 DOI: 10.18231/2348-7682.2017.0007

Magnetic resonance imaging of the placenta in intrauterine fetal growth restriction

S. Kalpana[1,*], H. Iyengeran[2], Ravi[3], Malathy[4], R. Karthick[5]

[1,3,4]Professor, [2]Assistant Professor, Barnard Institute of Radiology, Madras Medical College, Chennai, Tamil Nadu, [5]Research Scientist, Multi-disciplinary Research Unit, Chennai, Tamil Nadu

***Corresponding Author:**
Email: kapudr@gmail.com

Abstract

Intrauterine growth restriction occurs when the foetus fails to attain its genetically determined potential size. The present study was carried out to test the hypothesis that placental MR morphology and signal intensity measurements could differentiate between normal placentas and placentas in early or late intrauterine growth restriction. Normal and growth restricted foetuses were studied by Ultrasound and MRI at varying weeks of gestation. 98 growth restricted foetuses and 61 normal foetuses were included in the study. Ultrasound was done on a Siemens Antares ultrasound machine and MRI on a Siemens 1.5 Tesla system. Data was collected pertaining to gestational age, foetal weight and placental appearance by Ultrasound and MRI. Post processing signal intensity measurements of placenta were obtained. Echogenic cysts and echogenic cotyledons were seen more frequently in the placenta of IUGR foetuses by ultrasound. Globoid appearance of placenta in MRI denoted IUGR ($p < .005$).Placental signal intensity calculated by Region of Interest (ROI) showed a decline in normal pregnancies with advancing gestational age and significant difference between normal and IUGR placentas. Significant difference was found in T2 weighted Amniotic Fluid/Placental signal intensity ratios between normal and growth restricted pregnancies. MR evaluation of the placenta provides significant contribution towards assessment of IUGR placentas. Evaluation of the placenta should be done in any antenatal MRI study and MRI may play a role in future in management of Placental insufficiency.

Keywords: Placenta, Intrauterine growth restriction, Placental MRI, Placental signal intensity.

Introduction

Intrauterine growth restriction occurs when the foetus fails to attain its genetically determined potential size. Currently, estimated foetal weight by ultrasound or birth weight below the 10th percentile, at a given gestational age is defined as intra uterine foetal growth restriction (IUGR). The cause of foetal growth restriction can be due to maternal, foetal or environmental/placental causes.(1) Coexisting Maternal diseases like diabetes or hypertension, foetal causes like congenital anomalies and genetic abnormalities, placental/environmental causes like malnutrition and infections(1)can all result in IUGR. Early diagnosis by non-invasive means is the key stone to management of these growth restricted foetuses to prevent morbidity and mortality. The growth restricted foetus is at higher risk for perinatal morbidity and mortality,(2) as well as adult onset problems like diabetes and hypertension.(3)

Ultrasound evaluation of the placenta in pregnancies typically includes assessment of location and appearance. In third trimester ultrasound evaluation is limited by poor soft tissue contrast resolution, maternal body habitus and posterior location of the Placenta. Previous studies have proved that Placental grading by Ultrasound[4] is inconsequential in its prediction of IUGR.

Antenatal MRI due to its lack of Radiation exposure is frequently done as an additional investigation in pregnancy. Recent articles are now focussing on other aspects of placental imaging by MRI especially, MR characteristics of Placenta in normal and IUGR pregnancies. MR can demonstrate the uterine wall, the placenta, amniotic fluid as well as the foetus with excellent contrast. This study was undertaken to evaluate the role of MR in imaging the placenta in early and late IUGR. Comparison of MR placental imaging in IUGR foetuses according to gestational age has not been reported so far.

Aims and Objectives

To test the hypothesis that placental MR morphology and signal intensity measurements could differentiate between normal placentas and placentas in early or late intrauterine growth restriction.

Material and Methods

This Quantitative, Observational, Case control study was a prospective study carried out between June 2012 and July 2014.Approval for the study was obtained from College Ethical Committee. Written maternal consent was obtained from individual antenatal mothers before screening.

