPI ≤ 1 indicative of brain sparing effect were significantlyhigher in the SGA foetus group as shown in table.

Table 15: Sensitivity, specificity, positive predictive value and negative predictivevalue of CPI in detecting brain sparing

CPI or MCA RI / UA RI	SGA	AGA	TOTAL
≤1	17	4	21
>1	18	61	79
TOTAL	35	65	100

SENSITIVITY 48.5%, SPECIFICITY 93.8%,PPV 80.9%,NPV 77.2

Table 16: Comparision of Gestational outcome by Cerebro-umbilical index(CUI=MCA PI/UA PI) (N=100)

CUI MCA PI / UA PI	Outcome, N (%)		P-value
	SGA	AGA	
>1.08	19(22.6%)	65(77.4%)	0.000
≤ 1.08	16(100%)	0(0)	

The proportion CU index ≤ 1.08 indicative of brain sparing effect were significantly higher in the SGA foetus group as shown in table

Table 17: Comparison of Gestational outcome by foetal maturity (N=100)

Maturity	Outcome, N(%)		P-value
	SGA	AGA	
Preterm	3(75.0)	1(25.0)	0.087*
Term	32(33.3)	64(66.7)	

*Fisher's exact test

Overall there were 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 inthe gestational outcome by maturity of the babies as shown in the table.

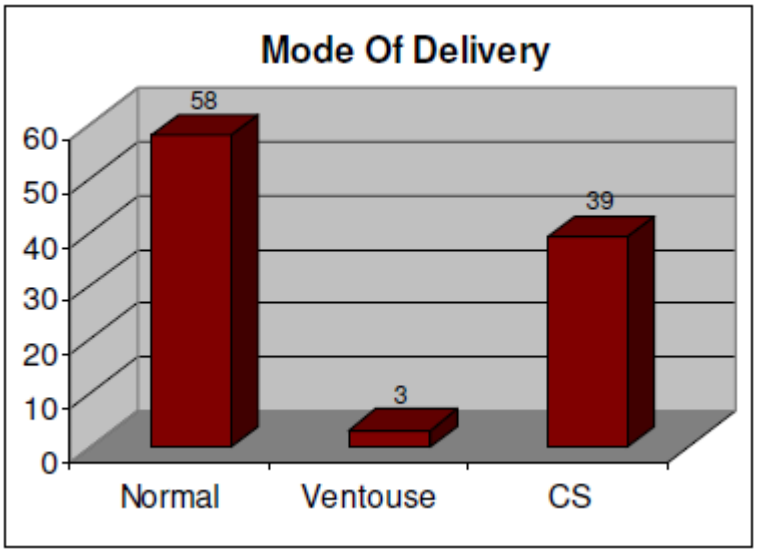


Figure 2: Bar chart showing mode of delivery

Out of 100 cases, 61 cases delivered vaginally of whom 3 cases required instrumental delivery. Casesarean sections were performed in 39 cases.

