

**ASSOCIATION OF DIFFERENT SONOGRAPHIC PARAMETERS WITH ONSET OF IUGR**

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**ABSTRACT****BACKGROUND**

Ultrasound has become the essential tool of modern obstetric practice as it is non-invasive, safe and radiation free. IUGR is defined as the pathologic inhibition of intrauterine foetal growth and the failure of the foetus to achieve its growth potential. Over the last decade, two different patterns of IUGR has been characterised on the basis of gestational age of onset. IUGR has a different phenotypic expression, evolution and outcome when it starts early in gestation called early-onset IUGR and it is different when it starts late in gestation known as late-onset IUGR. Early diagnosis and timely management decisions are the cornerstones for optimum outcome in these cases.

**MATERIALS AND METHODS**

This was a cross-sectional study collected from 152 pregnant women with IUGR fetuses, attending/ referred to Maharani Laxmi Bai Medical College and Hospital, Jhansi, Uttar Pradesh. The gray scale and colour Doppler sonography was routinely performed in all these IUGR pregnancies. Subsequently, the results were statistically analysed to find the association between different colour Doppler and gray scale parameters and time of onset of IUGR.

**RESULTS**

Abnormality in placenta, increased FL/AC ratio, increased S/D ratio and PI of umbilical artery, decreased S/D ratio and PI of middle cerebral artery and increased mean PI of uterine artery were more strongly associated with early-onset IUGR, while oligohydramnios was more strongly associated with late-onset IUGR. Low lying placenta, increased HC/AC ratio, decreased cerebroplacental ratio (CPR), increased S/D ratio of uterine artery, umbilical vein pulsation and increased PI of ductus venosus were equally associated with both early- and late-onset IUGR.

**CONCLUSION**

With the help of non-invasive, single study, sonographic gray scale and colour Doppler parameters, we can diagnose both types of IUGR, but most of the parameters were found to be more commonly associated with early-onset IUGR. So, we can use them to predict IUGR at an early stage and act accordingly for better perinatal outcome.

**KEYWORDS**

IUGR, Early Onset, Late Onset, Gray Scale, Colour Doppler.

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**BACKGROUND**

Ultrasound has become the essential tool of modern obstetric practice as it is non-invasive, safe and radiation free. With advances in technology and computer processing, what was once a mere curiosity has now become modality of choice for the assessment of the placenta, membranes, fluid, foetal structure and its growth.

IUGR is defined as the pathologic inhibition of intrauterine foetal growth and the failure of the foetus to achieve its growth potential, most often defined on the basis of a weight below the 10th percentile for gestational age.

Over the last decade, two different patterns of IUGR has been characterised on the basis of gestational age of onset. IUGR has a different phenotypic expression, evolution and outcome when it starts early in gestation called early-onset IUGR and it is different when it starts late in gestation known as late-onset IUGR. Early diagnosis and timely management decisions are the cornerstones for optimum outcome in these cases.

**Aims and Objectives**

**The study carried out with the following aims and objectives-**

- Sonographic evaluation of different parameters on gray scale and Colour Doppler in early- and late-onset IUGR.
- Gray scale parameters- Placental lesions, Amniotic Fluid Index (AFI); Head Circumference/ Abdominal Circumference (HC/ AC); Femur Length/ Abdominal Circumference (FL/ AC) and Foetal Weight.
- Colour Doppler parameters- Characteristics of Umbilical Artery (UA); Middle Cerebral Artery (MCA); Uterine Arteries (Ut. A), Umbilical Vein (UV) and Ductus venosus (DV).

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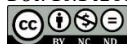
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- To find out the association of different parameters on Sonography on Gray scale and Colour Doppler with early- and late-onset IUGR.

