Original Research Article

US Doppler Indices in Umbilical and Fetal MCA in Diagnosis of IUGR Fetuses

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Abstract

Background: Intrauterine growth restriction remains a leading contributor to perinatal mortality and morbidity. There is no cure, management is reliant on a structured antenatal surveillance program with timely intervention. Recent advances in ultrasound and Doppler have elucidated several mechanisms of evolution of disease and prediction of threat of intrauterine hypoxia and acidaemia well in advance of other surveillance tests.

Materials and methods: This prospective study was conducted in 110 high risk pregnant women attending OPD, admitted in antenatal wards and labor room at Government General Hospital, Siddipet, over a period of 2 years from October-2016 to September 2018; Ultrasound examination was done for interval growth, AFI, placental pathology. Fetal well-being was assessed with Doppler studies of UA and MCA, daily fetal movement count, NST, BPP.

Results: In the present study, PIH was found to be the commonest (50.9%) cause of IUGR. Abnormal Doppler Indices in Umbilical and MCA correlated statistically with lower birth weight, higher rates of caesarean delivery, oligohydramnios, lower Apgar scores, perinatal death, and higher admissions to NICU. AEDF/REDF was associated with highest perinatal loss, poor perinatal outcome. Cerebroplacental ratio < 1 (C/U<1) had 100% specificity and 100% PPV.

Conclusion: Doppler technology enables a better understanding of the hemodynamic changes in the fetus. It can help in identifying the changes in the fetal circulation well in advance of other surveillance tests, thus identify the truly hypoxic fetus. Interval changes in Doppler indices are useful in determining monitoring frequencies and optional time for delivery.

Key words

IUGR, Ultra sound, Doppler, Umbilical artery.

Introduction

Intrauterine growth restriction is defined as the sonographically estimated fetal weight less than 10^{th} percentile for the gestational age [1]. IUGR is the result of numerous pathologies that reduce fetal cell size and when early and severe enough in cell number [2].

IUGR can be classified into [3]

- Type 1/intrinsic/symmetrical
- Type 2/ extrinsic/asymmetrical

Intrinsic IUGR arises from fetal conditions such as infections or chromosomal abnormalities. These fetuses grow slowly because their growth potential has been permanently affected usually by a severe insult in the first trimester and tend to grow in a low percentile on growth chart. Medical interventions to improve fetal growth usually have little effect.

Extrinsic IUGR results when the growth failure is due to an element outside of the fetus such as uteroplacental insufficiency, restriction in nutrients supply. Accurate antenatal diagnosis offers the best opportunity to reduce complications associated with IUGR.

In India according to recent UNICEF surveys, the incidence of IUGR is 25-30%. IUGR due to placental vascular insufficiency is rampant in developing countries like India [4]. Current challenges in the clinical management of IUGR include accurate diagnosis of truly growth restricted fetuses, selection of appropriate fetal surveillance and optimizing the timing of delivery. Despite the potential for a complicated course, antenatal detection of IUGR and its antepartum surveillance can improve outcomes in high risk pregnancies.

Doppler sonography offers a unique tool for the non-invasive evaluation of uteroplacental and fetoplacental circulation [5]. Trials have shown that there is significant decrease in perinatal mortality when evaluation of umbilical artery Doppler waveform is included in the management protocol for high risk pregnancies [6] in antenatal period. The absence of end diastolic frequencies is correlated with fetal acidosis and hypoxia.

In cases of IUGR, Wladimiroff (1986) have described compensatory reduction in vascular résistance in fetal brain during hypoxia referred to as brain sparing effect [7, 8]. Increased resistance in uterine artery as indicated by an elevated S/D ratio and persistence of an early diastolic notch often precedes the onset of intrauterine growth restriction [9]. Doppler interrogation of the UA and MCA remains the most useful and practical tool in identifying fetuses at risk of adverse perinatal outcome, capturing 88% of all adverse outcomes [10].

Doppler Waveform Analysis

Because of inherent difficulties in quantitatively evaluating blood flow, the blood flow velocity waveform (FVW) is described to distinguish patterns associated with high and low resistance in the distal vascular tree. A unique characteristic of uteroplacental, fetoplacental and carotid circulations in the fetus is the continuous forward flow during diastole so that the perfusion of vital organs is uninterrupted throughout the cardiac cycle. This feature progressively develops in the fetoplacental circulation resulting in progressive increase in the end diastolic component of the flow velocity and concomitant decrease in the pulsatality, which is the difference between the maximum systolic and the end diastolic components.

