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ORIGINAL ARTICLE

Structural Analysis of the Umbilical Cord and Its Vessels in Intrauterine Growth Restriction and Pre-eclampsia

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Abstract Both intrauterine growth restriction (IUGR) and pre-eclampsia (PE) are accompanied by alterations in the vascular structures of the umbilical cord (UC). However, it is unclear if the vasculature is significantly different when both conditions co-exist. Digitized sections of 77 UC from four groups of women were analyzed morphometrically. The groups included women with PE (group I), IUGR and PE (group II), IUGR (group III) and women with uncomplicated pregnancy as controls (group IV). The effect of PE, IUGR and their combination on UC parameters were examined using two-way ANOVA and the correlation of birth weight and placental weight in these parameters were measured. There were 12 cases in group I, 22 in group II, 26 in group III and 17 in group IV. The umbilical vein (UV) parameters like wall thickness (0.33 vs 0.42 mm, $p = 0.04$), cross sectional area, (2.9 vs 4.1 mm^2, $p = 0.01$), diameter (2.2 vs 2.6 mm, $p = 0.04$) and muscle cross sectional area (1.53 vs 2.4 mm^2, $p = 0.01$) were lower in the IUGR group as compared to other groups. In the group with PE, UV wall:lumen ratio (0.28 vs 0.2, $p = 0.05$), UA D (0.77 vs 0.63 mm, $p = 0.04$) and UA CSA (0.99 vs 0.8 mm^2, $p = 0.04$) were significantly higher compared to other groups. The interaction effect of PE and IUGR was not significant for any of the umbilical vessel parameters. The UV dimensions are significantly smaller in IUGR and PE pregnancies. These differences were mainly seen in the IUGR group and the presence of PE did not amplify the differences.

Keywords Intrauterine growth restriction · Morphometry · Pre-eclampsia · Umbilical vein · Umbilical cord

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Introduction

Intrauterine growth restriction (IUGR) is defined as the inability of the fetus to acquire its genetically determined growth potential [1]. It is now widely accepted that these fetuses with impaired fetal programming and growth restriction are at a risk for developing chronic diseases of adulthood like neurological disorders and cardiovascular diseases. Though the aetiology of IUGR is varied, ranging from maternal, fetal, and placental causes, the most commonly cited cause is placental insufficiency [2].

Pre-eclampsia (PE) is another well known pregnancy complication with an incidence of approximately 7–9% in Indian population [3]. The most common pregnancy complication associated with pre-eclampsia is IUGR with a reported incidence of 15.5% in Indian population [4]. Data across the world also suggest that PE is the most common cause of maternal mortality and fetal prematurity [5, 6]. The underlying pathogenesis in PE is placental underperfusion due to defective trophoblastic invasion and defective transformation of decidual arterioles into low resistance circulation [7].

The umbilical cord serves as a conduit for blood flow to the developing fetus. It is considered as an extension of fetal cardiovascular system. The changes in the physical dimension and composition can be considered as a reflection of changes in fetal vascular tissue. The cord has three blood vessels surrounded by Wharton's jelly, which supports these vessels. This coiled structure is twisted either in right- or left-handed directions. Various physical characteristics of the cord, like length, diameter, coiling index, number of vessels and their calibre, presence of knots, Wharton's jelly, modulate blood flow through it. These determine the pattern of blood flow through the umbilical cord vessels, which, as assessed by Doppler, indicate the status of fetal well-being in utero.

Ultrasonography, coupled with Doppler studies is now widely used antenatal investigations to assess and monitor fetal growth in high-risk pregnancies. The Doppler flow velocities in the uterine and umbilical arteries may be altered in IUGR and PE and show high S/D ratio (>95th percentile from standard values for the reference population), elevated resistivity index (RI), pulsatility index (PI), absent/reversal of end diastolic velocity and early diastolic notching. In IUGR, the diagnosis rests on finding a lag in intrauterine growth as measured by fetal biometry. The Doppler findings in IUGR assists in assessing the severity of circulatory compromise and is used as an indicator for termination of pregnancy. In PE, sonological changes are seen mostly in the uterine artery, as the pathology is more related to the decidual arterioles [8]. Some of these individual umbilical artery parameters are considered diagnostic tools in assessing the hemodynamic changes caused by PE which influence the fetal outcome [9]. While IUGR and PE can occur independently or co-exist in pregnancy, both the conditions are associated with alterations in Doppler velocimetry of the umbilical vessels.