### MATERIALS AND METHODS

This was a cross-sectional study conducted for 18 months (Feb. 2016 to July 2017), which included 152 pregnant ladies of age between 18 years to 35 years having singleton, non-

#### Parameters studied on Grey Scale:

- Fetal weight : < 10th percentile for GA was taken as abnormal
- FL/AC : > 23.5 was taken as abnormal
- HC/AC : > 2 SD for GA was taken as abnormal
- Placenta : Location and lesion (if any)
- AFI (Amniotic fluid index) : < 8 considered abnormal

#### Parameters Studied on Colour Doppler

- Umbilical artery : S/D ratio with 3 as cut-off (> 3 abnormal) and PI with 1 as cut-off (> 1 Abnormal)
- Middle cerebral artery : S/D ratio with 3 as cut-off (< 3 abnormal) and PI with 1 as cut-off (< 1 Abnormal)
- Cerebroplacental ratio : MCA RI/UA RI with 1 as cut-off (< 1 Abnormal)
- Uterine artery : Mean S/D ratio with 3 as cut-off (> 3 Abnormal) and PI with 1.45 as cut-off (> 1.45 Abnormal) and presence of diastolic notch is considered abnormal
- Umbilical vein : Waveform, pulsation is considered abnormal
- Ductus venosus : PI with 0.8 as cut-off (> 0.8 Abnormal)

#### Statistical Analyses

After all the data were collected, the statistical tools were applied to find out the association between the gray scale and colour Doppler parameters and timing of onset of IUGR. The Chi-square test is used to compare the categorical data and degree of freedom. P value of < 0.05 was considered statistically significant.

### RESULTS

- 104 (68.42%) women were from age group of 18 to 25 years, while 48 (31.58%) were from age group of 26 to 35 years.
- 95 (62.5%) women were Primiparous and 57 (37.5%) were Multiparous.
- Taking 32 weeks as cut-off, 42 (27.63%) cases belonged to early-onset IUGR, while 110 (72.37%) cases were from late-onset IUGR.
- Most common medical condition found to be present in mother with IUGR foetus was anaemia followed by pregnancy induced hypertension (Figure 1).

#### Gray Scale Parameters:

##### Placental Position and its Abnormality

Placental position was commonly found to be normal in both early- and late-onset IUGR, while low lying was more common in late-onset IUGR (Table 1). Similarly, placenta was usually normal in both types of IUGR, though abnormality was more common in early-onset IUGR (Table 2).

##### Amniotic Fluid Index (AFI)

49 cases showed reduced AFI, which were more common in late-onset IUGR (Table 3).

##### HC/ AC Ratio

It was found to be increased in 129 cases, more commonly in early-onset IUGR (Table 4).

anomalous foetus, beyond 28 weeks of gestation with features of IUGR.

After taking an informed consent and detailed history from all the patients, all the required parameters on Gray scale and Colour Doppler were obtained using ultrasound machines Medison SA 9900 and Medison SonoAce X8.

#### FL/ AC Ratio

It was found to be increased in 116 cases, more commonly in early-onset IUGR (Table 5).

#### Weight

It was found to be low in 110 cases, more commonly in early-onset IUGR (Table 6).

#### Colour Doppler Parameters

##### Umbilical Artery (UA)

S/D Ratio: It was found to be increased in 86 cases and more common in early-onset IUGR (Table 7).

PI: 88 cases showed increased PI and were more common in early-onset IUGR (Table 8).

##### Middle Cerebral Artery (MCA)

S/D Ratio: It was found to be decreased in 54 cases and more common in early-onset IUGR (Table 9).

PI: 42 cases showed decreased PI and were more common in early-onset IUGR (Table 10).

##### Cerebroplacental Ratio (CPR)

It was found to be decreased in 24 cases and more common in late-onset IUGR (Table 11).

##### Uterine Artery

Mean S/D ratio: 42 cases showed increased S/D ratio and were more common in early-onset IUGR (Table 12).

Mean PI: 28 cases showed increased PI and were more common in early-onset IUGR (Table 13).

##### Umbilical Vein

Only 4 cases showed abnormal umbilical vein, which were slightly more common in late-onset IUGR (Table 14).

##### Ductus Venosus

PI: 7 cases showed increased PI, which were slightly more common in early-onset IUGR (Table 15).