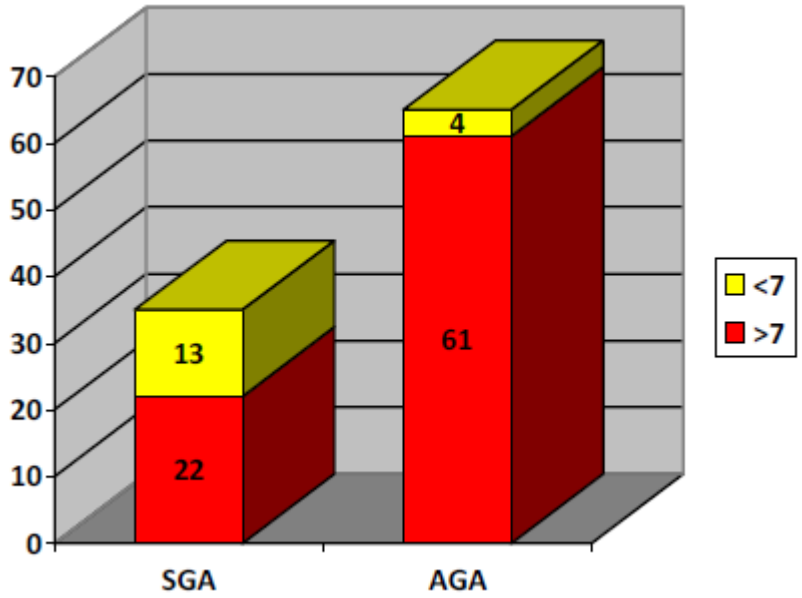
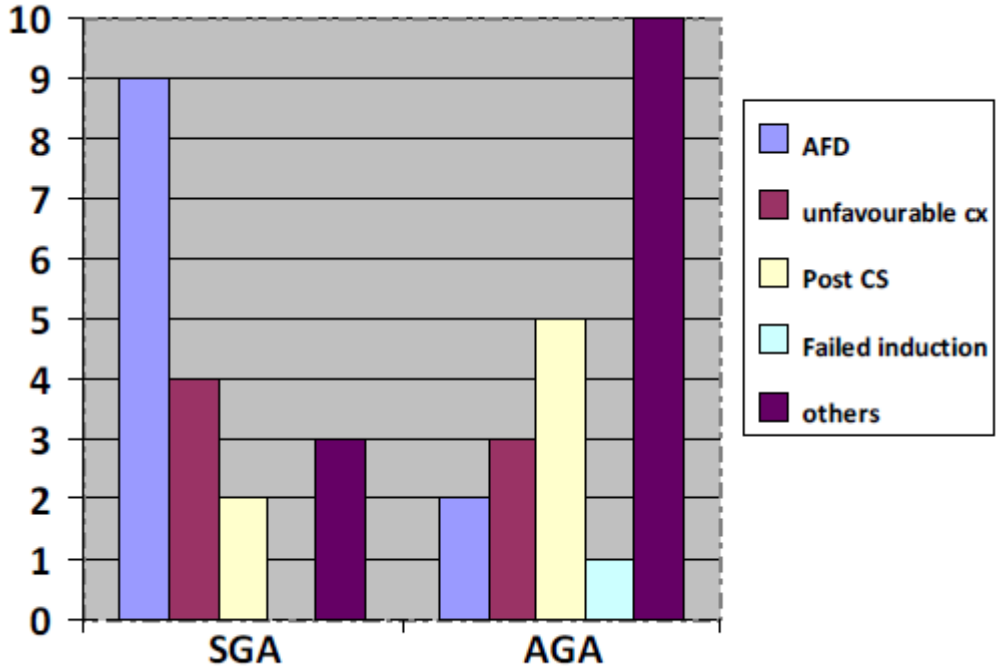


Figure 3: Bar chart showing indication of CS among SGA & AGA babies

In case of SGA babies' acute foetal distress (AFD) was the indication for CS inmajority of cases.



Poor Apgar score was mostly seen in SGA babies.

Figure 4: Bar chart showing Apgar score by outcome

Table 18: Comparison of Gestational outcome by NICU admission (N=100)

NICU admission	Outcome, N(%)		P-value
	SGA	AGA	
Yes	14(87.5)	2(12.5)	0.000
No	21(25.0)	63(75.0)	

SGA babies were more likely to be admitted in the NICU as compared to theAGA babies and the difference was found to be statistically significant (P<0.000).