Although studies on the effect of PE and IUGR on cord structure or biochemical composition exist, the interaction effect of these pathological conditions is not explicitly analyzed. Also studies that relate biomechanical functioning of the umbilical cord to its structure are lacking in literature. This morphometric study is intended to assess alterations in the various structural components of the umbilical cord, in four groups: Women with PE, IUGR, both PE and IUGR, and Control (women with a normal pregnancy outcome) and attempts to relate these changes to Doppler findings in the pathological group.

Materials and Methods

Sample Selection

In this retrospective study, the database of placentas in the Department of Pathology, St. John's Medical College, was searched with the key words "pre-eclampsia" and "intrauterine growth restriction" over a period of one year. Clinical records and ultrasound records for fetal biometry were reviewed to confirm the diagnosis. PE was defined as detection of high blood pressure (>140/90 mm Hg) and proteinuria (urine protein excretion of >2 g/24 h). IUGR was defined as effective birth weight less than 10th percentile and lag in the fetal growth curve between two independent measurements. These cases were categorized into three groups: those with PE (Group I), PE with IUGR (Group II) and IUGR alone (Group III). The control (Group IV) comprised placentas of patients enrolled in the pregnancy cohort of St. John's Research Institute, where the antenatal history/routine ultrasound did not reveal any complications. Gestational ages of more than 30 weeks were included as the umbilical cord parameters stabilize beyond 30–32 weeks [10]. Multiple gestation and cords with single umbilical artery were excluded. The umbilical cord sections of the different groups were retrieved and analyzed for orientation of the sections and those which were strictly transverse were considered for further analysis. The gross placental examination was done as per the international guidelines and the various recommended parameters were recorded for all the placentas received in the department [11, 12]. As per this standard grossing protocol, the umbilical cord sampling was done at a fixed distance from the insertion site in all the samples to reduce the effect of nonuniformity. In the cords which had any obvious gross abnormality at this point, sampling was done further away to avoid errors in morphometric

measurements. No strictures or hypercoiling was observed. Relevant parameters were collected from the clinical records including birth weight, placental weight, presence of oligohydramnios, parity, and gender. Doppler findings wherever available, were recorded. The informed consent was obtained from the patients. The study was approved by the Institutional Ethics committee (IEC reference no. 202/12), as a part of larger histomorphological study of placentas.

Morphometric Analysis of the Cord

The H and E stained section were digitised to examine the entire circumference of the cord. The digitised slides were photographed at different magnifications with an inbuilt ruler to measure the various parameters. Multiple pictures were taken to ensure adequate visualisation of the vessels. The captured photomicrographs were analysed using image analyser software, Image J software (version 1.48) downloaded from http://rsb.info.nih.gov/ij/. The software was calibrated by measuring two points of known distance on the ruler converted to pixels by the software and the measurements of the image in pixels was automatically converted into distance (mm) by the software. Calibration was repeated for each cord section before obtaining the set of measurements. The various parameters measured are listed in Table 1.

Statistical Analysis

Data analysis was performed using SPSS version 18.0 (PASW Statistics, 18.0, SPSS Inc, Chicago, IL, USA). The umbilical cord parameters are represented as median (25th percentile, 75th percentile). The normal distribution of data was examined using Q–Q plots. Natural logarithm of all variables that did not follow normal distribution were used for comparison between the groups using two-way ANOVA, where the main effects of IUGR (IUGR vs non-IUGR), PE (PE vs nonPE) and their interaction effects (Normal vs IUGR alone vs PE alone vs IUGR + PE) were considered. The association of the umbilical cord parameters with birth weight and placental weight were examined using Spearman's rank correlation. The p values corresponding to the correlation coefficients were Bonferroni adjusted to account for multiple testing. Statistical significance was considered at $p < 0.05$.

Results

Umbilical cord sections from 77 placentas were analyzed which comprised of Group I: PE, n = 12, Group II: IUGR with PE, n = 22, Group III: IUGR alone, n = 26, Group IV: Control, n = 17. The gestational age of the patients' ranged from 30 weeks ± 2 days to 40 weeks ± 4 days. There were 39 placentas from primigravid and 38 from multigravid women. Oligohydramnios was present in 42% of cases, predominantly from the IUGR group. Table 2 shows the clinical characteristics of the study group.