Placental Position	Onset of IUGR				$\chi^2$	df	P-value
	Early Onset (n <sub>1</sub> = 42)		Late Onset (n <sub>2</sub> = 110)				
	f	%	f	%			
Normal	40	95.24	99	90.00	0.502	1	0.4786
Low Lying/Previa	02	04.76	11	10.00			

**Table 1. Distribution of IUGR Pregnancy on the basis of Placental Position and Onset of IUGR**

Placenta	Onset of IUGR				$\chi^2$	df	P-value
	Early Onset (n <sub>1</sub> = 42)		Late Onset (n <sub>2</sub> = 110)				
	f	%	f	%			
Normal	30	71.43	108	98.18	22.915	1	0.0002
Abnormal	12	28.57	02	01.82			

**Table 2. Distribution of IUGR Pregnancy on the basis of Placental Abnormality and Onset of IUGR**

AFI	Onset of IUGR				$\chi^2$	df	P-value
	Early Onset (n <sub>1</sub> = 42)		Late Onset (n <sub>2</sub> = 110)				
	f	%	f	%			
Normal	34	80.95	69	62.73	4.622	1	0.0315
Oligohydramnios	08	19.05	41	37.27			

**Table 3. Distribution of IUGR Pregnancy on the basis of AFI and Onset of IUGR**

HC/AC	Onset of IUGR				$\chi^2$	df	P-value
	Early Onset (n <sub>1</sub> = 42)		Late Onset (n = 110)				
	f	%	f	%			
Normal	05	11.90	18	16.36	0.471	1	0.4925
Increased	37	88.10	92	83.64			

**Table 4. Distribution of IUGR Pregnancy on the basis of HC/AC and Onset of IUGR**

FL/AC	Onset of IUGR				$\chi^2$	df	P-value
	Early Onset (n <sub>1</sub> = 42)		Late Onset (n <sub>2</sub> = 110)				
	f	%	f	%			
Normal	04	09.52	32	29.09	6.438	1	0.0112
Increased	38	90.48	78	70.91			

**Table 5. Distribution of IUGR Pregnancy on the basis of FL/AC and Onset of IUGR**

Foetal Weight	Onset of IUGR				$\chi^2$	df	P-value
	Early Onset (n <sub>1</sub> = 42)		Late Onset (n <sub>2</sub> = 110)				
	f	%	f	%			
Normal	10	23.81	32	29.09	0.424	1	0.5149
Low	32	76.19	78	70.91			

**Table 6. Distribution of IUGR pregnancy on the basis of Foetal Weight and Onset of IUGR**

S/D Ratio of UA	Onset of IUGR				$\chi^2$	df	P-value
	Early Onset (n <sub>1</sub> = 42)		Late Onset (n <sub>2</sub> = 110)				
	f	%	f	%			
Normal	07	16.67	59	53.64	16.91	1	0.0004
Increased	35	83.33	51	46.36			

**Table 7. Distribution of IUGR Pregnancy on the basis of S/D Ratio of UA and Onset of IUGR**

PI of UA	Onset of IUGR				$\chi^2$	df	P-value
	Early Onset (n <sub>1</sub> = 42)		Late Onset (n <sub>2</sub> = 110)				
	f	%	f	%			
Normal	06	14.29	58	52.73	18.43	1	0.0002
Increased	36	85.71	52	47.27			

**Table 8. Distribution of IUGR Pregnancy on the basis of PI of UA and Onset of IUGR**

S/D Ratio of MCA	Onset of IUGR				$\chi^2$	df	P-value
	Early Onset (n <sub>1</sub> = 42)		Late Onset (n <sub>2</sub> = 110)				
	f	%	f	%			
Normal	21	50.00	77	70.00	5.308	1	0.0212
Decreased	21	50.00	33	30.00			

**Table 9. Distribution of IUGR Pregnancy on the basis of SD Ratio of MCA and Onset of IUGR**

PI of MCA	Onset of IUGR				$\chi^2$	df	P-value
	Early Onset (n <sub>1</sub> = 42)		Late Onset (n <sub>2</sub> = 110)				
	f	%	f	%			
Normal	25	59.52	85	77.27	4.788	1	0.0287
Decreased	17	40.48	25	22.73			