Antenatal mothers referred for imaging studies to the Radiology department were screened by Ultrasound and recruited for the study. Inclusion criteria were antenatal singleton pregnancies between 20 - 40 weeks of gestational age. Mothers with multiple pregnancies or with foetuses with congenital anomalies were excluded from the study. Recruited mothers were screened for Diabetes, hypertension and preeclampsia according to standard hospital protocol.

Selected singleton antenatal mothers underwent ultrasound screening by a Siemens Antares machine. Assessment of foetal weight, placental location, foetal

biometry and liquor volume were obtained transabdominally by a 3.5 MHz curvilinear probe. A foetus was assigned as IUGR if the ultrasound estimated foetal weight was below the 10th percentile for gestational age. Foetuses weighing above the 10th percentile were assigned to the control group. Based on estimated foetal weight by ultrasound, they were grouped into three categories. Category A- Severe IUGR foetuses with less than 5th percentile of expected weight for gestational age, Category B- Mild IUGR foetuses with weight between 5th to 10th percentile of expected weight and Category C- normal foetuses with weight above 10th percentile of expected weight for gestational age.

Obstetric MRI was performed according to standard protocol using a 1.5 Tesla Siemens MRI system (Germany). Six of the MRI studies were done on a 3 Tesla Siemens MRI system. T1 and T2 weighted spin echo sequence through the entire uterus was performed. No sedation or contrast was used. MRI images of the uterus and placenta were obtained in Axial, Sagittal and Coronal planes.

MR images were assessed for placental location, volume and appearance. Placental volume was calculated by measuring 2 longest measurements in axial and sagittal plane and placental thickness at site of cord insertion on axial plane. Placental T1 and T2 signal intensity was calculated as an average of three readings. The measurements were obtained by placing circular Region of Interest (ROI's) markers, on the axial slice in which the placental thickness was maximum. The Placenta was arbitrarily divided into three parts central, right and left. Three readings were taken from the centre of each part well away from the edges of the placenta. Amniotic fluid signal intensity was obtained as an average of three ROI's placed in three deepest pockets, preferably on a single T2W axial slice or on adjacent axial slices in presence of oligohydramnios. Placental signal intensity was assessed in relation to amniotic fluid signal intensity.

All statistical analysis was done using SPSS software. Frequency distribution and Descriptive statistics were obtained. Students T- Test, Anova and Levennes test for equality of means were done both between categories and between groups. Sensitivity and Specificity ratios were calculated.

Results

147 singleton antenatal mothers with ages ranging from 18 to 38 years underwent ultrasound screening. Foetal weight ranged between 446 gm to 3791 gm. A total of 90 growth restricted foetuses and 57 normal foetuses were screened. Foetal weight of all 90 growth restricted foetuses was below the 10th percentile. Further sub grouping (Table 1) was done based on gestational age at time of ultrasound. Group 1- premature i.e. less than 29 weeks, Group 2 -early presentation i.e. between 29 to 34 weeks and group 3- late presentation i.e. between 34 weeks to term. Demographics of sample volume are given in Table 1.

Table 1: Grouping of antenatal mothers included in study

Category	Percentile of Gestational weight(N=147)	Group: Gestational age in Wks	Number (%)
A	<5% IUGR (70)	1-<29Wks	0
		2 -29-34 wks	16 (22.8)
		3 ->34 wks	54 (77.1)
B	5- 10 % IUGR (20)	1 -<29Wks	2 (10)
		2-29-34 wks	6 (30)
		3->34 wks	12 (60)
C	> 10 % Normal (57)	1-<29Wks	4 (7.0)
		2 -29-34 wks	17 (29.8)
		3->34 wks	36 (63.1)