The median (25th percentile, 75th percentile) values of the various umbilical cord parameters and vessel dimensions are detailed in Table 3. Numerically, the umbilical cord measurements, i.e., the umbilical cord diameter (UC-D), cross-sectional area (UC-CSA), and Wharton's jelly area (WJA) were greater in the normal placenta cords compared to the IUGR and PE cords, whereas the total vessel area (UVS-A) was more in Group I (PE) and Group II (IUGR + PE) placentas and lower in Group III (IUGR) placentas compared to Group IV (Control). However, these differences between the groups did not reach statistical significance.

The vessel parameters were compared between the study groups using two-factor ANOVA where the main effects of IUGR, PE, and their interaction effect were examined. The umbilical vein (UV) parameters: Diameter (UV-D) ($p = 0.043$), wall thickness (UV-WALL) ($p = 0.03$), cross sectional area (UV-CSA) ($p = 0.014$) and muscle cross-sectional area (UV-MCSA) ($p = 0.011$) were lower in IUGR placenta as compared to nonIUGR placenta. A similar observation was seen with umbilical artery (UA) parameters: wall-lumen ratio (UA-W/L ratio) ($p = 0.048$). The muscle cross-sectional area (UA-MCSA) and outer muscle area (UA-OMA) tended to be lower in IUGR placenta though not statistically significant ($p = 0.07$ and 0.05, respectively). The luminal cross-sectional area of umbilical artery tended to be higher in IUGR reflecting the hypoplastic nature of the umbilical artery ($p = 0.09$). The presence of PE influenced UV-W/L ratio ($p = 0.05$), UA-D ($p = 0.044$), and UA-CSA ($p = 0.047$) significantly and were higher in PE placentae compared to nonPE placentae. Figure 1 plots the least square means for the main effects of IUGR and PE. The interaction effect of PE and IUGR was not significant for any of the umbilical cord parameters. Doppler velocimetry was available for 18 (n = 22) cases in Group II and 19 (n = 26) cases of Group III. When IUGR and PE co-existed (Group II), most of the cases (11/18) had findings of uteroplacental (UPI), and fetoplacental insufficiency (FPI), whereas isolated findings of UPI and FPI were seen only in three and two cases, respectively. In two others, normal Doppler finding was recorded. When IUGR was not associated with PE (Group III), FPI was the most frequently recorded finding (8/19 cases) and UPI with FPI was found in five cases. Normal Doppler finding was noted in six cases. However, none of them had isolated finding of UPI.

Although definite conclusions cannot be drawn from the Doppler findings, as velocimetry for Group I and IV are not available, the findings suggest that IUGR is more often

Table 1 The various morphometric parameters measured on the cord

I. Umbilical cord (UC) parameters	IIA. Umbilical vein (UV) parameters	IIB. Umbilical artery (UA) parameters
a. Diameter (UC-D)	a. Diameter (total {UV-D} and luminal {UV-L})	a. Diameter (total {UA-D} and luminal {UA-L})
b. Total cross-sectional area (UC-CSA)	b. Wall thickness {UV-WALL} and wall/lumen ratio {UV-W/L ratio}	b. Wall thickness {UA-WALL} and wall/lumen ratio {UA-W/L ratio}
c. Total umbilical vessels area (UVS-A)	c. Cross-sectional area: Total {UV-CSA}, luminal {UVL-CSA}, and smooth muscle {UV-MCSA})	c. Cross-sectional area: Total {UA-CSA}, luminal {UAL-CSA}, and smooth muscle {outer [UA-OMA] and inner [UA-IMA] muscle}
d. Wharton's Jelly area (WJA)		d. For umbilical arteries the average measurement (UA MEAN) of the two arteries was also calculated

Table 2 Characterization of normal, PE, and IUGR pregnancies

Parameters	Normal	IUGR	PE	IUGR + PE
No. of cases	17	26	12	22
Gender (75 cases) M:F, n	6:10	17:9	3:8	12:10
Oligohydramnios, n (%)	1 (6%)	11 (42%)	1 (8%)	7 (32%)
Gravida (primi: multi), n	10:7	13:13	7:5	9:13
Birth weight (kg)				
Min–Max	2.16–3.99	0.84–2.53	0.79–3.6	0.36–2.18
Mean (SD)	2.97 (0.46)	1.73 (0.48)	1.9 (0.77)	1.44 (0.44)
Placental weight (g)				
Min–Max	290–518	166–454	148–426	106–380
Mean (SD)	405 (63.3)	273 (75.9)	269 (84.6)	247 (58.8)
Gestational age				
Min–Max	35.9–40.6	30.3–39.7	28–38	27.6–37.9
Mean (SD)	38.6 (1.4)	36 (2.8)	33.9 (3.1)	34.4 (2.6)