**Table 10. Distribution of IUGR Pregnancy on the basis of PI of MCA and Onset of IUGR**

CPR (MCARI/UARI)	Onset of IUGR				$\chi^2$	df	P-value
	Early Onset (n <sub>1</sub> = 42)		Late Onset (n <sub>2</sub> = 110)				
	f	%	f	%			
Normal	37	88.10	91	82.73	0.659	1	0.4169
Decreased	05	11.90	19	17.27			

**Table 11. Distribution of IUGR Pregnancy on the basis of Cerebroplacental Ratio (CPR) and Onset of IUGR**

Mean S/D Ratio of Ut.A	Onset of IUGR				$\chi^2$	df	P-value
	Early Onset (n <sub>1</sub> = 42)		Late Onset (n <sub>2</sub> = 110)				
	f	%	f	%			
Normal	26	61.90	84	76.36	3.178	1	0.0746
Increased	16	38.10	26	23.64			

**Table 12. Distribution of IUGR Pregnancy on the basis of Mean S/D Ratio of Ut. A and Onset of IUGR**

Mean PI of Ut. A	Onset of IUGR				$\chi^2$	df	P-value
	Early Onset (n <sub>1</sub> = 42)		Late Onset (n <sub>2</sub> = 110)				
	f	%	f	%			
Normal	25	59.52	99	90.00	18.79	1	0.0001
Increased	17	40.48	11	10.00			

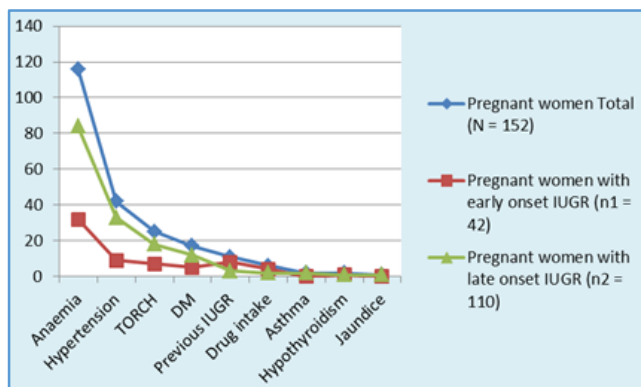
**Table 13. Distribution of IUGR Pregnancy on the basis of Mean PI of Ut. A and Onset of IUGR**

Umbilical Vein Waveform	Onset of IUGR				$\chi^2$	df	P-value
	Early Onset (n <sub>1</sub> = 42)		Late Onset (n <sub>2</sub> = 110)				
	f	%	f	%			
Normal	41	97.62	107	97.27	0.20	1	0.6547
Abnormal	01	02.38	003	02.73			

**Table 14. Distribution of IUGR Pregnancy on the basis of Umbilical Vein Waveform and Onset of IUGR**

PI of Ductus Venosus	Onset of IUGR				$\chi^2$	df	P-value
	Early Onset (n <sub>1</sub> = 42)		Late Onset (n <sub>2</sub> = 110)				
	f	%	f	%			
Normal	40	95.24	105	95.45	0.141	1	0.7073
Increased	02	04.76	005	04.55			

**Table 15. Distribution of IUGR Pregnancy on the basis of PI of Ductus Venosus and Onset of IUGR**



**Figure 1. Distribution of IUGR Pregnancy on basis of Onset and Medical Condition/History**

**DISCUSSION**

Foetal growth and development is a dynamic process since not all foetuses grow or develop equally, extensive research in this sphere has been done. The pathophysiology of intrauterine growth restriction cannot be pinned down to one specific cause. It results due to a series of events occurring along several possible pathways.

Our study included 152 pregnant women, who were suspected to have foetuses with intrauterine growth restriction after considering the inclusion and exclusion criteria. Literature shows diversified results on this challenging and emerging issue. Controversies in the results and inability to compare results could be attributed to various factors such as the sample size in a particular study, varying techniques and different cut-off values.