Group 1- <29 weeks = 6.Group 2- 29-34 weeks = 39.Group 3 - > 34weeks =102

The ultrasound assessment of placenta included placental grading, calcification and placental appearance. Placental grading was done according to Grannum et al classification.[4] In the second group(29-34 weeks GA), 81.2% of normal foetuses were grade 1 or 2 while 82.6% of IUGR foetuses belonged to grade 2 or 3. In group 3(late gestation)97.5% of the 36normal foetuses were associated with grade 2 or 3 placentas while only less than 3% had grade 1 placentas. Of the 66IUGR foetuses scanned at late gestation95.7% had grade 2 or 3 placentas and less than 4% had grade 1 placentas. Grading of placentas was a poor indicator of growth restriction.

Placental USG appearance was graded based on homogenous or heterogenous appearance, presence of cysts with or without echogenic margins and presence of hyperechoic cotyledons. Cysts with thin margins were noticed in both mature and IUGR placentas while cysts with echogenic margins were noted in 17.5% (10/57) of normal and 24.4% (22/90) of IUGR placentas. Echogenic cotyledons (Fig. 3) were seen in 17% (5/39) of mature placentas and in 5% (5/94) of IUGR placentas. Sensitivity, Specificity of cysts with echogenic margins was 0.31 and 0.87

respectively. Positive Predictive value was 0.68 and negative predictive value was 0.59. Odds ratio was 1.18. Echogenic cotyledons had a sensitivity of 0.05 and specificity 0.87with a PPR of 0.5 and NPR of 0.27.

Placental calcification was graded as 1-no calcification, 2-specks of calcification, 3-basal calcification and 4-calcified cotyledons. Basal and cotyledon calcification was seen in only 12% of normal placentas in group 3 and in 22% of severe IUGR and 7% of mild IUGR. The sensitivity of presence of calcification in less than 34 weeks as a predictor of IUGR was 0.16 and specificity was 0.09.Positive predictive value was 66. P value was not significant between categories but was .01 between the groups in category B.

Table 2: Distribution of placenta based on shape by MRI

PLAC	Group 1 (<29 weeks)			Group 2(29-34 weeks)			Group 3(-above 34 weeks)			Total
Category IUGR	5% IUGR	5-10%	>10%	5%	5-10	>10%	5%	5-10%	>10 %	
1-disc	-	2(100)	2(50)	9(69.2)	4(66.7)	14(87.5)	37(74)	11(91.7)	32(78)	111
2-thin and long	-	0	0	1(7.7)	0	1(5.8)	3(6)	0	1(2.8)	6
3-globoid	-	0	2(50)	3(23.1)	2(33.3)	2(6.3)	10(20)	1(8.3)	2(8.3)	22
Total		2	4	13	6	17	50	12	35	
Group total	6			36			97			
Grand total	139									

Note: Percentages given in brackets adjacent to actual number in each category.

MRI of placenta was done in all pregnancies. Artefact free valid MRI images were obtained in 139 pregnancies. Placental shape was grouped as disc shape, thin and elongated shape and globoid shape. (Table 2).Of the 22 placentas with globoid shape 13(59%) belonged to category A, 3 (13.6%) to category B and 6 (27%) to category C. Of the 6 globoid placentas in normal Category C pregnancies, 3 mothers had associated conditions like diabetes, hypertension or cardiac pathology. Of the 16 globoid placentas in the IUGR category, 5 (31%) presented during early IUGR (group 2) and 11 (68%) in late IUGR (i.e. group 3). The correlation of globoid appearance of placenta with IUGR had P value 0.001.The sensitivity; specificity was 0.22 and 0.88 respectively with a positive predictive value of 71.