PE pre-eclampsia, *IUGR* intrauterine growth restricted

associated with umbilical vessel abnormality (as reflected by increased incidence of FPI) and when PE co-exist, the uterine vessel abnormality is coupled with abnormal umbilical vessels waveform (reflected as UPI with FPI).

Birth weight and placental weight showed significant positive correlation with each other (Spearman's $\rho = 0.774$, $p < 0.001$). The umbilical vein parameters such as UV-D, UV-CSA, and UV-MCSA correlated significantly with birth weight and placental weight (Table 4). The total vessel area of the umbilical cord was significantly lower when oligohydramnios was present ($p = 0.02$). There was no difference in these parameters between male and female genders.

Discussion

Intrauterine growth restriction and PE are the most common pregnancy complications causing low birth weight babies. There is no definite pathophysiological pathway delineated for the development of these conditions, which precludes the possibility of any intervention to prevent such an adverse outcome. Placental insufficiency due to inadequate vascular transformation of the maternal arterioles and abnormalities in the development of the placental fetal vasculature are considered the pathophysiological abnormalities in PE and IUGR, respectively. This compromises the blood flow and hence the fetomaternal exchange resulting in underdevelopment of the fetus.

The vascular changes occurring in the placental bed and in the microcirculation of the placenta will be reflected as morphometric changes in the umbilical vessels. These changes can be detected sonologically as well as on Doppler velocimetry.

The present study on morphometric analysis showed no significant difference in dimensions of the UC but a significant difference in dimensions of vascular components between IUGR and controls. The umbilical vein total CSA and smooth muscle area, the diameter and wall thickness were reduced in IUGR as compared to the control group.