Doppler indices (Figure – 1)

RI (Residtance Index) = S-D/S
Pulsatality index = S-D/M
S/D Ratio (Systolic/Diastolic) = S/D

Methodology for the calculation of the three most commonly used indices to calculate vascular impendence.

Certain considerations regarding the clinical and statistical properties of these indices:

- The three indices are highly correlated [11, 12]. Any one of the indices can be used.
- These indices are ratios, independent of the angle between ultrasound beam and insonated blood vessel and therefore not dependent on absolute measurement of true velocity.
- In cases with absent or reverse diastolic flow velocity RI, PI can provide a measurable entity for future reference, as S/D ratio becomes infinite
- In a normal pregnancy, neither the S/D ratio nor PI is normally distributed across all gestational ages. Hence comparisons should be done with non-parametric statistics
- The PI requires computer assisted calculation of mean velocity, which may be subject to experimental error

Figure - 1: Methodology for calculation of Doppler indices.

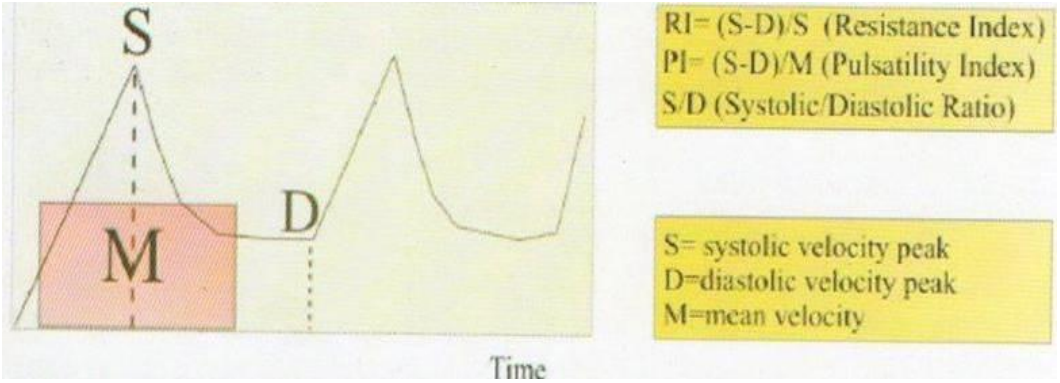

Table - 1: Hofer Classification of Umbilical Artery Doppler.

Class	Change in umbilical artery
I	PI < 2SD, continuous forward diastolic flow
II	PI > 2SD, continuous forward diastolic flow
III.a	Absent end diastolic flow
III.b	Reversal of end diastolic flow

Arterial Doppler

Umbilical Artery: The umbilical artery is the signature vessel in the Doppler study of the fetus as it is a direct reflection of the flow within the placenta. It is the first vessel to be studied when suspecting an IUGR fetus, The vessel is visible on ultra sound at 6-7 weeks, does not show diastolic flow till 10 weeks of gestation due to incomplete villous maturation.

With an increase in the number of tertiary stem villi and arterial channels, as the fetoplacental compartment develops, the impedance in the UA decreases, a diastolic component in UA flow velocity waveform (FVW) appears during the early second trimester, i.e. at 15 weeks of gestation and progressively increases with an increase in the gestational age. A mature FVW is usually achieved by 28-30 weeks [13].

The normal UA waveform pattern shows low impedance and high diastolic flow with a low PI. Normal RI: 0.5-0.7 S/D ratio $\leq$ 3 PI: 0.7-1.4.

All the three indices correlate well with clinical outcome. Resistances at the abdominal cord insertion tend to be higher and those at the placental insertion tend to be lower than those at midcord [14]. Giles, et al. [15] have found that a decrease in the number of vessels in the tertiary stem villi in placenta causes increase in resistance in leading to decreased flow through UA and increase in UA PI. In fetuses developing IUGR the FVW of UA changes in a progressive

manner as given by Hofer classification (**Table – 1**).