Table 3: MR appearance of placenta according to gestational age

Placental MR appearance	Group 1 (<29 weeks GA)		Group 2 (29-34 weeks GA)		Group 3 (above 34 weeks GA)		Total
	IUGR	>10% Weight	IUGR	>10% Weight	IUGR	>10 % Weight	
1- homo +iso	1	3(75)	4(25)	4(26)	8(14)	8(22)	28
2-homo +hyper	0	0	0	0	2(3)	5(14)	7
3-homo+hypo	0	1 (25)	1(6.2)	1(6)	3(5)	4(11)	10
4-heter+hyper	1	0	8(50)	5(33)	26(45)	11(31)	51
5 -heter+hypo	0	0	0	2 (13)	4(7)	0	6
6 -heter+hypercots	0	0	3(18)	3(20)	10(17)	6(17)	22
7 -hetero hypocots.	0	0	0	0	4(7)	1(2)	5
Total	2	4	16	15	57	35	
Total in group	6		31		92		
Grand total	129						

Key: homo- homogenous, iso -isointense, hyper- hyperintense, hypo -hypointense, heter -heterointense, cots-cotyledons. Note: Percentages rounded off to nearest number given in brackets adjacent to actual number in each group.

Placentas were graded by appearance into 7 types based on appearance (Table 3). Of the 129 placentas graded by appearance 6 were screened in group 1, 31 in group 2, and 92 in group 3.P value for MR intensity of placenta was .05 between category A and C. Presence of hypointensity in placenta (i.e. type 3, type 5 or type 7) as a predictor of IUGR had a sensitivity, specificity, Positive and Negative predicative value of 0.16, 0.83, 57 and 41 respectively.

Table 4: Gestational age wise MRI signal intensity measurements of normal and IUGR placentas

PLAC	Group 1 (<29 weeks)			Group 2(29-34Weeks)			Group 2 (-above 34weeks)		
% FET WT	5% (0)	5-10% (2)	>10% (4)	< 5% (12)	5-10% (6)	>10% (16)	< 5% (46)	5-10% (12)	>10% (36)

(N)									
T1	-	172	108	130	95.6	96	108	95	84
T2mean	-	344	237	248	117	200	205	178	167

Placental signal intensity values were calculated for T1 and T2 weighted images. Mean T1 and mean T2 signal intensity of normal placentas decreased with advancing gestational age.(Table 4) This was in accordance with earlier studies.

Mean placental signal intensity in normal versus all category IUGR placentas is given in Table-5. Significant difference was found for T1W and T2W placental values.

Table 5: MRI placental signal intensity mean values

	Category C Normal	Category B IUGR 5-10%	Category A IUGR<5%	P value
T1	68.7	81.4	106	.042
T2	167	175	175	.036

Average T2 signal intensity of Amniotic fluid in normal pregnancies decreased with advancing gestational age.(Table 5)and was significantly higher in IUGR pregnancies.

T2 weighted Amniotic fluid signal intensity to Placental signal intensity ratios were calculated. Mean AF/PL ratios showed a decreasing trend in normal pregnancies with advancing gestational age. IUGR foetuses however showed an increasing trend with advancing gestational age. Within the same age groups the ratios in growth restricted foetuses were higher than in normal growth foetuses. Mean AF/PL ratios were 1.7 in normal pregnancies, 2.1 in Category B foetuses and 2.2 in Category A foetuses. P value was .003 for AF/PL ratios between normal and less than 5th percentile IUGR pregnancies.

Ultrasound placental morphology evaluation revealed no significant correlation of Placental grading, or degree of calcification with IUGR. Placental appearance of Cysts with echogenic margins (Fig. 1) was seen in 35% of IUGR placentas and echogenic cotyledons was visualised in 47% of IUGR placentas. Both were more specific than sensitive indicators for IUGR.