Table 3 Umbilical cord characteristics of normal, PE, and IUGR pregnancies

Umbilical cord parameters	Normal (n = 17)	IUGR (n = 26)	PE (n = 12)	IUGR + PE (n = 22)
UC-D (mm)	8.48 (7.22, 10)	7.74 (6.64, 9.4)	7.45 (6.31, 9.45)	7.36 (6.53, 8.79)
UC CSA (mm^2)	40.5 (29.2, 61.8)	32.03 (27.6, 48.9)	34.4 (25.3, 58.4)	32.1 (25.7, 43.03)
UVS A (mm^2)	8.03 (7.2, 11.91)	7.82 (6.2, 10.6)	9.65 (7.6, 16)	8.48 (6.17, 9.47)
WJA (mm^2)	32.5 (21.9, 45.6)	22.9 (19.6, 37.97)	21.5 (17.2, 44.3)	26.9 (17.5, 33.3)
UV D (mm)	2.36 (2.23, 2.96)	2.35 (1.88, 2.87)	2.44 (2.14, 3.69)	1.95 (1.7, 2.82)
UV-WALL (mm)	0.38 (0.31, 0.53)	0.28 (0.22, 0.39)	0.44 (0.32, 0.59)	0.37 (0.297, 0.53)
UV-L (mm)	1.67 (1.22, 2.02)	1.62 (1.3, 2.19)	1.55 (1.22, 2.49)	1.12 (0.87, 1.95)
UV W/L ratio	0.22 (0.18, 0.39)	0.22 (0.11, 0.27)	0.26 (0.17, 0.38)	0.41 (0.19, 0.55)
UV CSA (mm^2)	3.5 (3.06, 5.86)	3.69 (2.08, 5.14)	3.47 (2.8, 5.89)	2.48 (1.69, 3.91)
UV LCSA (mm^2)	1.53 (0.69, 2.26)	1.55 (0.43, 2.38)	1.35 (0.44, 2.35)	0.67 (0.37, 1.15)
UV MCSA (mm^2)	2.59 (1.89, 3.05)	1.66 (1.24, 2.47)	2.44 (1.55, 4.04)	1.51 (1.21, 2.2)
UA1-D (mm)	1.89 (1.57, 2.48)	1.96 (1.56, 2.36)	2.4 (1.7, 3.01)	2.06 (1.53, 2.49)
UA1-WALL (mm)	0.55 (0.46, 0.75)	0.58 (0.48, 0.66)	0.65 (0.45, 0.99)	0.56 (0.42, 0.77)
UA1-L (mm)	0.63 (0.54, 0.93)	0.65 (0.52, 1)	0.73 (0.51, 1.33)	0.64 (0.4, 1.32)
UA1 W/L ratio	0.92 (0.53, 1.25)	0.86 (0.64, 1.09)	0.92 (0.37, 1.39)	1.04 (0.32, 1.53)
UA1-CSA (mm^2)	2.41 (1.64, 3.38)	2.21 (1.63, 3.47)	2.66 (2.03, 4.25)	2.39 (1.83, 3.12)
UA1-LCSA (mm^2)	0.14 (0.069, 0.52)	0.14 (0.04, 0.59)	0.19 (0.11, 0.68)	0.14 (0.04, 0.73)