The prevalence of perinatal death in fetuses with absent or reversed end diastolic velocity in reported to be over 40%. Yoon, et al. demonstrated in their study that AEDF is strong and independent predictor of adverse perinatal outcome [16]. Bowley and colleagues demonstrated that UA velocimetry assessment decreases the perinatal mortality from IUGR without any increase in rate of unnecessary obstetric interventions in high risk pregnancies [17]. However, UA Doppler should not be used as a Screening tool in healthy pregnancies, as it has not been shown to be of value in this group.

Fetal Middle Cerebral Artery

The fetal middle cerebral artery Doppler is used to demonstrate fetal cerebral blood flow due to its easy accessibility and high reproducibility. During normal pregnancy, the MCA shows high resistance and low diastolic flow pattern with continuous forward flow throughout the cardiac cycle. It has high PI index. The Middle cerebral artery S/D ratio is always higher than Umbilical arterial S/D ratio.

In mild cases of fetal hypoxia when UA resistance is increased, no change may be demonstrated in the flow pattern of the MCA due to the adaptation of fetal circulation in maintaining the after load of left ventricle. An increase in the MCA PSV is the only perceivable finding at this early stage. In pregnancies with chronic fetal hypoxia, the blood volume in the fetal circulation is redistributed in favor of vitally important organs like heart, brain, adrenals, spleen, at the expense of kidneys and gastrointestinal systems .Vasodilatation of the MCA, with an increase in diastolic flow through it results in a decrease in PI. This phenomenon of brain sparing effect suggests a compromised fetus [8].

Paradoxically with continuing hypoxia, the over stressed fetus loses brain sparing effect and the diastolic flow returns to the normal level. This reflects a terminal decompensation in the setting of acidemia or brain edema and suggests grave irreversible fetal neurological outcome. A decreased PI in MCA indicates fetal adaptation, even in the presence of a normal UA Doppler. An abnormal UA waveform pattern is not universally the first Doppler sign of IUGR.

Aim and objectives

- To analyze the uteroplacental and fetoplacental blood flow using Doppler ultrasound in IUGR fetuses with reference to flow velocity and waveform indices i.e. Systolic/ diastolic ratio (S/D), resistance index (RI) and pulsatality index (PI).
- To select appropriate mode and time of delivery under optimal conditions of fetuses at risk.
- To analyze the perinatal outcome in IUGR pregnancy with respect to normal and abnormal Doppler waveforms.

Materials and methods

Source of Data: The study was conducted at the Government General Hospital, Siddipet, from October 2016 to September 2018, in the Department of Obstetrics and Gynecology in pregnant women attending OPD, admitted in antenatal wards and labor room, satisfying the inclusion and exclusion criteria.

55 cases of IUGR with abnormal Doppler were taken into this study and compared with equal number of IUGR cases with normal Doppler.

Study Design: Hospital based prospective, comparative study.

Inclusion criteria

- The last menstrual period (LMP) of the patient is well known / the gestational age is established by early antenatal scan prior to 22 weeks of gestation.
- The gestational age of patient is between 28 and 41 weeks.
- Singleton pregnancy.

- The patient is a clinically diagnosed case of IUGR (based on findings such as insufficient weight gain, no increase in fundal height and abdominal girth).
- Anyone of the risk factors is present
- Preeclampsia
- Chronic renal disease
- Connective tissue disorder
- Long standing diabetes with vascular lesion
- Cardiac disease class III or IV

Exclusion criteria

- Multiple gestation
- Documented major congenital anomaly

Method of Data Collection

A structured pre prepared case proforma was used to enter the patient details, clinical history, physical examination, who meets the inclusion criteria. After taking informed consent from the patient's antenatal ultrasound was performed in gray scale and color Doppler modes using a 3.5 to 5 MHZ, curvilinear array transducer of Esaote Mylab [18].

On gray scale parameters were assessed to establish the diagnosis of IUGR:

- Estimated Fetal Weight
- AC
- HC/AC ratio

On Doppler study the waveform analysis was done for the following vessels:

- Umbilical artery and
- Fetal Middle cerebral artery

Doppler indices of the following Vessels were studied

- Umbilical artery, PI, RI, S/D ratio
- Fetal middle cerebral artery, PI, RI, S/D ratio

The Doppler sample volume 2mm and the wall filter 50-100 HZ. The umbilical artery was sampled from free loop of cord midway between placental and abdominal wall insertion and measurements were taken when a clear waveform is acquired in the absence of fetal breathing or body movements.