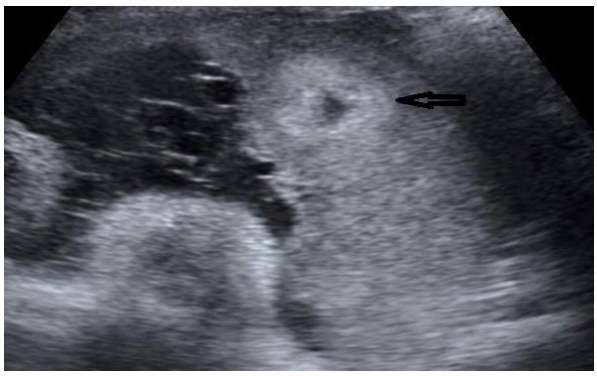

Fig. 1: Transverse zoomed Ultrasound image of the Placenta of Category A IUGR foetus showing cyst with echogenic walls (arrow)

Placental morphology evaluation by MRI showed that the presence of thick globular placenta (Fig. 2) was significantly associated with severe growth restriction (p = 0.001). Finding of Globoid placenta is more specific (0.88) than sensitive (0.22) indicator of IUGR. A Globoid appearance of the placenta in normal foetuses indicated underlying maternal medical conditions.

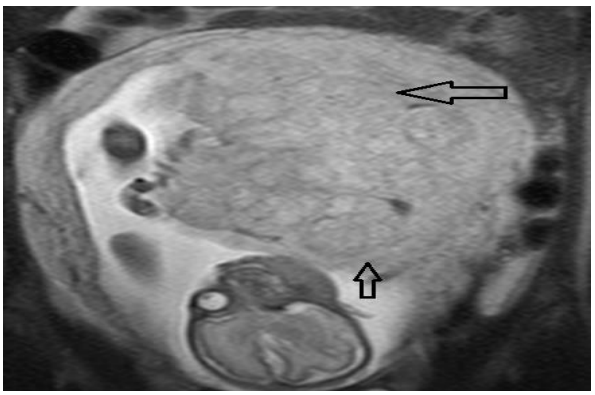

Fig.2: Coronal T2W MRI image of the uterus of a mother with Category A IUGR foetus reveals thick globoid shaped placenta. Baby died postnatal

Placental appearance by MRI in early gestation had a homogenous isointense appearance (Fig. 3) while IUGR placentas were hetero intense in appearance. Between 29-34 weeks normal placentas were homogenous in intensity or had hyper intense cotyledons or hyerintense ill-defined areas. Similar appearance was also seen in most IUGR placentas in this age group making differentiation difficult. In late gestation the normal placentas were predominantly heterointense in appearance with homo intense appearance seen in 22% of normal placentas. On the other hand homogenous placenta was seen in only 14% of IUGR placentas in this age group. The presence of hypo intensity in placenta (Fig. 4) was therefore assessed across age groups as a predictor of IUGR. This

revealed a less sensitive but more specific correlation with IUGR.

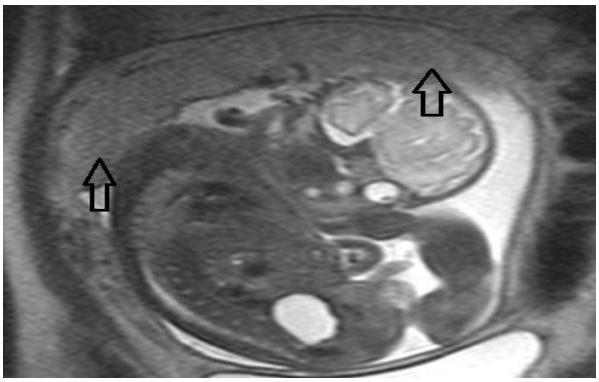

Fig.3: Coronal T2W MRI image ofnormal 29 weeks foetus with homogenous disc shaped (arrows) placenta

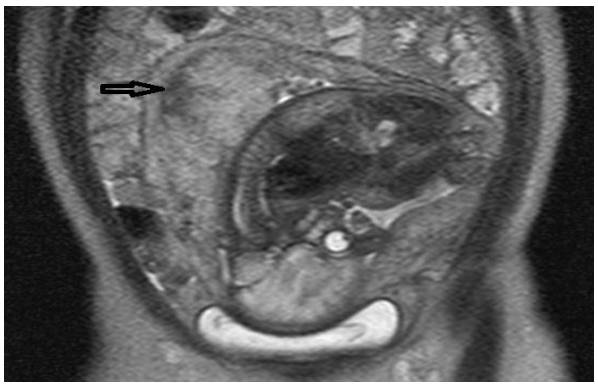

Fig. 4: T2 W coronal section of category A,group 2 foetus with hypointense basal area in placenta(arrow) andoligohydramnios who died three days postnatal