4. Discussion

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 ofSGA babies were higher. The failure of a foetus to attain its expected growth may result from differentcomplications but the final common pathway most often encountered is viauteroplacental insufficiency. In this series among the various risk factorshypertension was a very significant risk factor for IUGR which was in agreement with other workers (Thaler et al 1992, K Harrington e al 1999 and Coleman et al 2000).[8]

Benson and Dobuilet (2005)[9] noted that detection of IUGR with only weightestimation has some limitations because in 95% of cases the predicted weight falls upto 18% of the actual weight. Therefore additional sonogaphic criteria like elevatedHC/AC ratio, elevated FL/AC ratio, and presence of oligohydramnios withoutruptured membranes, presence of advanced placental grade are also used forimproving the accuracy of diagnosis as mentioned in Dutt DC (2004).[10]

In this study number of raised HC/ACratio (>1) were higher among the SGA babies as compared to AGA babies and thedifference was clinically significant (P<0.000). In this study 80% of SGA fetuses had abnormal HC/AC ratio. Benson et al in 1986[11] reported that elevated HC/AC ratiohas a sensitivity of 82%, specificity of 94%, positive predictive value 62% andnegative predictive value 98% for detecting IUGR & in this study Sensitivity 84.8%,specificity 92.3%, PPV 84.8%, specificity 92.3%, PPV 84.8% and NPV 89.5% werenoted.

In this study SGA babies were significantly more likely to have oligohydramnios ascompared to AGA babies. The proportion of advanced placental grade was alsohigher among SGA babies as compared to AGA babies in this study.

Uterine artery mean PI (1.5 vs.1), RI (.7 vs.0.5) and S/D (2.9 vs 2.4) ratio wereall significantly raised in SGA foetuses in comparison to AGA foetuses in this studyindicating raised impedance to blood flow.

In this series abnormal S/D ratio of > 2.6 in uterine artery were significantlymore in SGA foetuses. Fleicher et al (1986)[12] noted that if the S/D ratio of uterineartery exceeds 2.6 the situation in predictive of adverse perinatal outcome. Here S/Dratio of >2.6 had a sensitivity of 60%, specificity 87.6%, PPV 72.4% and NPV 80.2%.Bhushan and Shefeek (1999)[13] reported that sensitivity, specificity, PPV and NPV ofuterine artery S/D ratio for detecting SGA babies are 67%, 90.3%, 80% and 82.6%.

In this study uterine artery notching were found in 11 cases and all of them had SGA babies. 8 of them were associated with hypertension. Thaler et al (1992),Bower et al (1993), Park et al (1996) and AxtFliedner R (2004)[14] also noted higherassociation of uterine notching with hypertension.

MCA is suggestive of brain sparing effect.The proportion of CPI (MCA RI/UA RI) ≤ 1 indicative of brain sparing effectwas 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(2005)[16] considered MCARI/UA RI < 1.0 abnormal. It had a sensitivity of 64.1%, specificity 72.7%, PPV 89.2% and NPV 36.3% respectively. There was a strong correlation between theMCA RI/UA RI and neonatal outcome. They concluded that MCA RI/UA RI< 1.0may be helpful in the identification of newborns at risk of morbidity, irrespective ofwhether they are small or appropriate for the gestational age.

Malhotra et al (2001)[17] remarked that the PI ratio of MCA/ UA (CU index) isvaluable for monitoring growth retarded and small for gestational age fetuses,particularly those, whose umbilical artery PI is high. In this study the proportion CUindex (MCA PI/UA PI) ≤ 1.08 indicative of brain sparing effect was significantlyhigher in the SGA foetus group. It was associated with a sensitivity of 45.7%,specificity 100%, PPV 100% and NPV 77.3%. Odibo AO et al (2005) reported thatwith a MCA PI/UA PI threshold of less than 1.08, the sensitivity, specificity, positiveand negative predictive values were 72%, 62%, 68% and 67%. They concluded thatthe accuracy of using gestational age-specific reference levels was similar to that ofusing a categorical threshold.
Padmagirison and Rai (2006)[18] noted that when brainsparing effect occurs (CU index < 1.08) and if the prospects for neonatal survival aregood, it is better to deliver the foetus.

Amniotic fluid index and umbilical artery pulsatility index werethe first variable to become abnormal, followed by the middle cerebral artery,aorta,and variation of foetal heart rate, ductus venosus and inferior vena cava.