UA1 MCSA (mm^2)	2.12 (1.43, 2.83)	1.92 (1.39, 2.27)	2.42 (1.72, 3.97)	1.87 (1.55, 2.69)
UA2-D (mm)	1.69 (1.58, 2.20)	1.99 (1.54, 2.28)	2.12 (1.59, 3.11)	1.98 (1.77, 2.73)
UA2-WALL (mm)	0.57 (0.54, 0.60)	0.47 (0.34, 0.56)	0.62 (0.48, 0.83)	0.59 (0.38, 0.79)
UA2-L (mm)	0.52 (0.43, 0.87)	0.86 (0.59, 1.26)	0.78 (0.64, 0.95)	0.82 (0.55, 1.24)
UA2 W/L ratio	1.12 (0.64, 1.4)	0.62 (0.33, 0.96)	0.97 (0.64, 1.13)	0.86 (0.35, 1.28)
UA2 CSA (mm^2)	2.28 (1.74, 2.85)	2.24 (1.77, 2.98)	2.57 (2.13, 3.99)	2.39 (2.02, 3.68)
UA2-LCSA (mm^2)	0.095 (0.054, 0.28)	0.36 (0.11, 0.78)	0.2 (0.1, 0.4)	0.27 (0.07, 0.67)
UA2-MCSA (mm^2)	2.01 (1.66, 2.56)	1.63 (1.27, 2.21)	2.19 (1.83, 3.16)	1.97 (1.45, 2.4)
UA-MEAN DIA (mm)	1.89 (1.64, 2.15)	1.9 (1.73, 2.12)	2.25 (1.71, 3.06)	1.99 (1.77, 2.58)
UA MEAN WALL THICKNESS (mm)	0.59 (0.49, 0.68)	0.54 (0.43, 0.59)	0.61 (0.48, 0.87)	0.59 (0.45, 0.77)
UA MEAN LUMEN LENGTH (mm)	0.59 (0.52, 0.87)	0.82 (0.59, 1.12)	0.81 (0.66, 1.06)	0.92 (0.55, 1.27)
UA MEAN W/L ratio	1.06 (0.69, 1.26)	0.75 (0.58, 1.09)	0.93 (0.56, 1.32)	0.81 (0.49, 1.56)
UA MEAN TCSA (mm^2)	2.29 (1.93, 2.75)	2.35 (1.76, 2.71)	2.67 (2.13, 4.57)	2.33 (1.99, 3.29)
UA MEAN LCSA (mm^2)	0.12 (0.09, 0.42)	0.43 (0.09, 0.91)	0.19 (0.13, 0.51)	0.30 (0.09, 0.67)
UA MEAN MCSA (mm^2)	2.07 (1.68, 2.43)	1.89 (1.38, 2.16)	2.5 (1.85, 3.73)	1.93 (1.64, 2.54)
UA1 IMA (mm^2)	0.62 (0.47, 1.20)	0.76 (0.41, 1.1)	0.99 (0.73, 1.44)	0.71 (0.52, 1.4)
UA1OMA (mm^2)	1.60 (0.98, 1.99)	1.43 (0.92, 1.72)	1.69 (1.13, 2.88)	1.35 (1.13, 1.74)
UA2IMA (mm^2)	0.65 (0.41, 1.03)	0.94 (0.5, 1.33)	0.9 (0.68, 1.33)	0.85 (0.53, 1.81)
UA2OMA (mm^2)	1.43 (1.31, 1.9)	1.18 (0.89, 1.54)	1.52 (1.27, 2.27)	1.47 (0.93, 1.97)