For MCA Doppler US, a transverse image of fetal head was obtained at the level of the sphenoid bones. Color flow imaging was used to display the circle of Willis. The MCA in the near field was insonated about 1 cm distal to its origin from the internal carotid artery.

The waveform and the Doppler indices were analyzed and noted down. The sensitivity and specificity of these parameters were used to analyze taking the perinatal outcome as reference standard. The patients enrolled for the study were followed up from the point of the recruitment up to the time of delivery. Exact gestational age established based on LMP and first trimester ultrasound.

Antenatal steroids were given between 28-36 weeks to enhance fetal lung maturity if delivery anticipated within one week. Induction of labour with PGE2 gel was done if liquor was adequate and increased S/D ratio in UA more than 2SD, decreased PI $<5^{th}$ percentile in MCA Doppler. For severe oligohydramnios, AEDF/REDF delivered by Emergency caesarean section.

Various parameters studied include mean gestational age, scan to delivery interval, and mode of delivery. Perinatal outcome considered adverse if one or more of the following complications occur; The adverse outcome parameters include:

- Apgar score at 5 min<7 (Birth asphyxia) (HIE by clinical diagnosis)
- Caesarean section for fetal distress
- Admission to NICU
- Perinatal death
- Meconium stained liquor.

Results

A group of 110 cases were studied 55 cases of IUGR with abnormal Doppler formed the study group, the results compared with group of 55 cases of IUGR with normal Doppler. 43.6% cases in abnormal Doppler group were of 21 – 25

years age group and 41.8% in normal Doppler group. There were 36.3% cases of primigravidae in abnormal Doppler IUGR group, 32.7% in normal Doppler group, comprising 69% of IUGR, showed that primis were at risk for IUGR as PIH was a predisposing factor in primigravidae, the commonest cause of IUGR (**Table – 2**).

Table – 2: Age Wise Distribution of Cases.

	Abnormal Doppler IUGR		**Normal Doppler IUGR**	
	(n=55)	**Percentage**	**(n=55)**	**Percentage**
< 20 years	21	38.1	19	34.5
21 – 25 years	24	43.6	23	41.8
26 – 30 years	9	16.3	10	18.1
31 – 35 years	1	1.8	3	5.4

Table – 3: Predisposing Factors in Both Groups.

Factor	**Abnormal Doppler IUGR**		**Normal Doppler IUGR**	
	(n=55)	**Percentage**	**(n=55)**	**Percentage**
PIH	28	50.9	14	25.4
Anemia (Malnutrition)	10	18.18	24	43.6
BOH	6	10.9	5	9
Diabetes	2	3.63	1	1.81
Epilepsy	2	2.63	1	1.81
Heart Disease	1	1.81	---	---
Chronic renal disease	1	1.81	---	---
Cirrhosis of Liver	1	1.81	---	---
Placenta praevia	1	1.81	---	---
Anomalies	---	---	8	14.6
Previous IUGR baby	4	72	---	---

Table – 4: Distributions of Cases According To Doppler Derangement.

Doppler Derangement	**No. of cases (n=55)**	**Percentage**
Decreased end diastolic flow in UA with normal MCA	12	21.8
Decreased end diastolic flow in UA with abnormal MCA	7	12.7
AEDF/REDF in UA with normal MCA	1	1.8
AEDF/REDF in UA with abnormal MCA	9	16.3
Abnormal MCA with decreased end diastolic flow in UA	26	42

Table – 5: Perinatal Outcomes in Abnormal Doppler IUGR Cases.

Perinatal Outcome	**No. of cases (n=55)**	**Percentage**
Live Birth	51	92.3
Still birth	4	7.2
Neonatal Death	5	9.09
Apgar at 5 min <7	23	41.8
NICU admission	33	60
EMLSCS	37	67.2
Neonatal Complications	21	38.1

Table – 6: Comparison of Mode of Delivery.

Doppler	Vaginal Route	Caesarean Section	Total
Abnormal	8	47	55
Normal	19	36	55
P value : 0.02 = < 0.05			

(X^2 = 5.4017, P Value = 0.02 < 0.05 = Statistically Significant). Abnormal Doppler is associated with high rates of caesarean section)

Table – 7: Oligohydramnios in Relation with IUGR.