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& birthweight 3.1Kg).Patrizia et al (2002)[19] also observed lower gestational age at delivery (37.7 ± 20 vs. 38.8 ± 1.6,) and lowerbirth weight (2193 ± 446 vs. 2524 ± 379,) in growth restricted foetuses near term.

Caesarean section rate noted in this study were significantly higher in SGA foetus group. In SGA group CS rate was 51% and in AGA group 32%.

Low APGAR score of < 7 and NICU admissions in this study weresignificantly more in SGA babies in comparison to AGA babies.

In this study SGA foetuses with abnormal Doppler study had a poor outcome in comparison to those with normal Doppler study.SGA babies with abnormal Doppler had lower fetal weight, poor Apgar score, NICUadmissions and higher CS rate.

5. Conclusion

The most common definition accepted for diagnosing IUGR is when the expected foetal weight is less than 10th percentile for gestational age.

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. RizaMadazli et al (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.

With the advent of ultrasonography (USG), it has become the most widely used, standard and simple way of detecting and confirming IUGR.Ultrasound biometry is the gold standard for assessment of foetal size. Foetalweight less than 10th percentile for gestational age is mostly used to diagnosis IUGRbut other criteria like elevated HC/AC ratio,

elevated FL/AC ratio, and presence ofoligohydramnios without reptured membranes, presence of advanced placental gradecan also be used for improving the accuracy of diagnosis. In this series among thevarious risk factors hypertension were more frequent is SGA babies.

Once diagnosis of IUGR is made Doppler imaging is valuable for monitoringthe pregnancy, it provides valuable information about the hemodynamic status of thefoetus.

Flow pattern of uterine artery reflects the evidence of uteroplacental vascularischemia. Umbilical artery Doppler waveforms reflect the status of the fetoplacentalcirculation. Doppler study of MCA provides information regarding hemodynamicrearrangements that occur in response to foetal hypoxia.

The uteroplacental insufficiency seen with IUGR is associated with a rise invascular resistance in uterine & umbilical arteries which can be estimated by raised pulsatility index, resistance index, systolic/diastolic ratio in these arteries, andpersistence of uterine artery diastolic notch, absent & reverse diastolic flow inumbilical artery. In the presence of foetal hypoxemia, central redistribution of bloodflow occurs, known as the Brain – Sparing Reflex manifested by a fall in Pulsatilityindex, resistance indes, systolic/diastolic ratio of MCA, CPI (MCA RI/UA RI) andCUI (MCA PI/UA PI).

Previously foetal arterial Doppler studies were mostly done in umbilical arteryand middle cerebral artery. In this series uterine artery, foetal Umbilical & MCA arterial Doppler velocimetry waveforms were studied.

In this series SGA babies were significantly associated with raised PI, RI andS/D ratio in uterine and umbilical arteries, persistence of notch in uterine artery,absent diastolic flow in umbilical artery, lowered PI, RI, S/D ratio In middle cerebralartey and decreased Cerebroplacental indices.

In SGA foetuses mean gestational age and birth weight were lower. CS ratewas high, low apgar score and NICU admissions were also higher.SGA foetuses with normal Doppler studies most likely represent constitutionally small, not pathologically growth restricted foetuses.

Because the changes in umbilical, uterine & MCA strongly correlate withpregnancy outcome in growth restricted fetuses the use of fetal biometry & Dopplerexamination is recommended in all cases of suspected IUGR cases.

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Author Profile

Dr. Harkiranpreet Kaur Kalsi MBBS (corresponding author): is currently post gradute junior resident in department of obstetrics and gynaecology MMIMSR, Mullana, Ambala, Haryana

Dr. Parminder Kaur Sachdev MBBS, MD is currently working as associate professor in department of obstetrics and gynaecology MMIMSR, Mullana, Ambala, Haryana