**Age**

In our study, the ages of pregnant women with IUGR babies were in range of 18 - 35 years. It was observed that the maximum number of IUGR pregnancy were in the age group of 18 - 25 years (68.4%). This could be due to the small sample size in our study or increased pregnancy rate in these age groups.

**Parity**

In this study the maximum IUGR pregnancy were primigravida constituting 62.5% (n= 95) of the sample population. This commensurate with Wen et al<sup>1</sup> research who found that IUGR was more common in primigravid women.

**Onset of IUGR**

In our study, all patients underwent Doppler study in the third trimester of their pregnancy with 27.6% being investigated before 32 weeks of gestation and constituted early-onset IUGR group. 72.4% were above 32 weeks of gestation and constituted late-onset IUGR group.

**Aetiology of IUGR**

Among women where a cause for IUGR was identified, 76.3% had anaemia, 27.6% had pregnancy induced hypertension (PIH) complicating pregnancy. Bad obstetric history as a cause is seen in 7.2%. 45.4% (n= 69) patients of the study group had no detectable cause for IUGR. In a study by Devoe and Ramos-Santos,<sup>2</sup> the association between PIH and IUGR was demonstrated. The reason for anaemia being most commonly associated in our study may be the fact that most of the pregnant women coming to medical college are from Bundelkhand region and belong to low socioeconomic status and most of them are anaemic.

**Placental Position and Abnormality**

V. Chaddha et al<sup>3</sup> showed that early-onset IUGR is strongly associated with poor placental implantation, but in our study no significant association was found between placental position and onset of IUGR.

However, the abnormality in placenta was found to be highly associated with early-onset IUGR. The abnormality that was maximally found in early-onset IUGR was advanced grade placenta. This has been highlighted in a study by Kazzi et al.<sup>4</sup> They demonstrated a direct relationship between high grade placenta and adverse perinatal outcome.

**Amniotic Fluid Index (AFI)**

In a study by Manning,<sup>5</sup> they highlighted the increased risk of oligohydramnios in growth restricted foetuses with abnormal Doppler indices as an associated finding. In our study, we found that although oligohydramnios was associated with both types of IUGR, it was more strongly associated with late onset type of IUGR.

**Head Circumference to Abdominal Circumference Ratio (HC/AC)**

In a study by Nihal and Melissa et al<sup>6</sup> in 2011, the increased HC/AC was found to be associated with early-onset IUGR. In our study, we found that this is equally associated with both early and late onset type of IUGR.

**Femur Length to Abdominal Circumference Ratio (FL/AC)**

Hadlock et al<sup>7</sup> reported that FL/AC is independent of GA. This ratio has been proposed as a very important indicator in the diagnosis of IUGR. Reason for using this ratio was the apparent length sparing effect of FL frequently observed in growth restricted foetus. We studied this parameter and found that it was more commonly associated with early-onset IUGR.

**Umbilical Artery Evaluation**

Burke et al<sup>8</sup> studied 179 women with singleton pregnancies and concluded that admission to neonatal intensive care and early delivery at less than 37 weeks are seen in those with S/D ratios greater than two standard deviations above the mean. Hecher<sup>9</sup> further concluded that it is more strongly associated with early-onset IUGR than the late onset one. Our study showed the similar trend.

Trudinger, Cook and Giles<sup>10</sup> reporting one of the largest outcome series to date (2178 pregnant women) showed that abnormal umbilical artery flow velocity waveforms are associated with a shorter gestation, light birth weight, shorter

length and lower Ponderal Index. Erskine and Ritchie<sup>11</sup> reported a series of significantly growth-restricted fetuses detected by an elevated PI. In our study, the increased PI of umbilical artery was also found to be more strongly associated with early onset type of IUGR. RY Fork et al<sup>12</sup> also found that the abnormal Doppler of UA was more often associated with early-onset IUGR.