Doppler	Oligohydramnios (AFI <5 Cm)		
	Present	Absent	Total
Abnormal	39	16	55
Normal	20	35	55

X^2 = 4.9384, P = 0.026 (Statistically significant). 70% of abnormal Doppler cases are associated with Oligohydramnios

Table – 8: Comparison of Fetal Outcome.

Doppler	Fetal Outcome		
	Live	Still Birth	Neonatal Death
Abnormal (n=55)	46	4	5
Normal (n=55)	52	0	3
Total (110)	98	4	8

X^2 = 8.38, P value = 0.0015 highly significant Abnormal Doppler IUGR babies are associated with more still birth and neonatal deaths.

50.9% had PIH. 18.1% and anemia as predisposing factor for IUGR with abnormal Doppler. PIH, anemia, were more common predisposing factors for IUGR (**Table – 3 to 8**).

- 10 – AEDF/REDF
- 26 – C/U<1
- 19 – EDF in UA reduced
- Reduced end diastolic flow in umbilical artery (n=19) (pi >95th percentile, s/d >3)

Discussion

Fetuses with estimated weight below the 10th percentile for their gestational age and sex are growth restricted [1]. Growth restricted fetus is one which has failed to achieve its genetic growth potential in utero [3], and is prone for adverse perinatal outcome. In India the incidence is as high as 25-30 %.In India more that 50% of the low birth weight babies are growth restricted [4].

The purpose of the present study was to analyze blood flow in umbilical and middle cerebral artery using Doppler ultrasound and to compare the perinatal outcome with respect to normal and abnormal Doppler waveforms. Doppler offers an unique tool for the non-invasive evaluation of uteroplacental and fetal placental circulations and thus form a basis for a structured antenatal surveillance program with timely intervention [19].

In the present study, 55 cases of IUGR with abnormal Doppler were included and compared with 55 cases of IUGR with normal Doppler. In this study, only 36% were booked either in our institution or outside. 43.7% were referred from peripheral centers, this institution being a tertiary referral centre. Majority of the patients were in the age group of 21-25 years, Most of the patients belonged to low socio-economic status. Duration of pregnancy ranged from 28-37 weeks of gestation. Mean Gestational age at which the

pregnancy was terminated was 34 weeks, showing early termination in cases of IUGR, comparable with the study by Tumbal PS, et al. 2012 [19] had termination at 34 weeks of gestation in 61.46% of cases.

IUGR was detected in the third trimester in majority of cases (71%) 39/55 cases of abnormal Doppler, in comparison with study by Vimla Jain, et al. [20] (1999) 65%. 36.36 % of the study group comprised primigravidae, comparable with study by Tumbal, et al. 2012 had 46%. Most the study group had PIH (50.9%) 28/55 cases of IUGR with abnormal Doppler as a major risk factor. 14/55 (25.4%) of IUGR with normal Doppler had PIH, in comparison to the study conducted by Dr. Arora Devendra, et al. [21] (2005) incidence of PIH was 21/44 (38.18%) for IUGR with abnormal Doppler, 26/40 (28.9%) for IUGR with normal Doppler.

Anemia, failure to gain weight (malnutrition) was the second common predisposing factor in the study group. 10/55 (18.1%) cases were associated with malnutrition, failure to gain weight and anemia, in comparison with study by Kushal Gandhi, et al. (2015) 26/113 (23%) [22]. Overt diabetes associated with IUGR in 3/110 cases (4.4%). Placental calcifications noted in 12/55 (21.81%) cases of abnormal Doppler IUGR. Placental infarcts noted in 4/55 (72%) cases of normal Doppler IUGR. Congenital anomalies were seen in 6/55 (14.5%) of cases of normal Doppler IUGR group.

45/55 cases (81.8%) delivered within 5 days of their Doppler detection and 50.90%., 28/55 delivered within 5 days in normal Doppler group. overlapping of Doppler abnormalities was seen in cases with abnormal Doppler IUGR. Cases divided into 3 Groups based on prominent abnormality affecting the perinatal outcome. The rate of LSCS in abnormal Doppler IUGR group was 85.4%, (47/55) cases and 65.45% (36/55) in normal Doppler IUGR cases, in comparison with study by Dr. Arora Devendra, et al. LSCS rate of (35/44), 79.5% Kushal Gandhi, et al. (2015) study had 69.6% (48/113) LSCS rate in abnormal Doppler IUGR cases Tumbal PS, et al. (2012) study had LSCS rate of 76% (73/96).