Values are median (25th percentile, 75th percentile)

PE pre-eclampsia, *IUGR* intrauterine growth restricted

Peyter et al. [13] in their study of 115 cord from IUGR and 170 cords from AGA newborns made similar observations. Sonographic studies have shown a significantly reduced UV area in utero in IUGR fetuses with [14, 15], small UV area being an indicator of adverse perinatal outcome [16].

Raio et al. studied umbilical cord characteristics in 84 IUGR fetuses and found that all the UC components including cord cross-sectional area, vein area, artery area and Wharton's jelly area were reduced in IUGR compared to controls. The lean umbilical cords (cross-sectional area <10th percentile for gestational age) are commonly encountered in IUGR. However, the proportion of lean umbilical cord was not significantly different between mothers with and without PE. This observation is in concordance with the present study that the cord vessel parameters which were significantly lower were due to IUGR and were not enhanced by the presence of PE. Raio et al. [15] also correlated the morphometric measurements

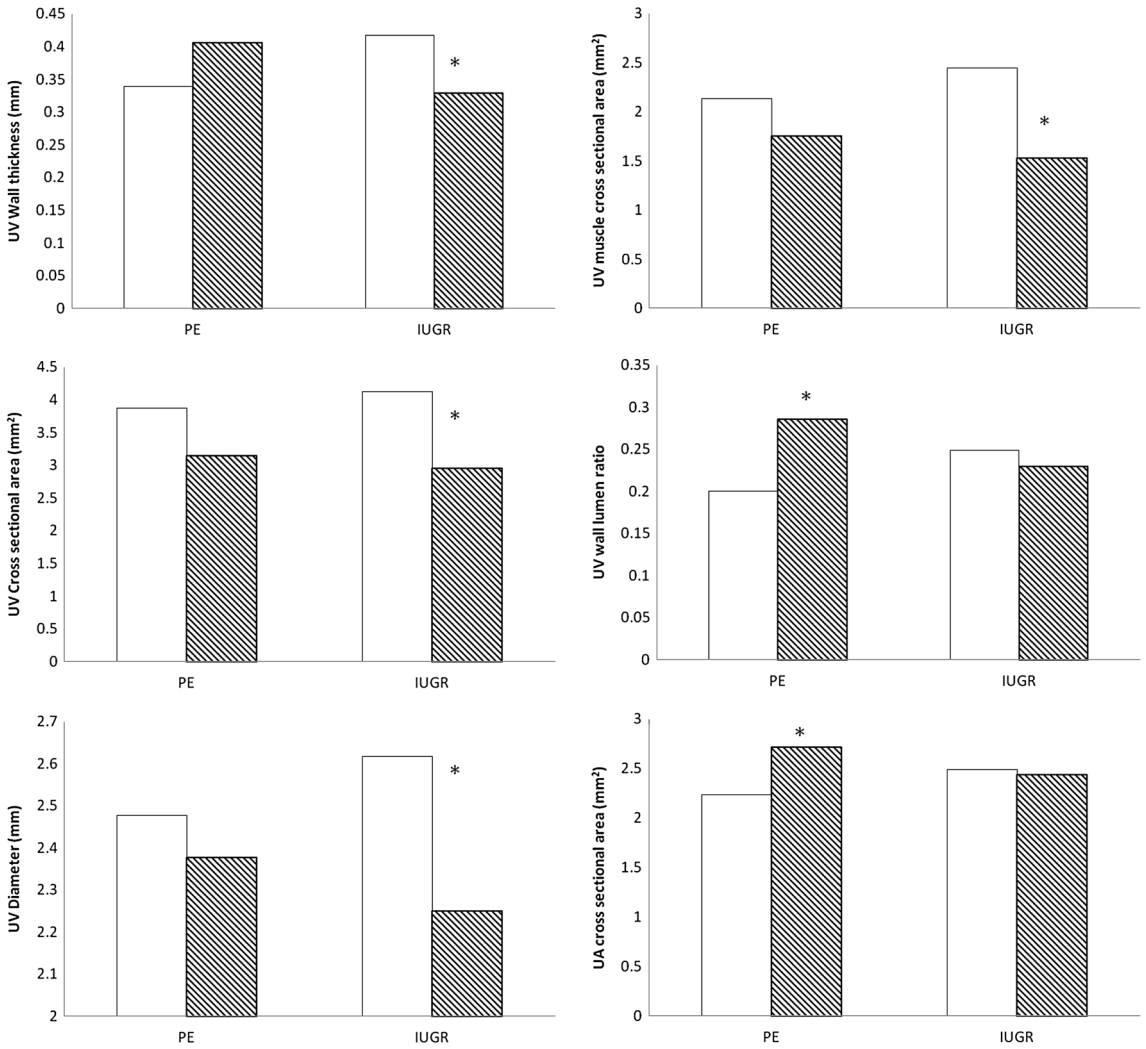

Fig. 1 The values presented are least-squares means for the main effects of intrauterine growth restriction (IUGR) and pre-eclampsia (PE) from two-way ANOVA with IUGR and PE as two factors. *Shaded bar* (presence of PE or IUGR). *Asterisk* represents $p < 0.05$ in main effect of PE or IUGR obtained from two-way ANOVA

of the cord vessels with umbilical artery Doppler findings and found that the umbilical vein calibre to decrease significantly with worsening resistance to blood flow in the umbilical arteries.

Based on the findings, Raio et al. study put forth a hypothesis that abnormal placentation may cause decreased umbilical venous blood flow. The increased fetoplacental impedance and the decreased flow lead to remodelling of the umbilical vessels, especially umbilical vein. As a result of decreased umbilical flow, the fetal growth velocity decreases. This sequence of events may culminate in altered umbilical artery Doppler parameters and redistribution of blood flow to vital organs. The findings from the above studies, including the present one, indicate that the UV undergoes structural modifications in IUGR fetuses. Since UV is the main supply of oxygenated blood to the fetus, it could be targeted in future therapeutic interventions to augment the fetoplacental circulation.

In pregnancies complicated by PE, we found a significant increase in the umbilical artery total cross sectional area and diameter along with increase wall lumen ratio in the umbilical vein. Barnwal et al. [17] also found 20% increase in UA thickness in PE group and Junek et al. [18] found 15% increase in arterial wall thickness. Therefore the present study along with previous other studies highlights the fact that PE is associated with increased UA thickness.

Birth weight and placental weight showed significant positive correlation with total umbilical vessel area, and umbilical vein diameter, cross sectional area and muscle cross sectional area as also reported by Peyter et al. [13] Oligohydramnios was associated with decreased cross sectional areas of umbilical vessels. Di Naro et al. stated that lean umbilical cord are associated with