### Middle Cerebral Artery Evaluation

**Hecher K<sup>9</sup>** Longitudinal studies on deteriorating early-onset IUGR fetuses have reported that the pulsatility index in the MCA progressively becomes abnormal. Severi<sup>13</sup> and Hershkovitz<sup>14</sup> showed that in late-onset IUGR, there was observational evidence that MCA vasodilatation was associated with adverse outcome independently of the umbilical artery. This suggests a role of MCA Doppler for foetal monitoring in late-onset IUGR cases. In our study, we found that the S/D ratio was lower in 35.5% of cases and PI was lower in 27.6% of cases and we found that the lower indices of MCA were more strongly associated with early-onset IUGR.

### Cerebroplacental Ratio (CPR)

In normal pregnancies, the diastolic component in cerebral arteries is lower than in the umbilical arteries at any gestational age. Therefore, cerebral vascular resistance remain higher than the placental resistance and MCA RI/UA RI remains > 1. If any flow redistribution in favour of the brain occurs, the ratio becomes < 1. Gramellini et al<sup>15</sup> highlighted that CPR provides a better diagnostic accuracy than either vessels, RI considered alone. Gregory R DeVore<sup>16</sup> found that low CPR was more strongly associated with late-onset IUGR. In our study also, low CPR looked to be more commonly associated with late-onset IUGR. However, the association was found insignificant on Chi-square test.

### Uterine Artery Evaluation

Uterine Doppler evaluation in the second or first trimester has been proposed by Martin et al<sup>17</sup> as a screening tool for early-onset IUGR with detection rates of about 75% and 25%, respectively, for a false-positive rate of 5% - 10%. In our study also, the mean PI of uterine arteries was more strongly associated with early-onset IUGR. However, the mean S/D ratio was found to be equally associated.

### Umbilical Vein Evaluation

Nakai et al<sup>18</sup> showed that fetuses with pulsation in the umbilical vein in the second and third trimesters have a higher morbidity and mortality even in the setting of normal UA blood flow. In our study, umbilical pulsation was noted in only 2.6% (n= 4) cases and no predominant association with either early or late-onset IUGR was noted. It can be attributed to small no. of cases.

### Ductus Venosus Evaluation

Hecher et al<sup>9</sup> found that ductus venosus PI is an important indicator for the optimal timing of delivery before 32 weeks of gestation and correlate with foetal outcome at delivery. Ferrazzi et al<sup>19</sup> identified the temporal sequence of abnormal Doppler changes in the foetal circulation in early growth restricted fetuses. However, in our study no such

association was found. It might be due to very less no. of cases 4.61% (n= 7), in which abnormal PI was found.

### CONCLUSION

Majority of the patients forming our study were in the age group of 18 to 25 years and most of them were primigravida and with late-onset IUGR.

Associated risk factors were anaemia, PIH, DM and previous IUGR, TORCH infection, history of drug intake and hypothyroidism with anaemia being the most common risk factor followed by PIH.

Abnormality in placenta, increased FL/AC ratio, increased S/D ratio and PI of umbilical artery, decreased S/D ratio and PI of middle cerebral artery and increased mean PI of uterine artery were more strongly associated with early-onset IUGR. Oligohydramnios was more strongly associated with late-onset IUGR.

Low lying Placenta, increased HC/AC ratio, decreased Cerebroplacental Ratio (CPR), increased S/D ratio of Uterine artery, Umbilical vein pulsation and increased PI of Ductus venosus were equally associated with both early- and late-onset IUGR.

We concluded that with the help of non-invasive, single study, sonographic gray scale and colour Doppler parameters we can diagnose both types of IUGR, but most of the parameters were found to be more commonly associated with early-onset IUGR. So, we can use them to predict IUGR at an early stage and act accordingly for better perinatal outcome.