Overall Mean placental T1 and T2 values were significantly higher in IUGR placentas (Fig. 5) as compared to normal placentas. Significant difference was found in AF/PL (Amniotic fluid /Placental signal intensity) ratios between normal and less than 5thpercentile IUGR pregnancies. MRI appearance of placenta, signal intensity measurements and ratios reflect a direct assessment of placental pathology not feasible by other modalities. Differences in these measurements between normal and IUGR placenta reflect placental infarcts, perivillous fibrin deposition and villous thrombosis occurring in IUGR placentas.

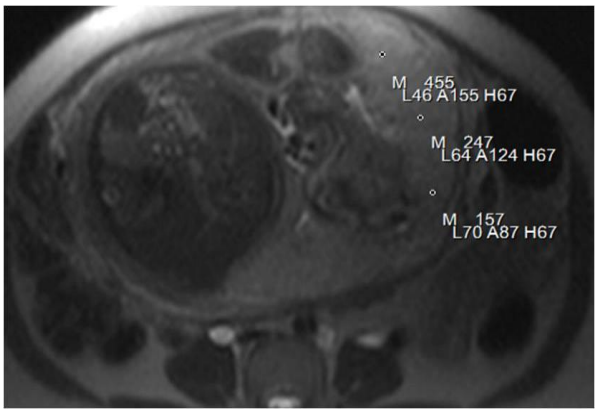

Fig. 5: T2W axial MRI image of Category A, Group 2 foetus with ROI markers measuring signal intensity of placenta. Note Oligohydramnios

Discussion

This is one of the first Indian studies investigating the MR Placental appearance in growth restricted foetuses versus normal foetuses. It is also the first study assessing MR placental appearance in IUGR foetuses according to gestational age. Singleton antenatal mothers with no foetal anomalies were recruited for the study to determine the relationship between placental ultrasound and placental MRI in IUGR. The cut of value for defining IUGR is below the 10th percentile of foetal weight for that particular gestational age.[5] The natural history of growth restriction differentiates between early onset and late onset[5] which have different biochemical, histological and clinical features.[6] IUGR is an important obstetric complication affecting 5% of all pregnancies.[7]

Ultrasound placental morphology evaluation revealed no significant correlation of Placental grading, or degree of calcification with IUGR. This agrees with previous studies which found that placental grading did not correlate with IUGR.[4] Placental appearance of Cysts with echogenic margins (Fig. 1) was seen in 35% of IUGR placentas and echogenic cotyledons was visualised in 47% of IUGR placentas. Both were more specific than sensitive indicators for IUGR. The same findings of echogenic cystic lesions indicating intervillous thrombosis and echo dense lesions suggesting villous infarction was found to correlate with placental insufficiency by earlier studies.[8]

Placental morphology evaluation by MRI showed that the presence of thick globular placenta significantly associated with severe growth restriction. This is comparable to earlier studies.[9]Placental appearance by MRI in early gestation had a homogenous isointense appearance while IUGR placentas were hetero intense in appearance. Between 29-34 weeks normal placentas were homogenous in intensity or had hyper intense cotyledons or hyerintense ill defined areas. Similar appearance was also seen in most IUGR placentas in this age group making differentiation difficult. In late gestation the normal placentas were predominantly

heterointense in appearance with homo intense appearance seen in 22% of normal placentas. On the other hand homogenous placenta was seen in only 14% of IUGR placentas in this age group. Previous studies correlated with pathology by Linduskaet al[10] have documented placental infarct as central hyper intensity with surrounding hypo intensity or as a diffuse region of hypo intensity. The presence of hypo intensity in placenta was therefore assessed across age groups as a predictor of IUGR. This revealed a less sensitive but more specific correlation with IUGR.