Oligohydramnios was present in (39/55) 70.9% in abnormal Doppler group and (20/55) 36.3% in normal Doppler group, in comparison with the study by Dr. Arora Devendra, et al. (2005) 56.81%, (25/44) had oligohydramnios. Meconium stained liquor was seen in 60% (33/55) cases of abnormal Doppler and 25.4% (14/55) of normal Doppler group. Average birth weight in abnormal Doppler group was 1.86 Kg and normal Doppler group 2.06 Kg is comparison with the study by Dr. Arora Devendra, et al. and Kushal Gandhi, et al. had average birth weight of 1.776 Kg and 1.82 Kg respectively. Perinatal mortality was (9/55), 16.3% in abnormal Doppler group and 5.45 % (3/55) of normal group. Dr. Devendra Arora, et al. study had no perinatal deaths.

Kushal Gandhi, et al. study had 13.2% (15/113), Tumbal PS, et al. study had 20.8% (20/96) and Katherine W Fong, et al. (1997) had 4.77% (14/293) perinatal mortality. Admission to NICU in 60% (33/55) abnormal Doppler group and 43.63 % (24/55) in normal Doppler IUGR cases. In Arora Devendra, et al. study 79.54% (35/44) in abnormal Doppler had NICU admissions. This study had 10/55, 18.1% cases with AEDF/REDF. LSCS rate in this group was 70%, delivered within 2 days of diagnosis. Median birth weight was 1.35 Kg perinatal mortality was 40% (4/10) with perinatal survival of 60%. This Doppler finding is indicative of impending fetal demise and has been associated with perinatal mortality in 40% cases and IUGR in 100% of cases. In this study the Doppler parameter C/U ratio had high specificity and positive predictive value of 100%.

Conclusion

Doppler technology enables a better understanding of the hemodynamic changes in the fetus. It can help in identifying the changes in the fetal circulation well in advance of other surveillance tests, thus identify the truly hypoxic

fetus. Interval changes in Doppler indices are useful in determining monitoring frequencies and optional time for delivery.

IUGR is associated with high perinatal mortality and morbidity. As the fetus with IUGR tolerates labour poorly, antenatal detection improves pregnancy outcomes. The purpose of our study was to evaluate Doppler indices in Umbilical and middle cerebral artery in diagnosis of IUGR fetuses and the prediction of adverse perinatal outcome in high risk pregnancies. A group of 110 cases were studied, 55 cases with IUGR abnormal Doppler formed the study group. The results were compared with group of 55 cases of IUGR with normal Doppler. Doppler indices have statistically significant relationship in this study.

- Abnormal Doppler indices in Umbilical artery were the initial Doppler abnormality in majority of the cases. Elevated umbilical artery PI 19/55 (34.5%) was associated with caesarean delivery in 78.9%, with median birth weight of 1.99 Kg, perinatal mortality of 10.5% and 57.8% admissions to NICU (18.18%).
- 10/55 cases of AEDF/REDF were identified in the study with mean gestational age at termination 30-31 weeks, caesarean rates of 70%, median birth weight of 1.35 Kg, perinatal mortality of 40% and 70% of NICU admissions. Hence gradual reduction in umbilical arterial diastolic flow and ultimate reversal may have correlation with severity of fetoplacental insufficiency. Thus identification of these findings creates possibility of early intervention.
- The finding of AEDF/REDF in Umbilical artery is an ominous sign, associated with adverse perinatal outcome and high perinatal loss.
- Overlapping of Doppler abnormalities in Umbilical and middle cerebral arteries was identified in the study group. MCA< 5th percentile was found in 7/55 (12.7%) cases but cerebro placental ratio was normal (C/U >1) 26/55 (42%) cases were identified to be having C/U < 1, had caesarean rates of 96.15% median birth weight of 1.85 Kg, perinatal mortality of 17.5%, 57.6% of NICU admissions. This Doppler parameter had 100% specificity and 100% positive predictive value. C/U ratio is a better predictor of growth restricted fetuses and adverse perinatal outcome than either UA PI or the MCA PI alone.

Doppler interrogation of UA and MCA is the most useful and practical tool in identifying fetuses as risk of acidemia and adverse perinatal outcome is high risk pregnancies.

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