### REFERENCES

- [1] Wen SW, Goldenberg RL, Cutter GR, et al. Intra-uterine growth retardation and preterm delivery: prenatal risk factors in an indigent population. *American Journal of Obstetrics and Gynaecology* 1990;162(1):213-8.
- [2] Devoe LD, Ramos-Santos E. Antepartum fetal assessment in hypertensive pregnancies. *Clinics in Perinatology* 1991;18(4):809-32.
- [3] Chaddha V, Viero S, Huppertz B, et al. Developmental biology of the placenta and the origins of placental insufficiency. *Semin Fetal Neonatal Med* 2004;9(5):357-69.
- [4] Kazzi GM, Gross TL, Sokol RJ, et al. Detection of intra-uterine growth retardation: a new use for sonographic placental grading. *American Journal of Obstetrics and Gynaecology* 1983;145(6):733-7.
- [5] Manning FA. Intra-uterine growth retardation, diagnosis, prognostication and management based on ultrasound methods. In: Fleischer A, Manning FA, Jeanty PH, et al. eds. *Sonography in obstetrics and gynaecology: principle and practise*. 5<sup>th</sup> edn. New York: Appleton & Lang 1996a; p. 517-36.
- [6] Nihal RA, Melissa GW, Leslie KP, et al. Utility of head/abdomen circumference ratio in the evaluation of severe early-onset intrauterine growth restriction. *J Obstet & Gynaecol Canada* 2011;33(7):715-9.
- [7] Hadlock FP, Deter RL, Harrist RB, et al. A date-independent predictor of intra-uterine growth retardation: femur length/abdominal circumference ratio. *American Journal of Reonatology* 1983;141(5):979-84.

- [8] Burke G, Stuart B, Crowley P, et al. Is Intrauterine growth retardation with normal umbilical artery blood flow a benign condition? *Br Med J* 1990;300:1044-5.
- [9] Hecher K, Bilardo CM, Stigter RH, et al. Monitoring of fetuses with intrauterine growth restriction: a longitudinal study. *Ultrasound Obstet Gynecol* 2001;18(6):564-70.
- [10] Trudinger BJ, Cook CM, Giles WB, et al. Fetal umbilical artery velocity waveforms and subsequent neonatal outcome: Clinical significance. *British Journal of Obstetrics and Gynaecology* 1991;98(4):378-84.
- [11] Erskine RL, Ritchie JW. Umbilical artery blood flow characteristics in normal and growth-retarded fetuses. *Br J Obstet Gynaecol* 1985;92(6):605-10.
- [12] Fok RY, Pavlova Z, Benirschke K, et al. The correlation of arterial lesions with umbilical artery Doppler velocimetry in the placentas of small-for-dates pregnancies. *Obstet Gynecol* 1990;75(4):578-83.
- [13] Severi FM, Bocchi C, Visentin A, et al. Uterine and fetal cerebral Doppler predict the outcome of third-trimester small-for-gestational age fetuses with normal umbilical artery Doppler. *Ultrasound Obstet Gynecol* 2002;19(3):225-8.
- [14] Hershkovitz R, Kingdom JC, Geary M, et al. Fetal cerebral blood flow redistribution in late gestation: identification of compromise in small fetuses with normal umbilical artery Doppler. *Ultrasound Obstet Gynecol* 2000;15(3):209-12.
- [15] Gramellini D, Folli MC, Raboni S, et al. Cerebral-umbilical Doppler ratio as a predictor of adverse perinatal outcome. *Obstetrics & Gynaecology* 1992;79(3):416-20.
- [16] DeVore GR. The importance of the cerebroplacental ratio in the evaluation of fetal well-being in SGA and AGA fetuses. *Am J Obstet Gynecol* 2015;213(1):5-15.
- [17] Martin AM, Bindra R, Curcio P, et al. Screening for pre-eclampsia and fetal growth restriction by uterine artery Doppler at 11-14 weeks of gestation. *Ultrasound Obstet Gynecol* 2001;18(6):583-6.
- [18] Nakai Y, Miyazaki Y, Matsuoka Y, et al. Pulsatile umbilical venous flow and its clinical significance. *Br J Obstet Gynaecol* 1992;99(12):977-80.
- [19] Ferrazzi E, Bozzo M, Rigano S, et al. Temporal sequence of abnormal Doppler changes in the peripheral and central circulatory systems of the severely growth-restricted fetus. *Ultrasound Obstet Gynecol* 2002;19(2):140-6.