The normal maturation sequence of placenta by MRI has been documented earlier by Blaicheret al,[11] with decreasing placental signal intensity with advancing gestational age. This study confirmed these findings in a larger study group. Within the same gestational age group IUGR placentas had higher signal intensity values as compared to normal placentas. This trend of increased signal intensity measurements was seen across all gestational age groups for both T1 and T2 signal intensities. Between groups T1 had a higher statistical significance of .008 to predict IUGR as compared to T2.

Overall Mean placental T1 and T2 values were significantly higher in IUGR placentas as compared to normal placentas. Both Placental T1 and T2 signal intensities were statistically significant between normal and IUGR pregnancies.

Significant difference was found in AF/PL (Amniotic fluid /Placental signal intensity) ratios between normal and less than 5th percentile IUGR pregnancies. MRI appearance of placenta, signal intensity measurements and ratios reflect a direct assessment of placental pathology not feasible by other modalities. Differences in these measurements between normal and IUGR placentas reflect placental infarcts, perivillous fibrin deposition and villous thrombosis occurring in IUGR placentas.

Conclusion

Although Currently Ultrasound still remains the best cost effective tool for evaluating placental morphology and Doppler the best tool to evaluate foetal outcome; this study brings out the fact that MRI also differentiates between normal and IUGR placentas. MRI may prove to be a more specific tool to evaluate placental pathology in future. Whenever MR imaging of growth restricted foetuses is done assessment of the placental shape, appearance and signal intensity measurements will provide additional information about the placental status.

References

1. Krishna Usha, Bhalerao Sarita. Placental insufficiency and foetal growth restriction. The Journal of Obstetrics and Gynecology of India September–October 2011;61(5):505–511.
2. Kady S, Gardosi J. Perinatal mortality and foetal growth restriction. Best Pract Res Clin Obstet Gynaecol 2004;18:397-410.
3. Chatelain P. Children born with intra-uterine growth retardation (iugr) or small for gestational age (sga): Long term Growth and metabolic consequences. Endocrine regulations 2000;33:36.
4. Grannum Pat, Berkowitz RL, Hobbins JC. The ultrasonic changes in the maturing placenta and their relation to foetal pulmonic maturity. Am J ObstetGynecol 1979;133:915.
5. Turan OM, Turan S, Gungor S, et al. Progression of Doppler abnormalities in intrauterine growth restriction. Ultrasound ObstetGynecol 2008;32:160-7.
6. Crispi F, Dominguez C, Llurba E, Martin- Gallan P, Cabero L, Gratacos E. Placental angiogenic growth factors and uterine artery Do ppler findings for characterization of different subsets in preeclampsia and in isolated intrauterine growth restriction. Am J ObstetGynecol 2006;195:201-7.
7. Romo A, Carceller R, Tobajas J. Intrauterine growth retardation (IUGR): epidemiology and etiology. PediatrEndocrinolRev 2009; 6Suppl 3:332-336.
8. MeghanaToal,Vandana Chadda, Rory Windrim et al.Ulrasound detection of Placental Insufficiency in Women with Elevated Second Trimester Serum Alpha Protein or Human Chorionic Gonadotropin. JOGC March 2008, 198206.
9. Damodaram M, Story L, Eixarch E. Placental MRI in foetal growth restriction. Placenta. 2010;31(6):491–8.
10. LinduskaN,DekanS,MesserschmidtA,KasprianG,Brugger PC,ChalubinskiK, et al.PlacentalpathologiesinfoetalMRIwithpathohistological correlation. Placenta 2009;30:555e9.
11. Blaicher W, Brugger PC, Mittermayer C, Schwindt J, Deutinger J, Bernaschek G, et al. Magnetic resonance imaging of the normal placenta. Eur J Radiol 2006;57:256–260.