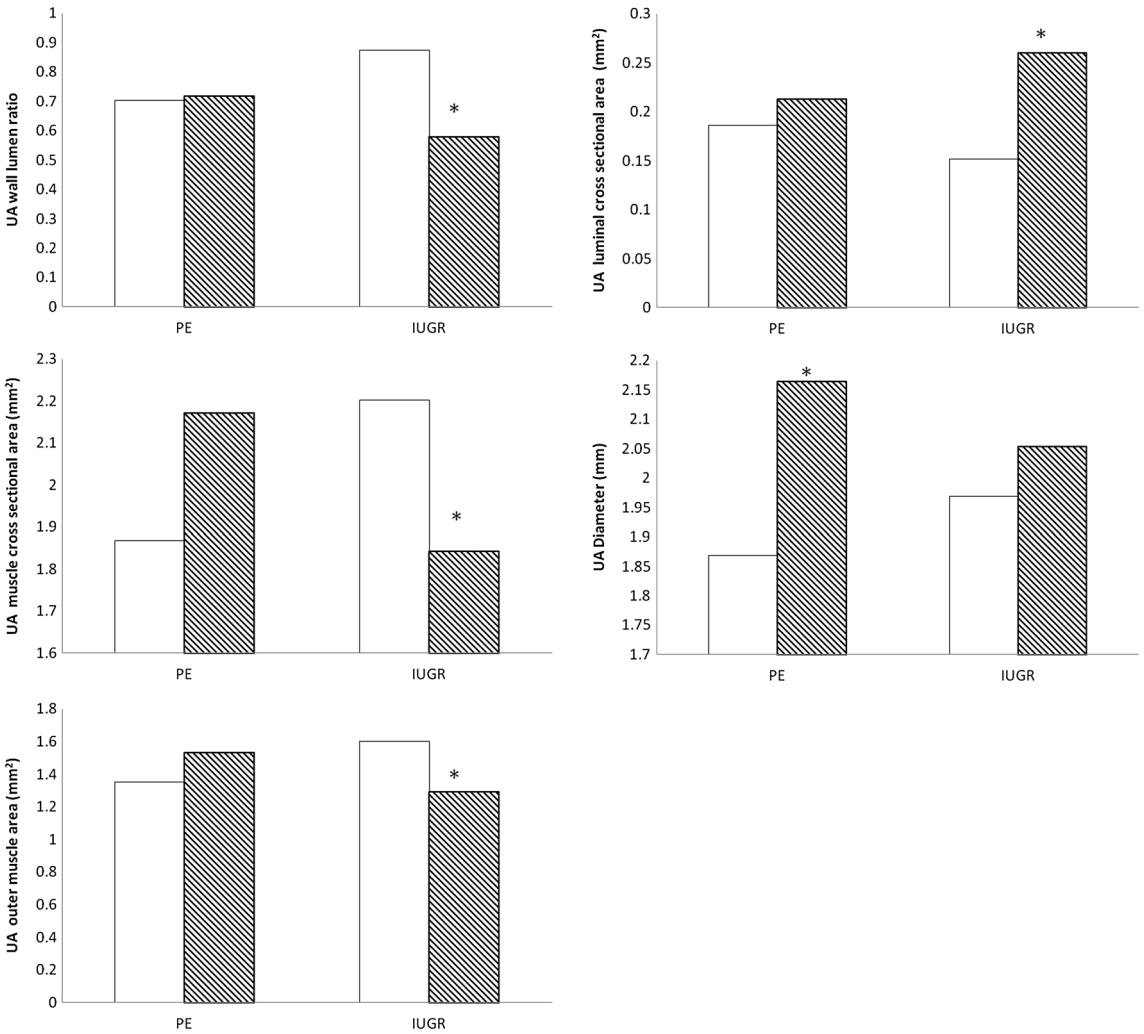

Fig. 1 continued

Table 4 Correlation between birth weight, placental weight, and umbilical cord parameters

Umbilical cord parameters	Birth weight	Placental weight
UVS A (mm^2)	0.39 (0.014)	0.41 (0.008)
UV D (mm)	0.43 (0.002)	0.36 (0.049)
UV CSA (mm^2)	0.53 (< 0.001)	0.47 ($p < 0.001$)
UV MCSA (mm^2)	0.62 ($p < 0.001$)	0.60 ($p < 0.001$)

Values are Spearman's correlation co-efficient (p value)

PE pre-eclampsia, *IUGR* intrauterine growth restricted

oligohydramnios [19] as also found by Silver et al., where umbilical cord diameter was much smaller in oligo hydramnios than in patients with normal amniotic fluid index [20].

The study has a few limitations. The umbilical cord sections were taken at fixed position of the cord. When there was gross abnomality at that position, sampling was done further away. This ensures that the results obtained in different groups should be comparable. The Doppler velocimetry reflects the functional properties of the cord. The dimensions of the cord or vessels on sonography is measured on a routine basis, therefore comparison between the postnatally measured parameters with antenatal sonographic measurement was not feasible.

In conclusion, the present study demonstrates the morphometric changes occurring in the umbilical vein associated with hypoplasia of umbilical artery are more marked in IUGR and these changes are not enhanced by the effect of PE. These changes along with a lean umbilical cord and abnormalities in Doppler velocimetry can be an early predictor of growth restriction and adverse perinatal outcome. Since umbilical vein is the main supply to the fetus, and with increasing evidence showing hypoplasia of umbilical vein in IUGR, this can be targeted for therapeutic intervention. However, multidisciplinary research involving biomechanics, structural analysis, biochemical, and biomolecular studies are mandated to provide unique

insight into cord abnormalities to identify targets for therapy to improve fetal blood supply.

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Compliance with Ethical Standards

Conflict of interest None.

Ethical Statement The work is has been approved by the Institutional Ethical Committee (Ref no. IEC 202/2012).

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