ORIGINAL ARTICLE

Umbilical cord morphology in pregnancies complicated by IUGR in cases of tobacco smoking and pregnancy-induced hypertension

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Abstract

OBJECTIVE: The aim of this study was to determine the characteristic features of the umbilical cord morphology in selected cases of intrauterine growth restriction (IUGR): tobacco smoking, pregnancy-induced hypertension and idiopathic IUGR.

MATERIALS AND METHODS: 136 pregnant women were included in the study – 86 patients with IUGR (IUGR group) and 50 women with uncomplicated course of pregnancy (control group). In the IUGR group 31 women were smokers, 27 suffered from pregnancy-induced hypertension, and 28 had an unknown reason for IUGR. Each of them underwent ultrasound examination to measure fetal growth and to assess morphological parameters of the umbilical cord.

RESULTS: Significant differences between the control group and the whole IUGR group in terms of the diameter of the umbilical cord and diameter of the umbilical vein – smaller diameters in the IUGR group than in the control group.

Significant differences among IUGR subgroups in terms of area of Wharton's jelly and diameters of the umbilical cord, vein and artery.

Significant difference in the length of the uncoiled section among the IUGR subgroups.

CONCLUSIONS: 1. The umbilical cord in IUGR and concomitant tobacco smoking is hyper-coiled with coiling index independent of fetal weight and high content of Wharton's jelly. 2. The umbilical cord in IUGR and concomitant pregnancy-induced hypertension is thinnest with thinnest vessels and the smallest content of Wharton's jelly. 3. The assessment of umbilical cord morphology should become an integral part of ultrasound exam in pregnancies complicated by IUGR.

INTRODUCTION

The causes and the reflection of fetal pathology can be sought in the structure and function of the placenta. Many diseases that complicate the pregnancy leave a vestige there, and this is where the cause for many can be found (Atalla *et al.* 1998; Biagiotti *et al.* 1998; de Laat *et al.* 2007; El Behery *et al.* 2009; Foltinova *et al.* 2010; Guiot *et al.* 2001; Kaplan *et al.* 2009; Karsdorp *et al.* 1996; Kashanian

2006; Rytlewski *et al.* 2009; Strong *et al.* 2010). The constantly improving imaging methods, such as the USG 2D, 3D, 4D, with the Doppler flow examination, allow for an even more precise assessment of fetal health and placenta function.

The authors of this paper were interested in studying the morphology of the umbilical cord as an integral part of the utero-placental unit in a selected pregnancy pathology, i.e. in the intrauterine growth restriction of the fetus.

We singled out in a particular way the pregnancies complicated by intrauterine growth restriction (IUGR) in tobacco smoking and pregnancy-induced hypertension, because of their unique character in the aspect of umbilical cord morphology, and which is related to yet another reason for fetal growth disorder in each of the groups.

Many correlations were observed between umbilical cord coiling and fetal pathology. A hypo-coiled umbilical cord accompanied fetal chromosomal abnormalities, decelerations and the need for instrumental delivery, and was more frequently observed in pregnancies complicated by intrauterine fetal death (de Laat *et al.* 2005; de Laat *et al.* 2007; Machin *et al.* 1999; Raio *et al.* 2003; Strong *et al.* 2010). A hyper-coiled umbilical cord was related to a low birth weight, drug abuse by gravida, decelerations and the need for instrumental delivery, although less frequently than a hypo-coiled umbilical cord. The intrauterine fetal death occured also less often than in the case of the hypo-coiled umbilical cord (de Laat *et al.* 2005; Degani *et al.* 2001).

The aim of this study is to assess umbilical cord morphology in terms of such parameters as: the diameter of the vein, artery, umbilical cord, size of Wharton's jelly and umbilical cord twist in selected cases of IUGR: tobacco smoking, pregnancy-induced hypertension (PIH) and idiopathic IUGR. The assessment of these parameters is to determine the characteristic features of the umbilical cord for each of the selected groups.

MATERIALS AND METHODS

The following group of patients was analyzed: 136 pregnant women in the 20^{th}–40^{th} week of pregnancy. 86 of them were diagnosed with fetal growth restriction (IUGR group). In this group 31 women were smokers, 27 suffered from pregnancy-induced hypertension, and 28 had an unknown reason for fetal hypotrophy. 50 healthy pregnant women with uncomplicated course of pregnancy were included into the control group.

Each of them underwent ultrasound examination to measure the size of the fetus, make mean umbilical cord parameter measurements, i.e. a mean result was calculated from three measurements in various sections of the umbilical cord. After estimation of exact time for pregnancy duration the criteria for IUGR diagnosis was fetal weight below 10 percentile for the fetal population of this age of pregnancy.

The umbilical cord was measured as follows: the diameter of the vessels, cross-sectional area of the vessels, umbilical cord area and Wharton's jelly area were measured in the cross-section, the length of the uncoiled section was measured on the vertical cross-section of the helix as the parameter that characterizes the coiling of the umbilical cord. We excluded the umbilical cord with only 2 vessels.

The study was conducted with the ultrasound device: Voluson Expert E8 (GE Medical Systems), the probe – 3.5 MHz volumetric abdominal.

RESULTS

1. A significant difference between the control group and the whole IUGR group in terms of the diameter of the umbilical cord (the Mann-Whitney Test p=0.049) – a smaller diameter in the IUGR than in the control group (Table 1, Figure 1).
2. A significant difference in the diameter of the vein between both groups, more evident than in the diameter of the umbilical cord (Mann-Whitney test, p=0.031) – smaller in IUGR than in the control group (Table 2, Figure 2).
3. Negligible difference between the control group and the IUGR group in terms of the diameter of the umbilical cord artery (Table 3).
4. Negligible difference between the IUGR group and the control group in terms of the area of Wharton's jelly (Table 4).
5. Negligible difference between the IUGR group and the control group in terms of the length of the uncoiled section (Table 5).
6. Correlation coefficients between each of the umbilical cord parameters and the neonate's birth weight for control group and IUGR group (Table 6).

A very interesting observation is that in the separation of IUGR subgroups, the uncoiled section of the umbilical cord is increasing with the weight of the fetus in idiopathic hypotrophy and PIH groups. At the same time, almost linear growth characterizes the PIH group, but remains unchanged in the smokers group. It remains very short, i.e. the umbilical cord is tightly hyper-coiled.

7. A significant difference among IUGR subgroups in terms of the area of Wharton's jelly – the smallest for pregnancy-induced hypertension (3), the biggest for smokers (2) (Figure 3).
8. The diameter of the umbilical cord in IUGR subgroups: the longest for smokers, shorter in the group of idiopathic IUGR and the shortest for PIH. It is the longest for smokers because of the large Wharton's jelly, since the diameters of the vessels do not differ significantly among the groups. Statistically significant differences – p=0.0436 (Figure 4).

Tab. 1. Values of the diameter of the umbilical cord in the control group (Group 2) and the whole IUGR group (Group 1).

	Rank Sum - Group 1	Rank Sum - Group 2	U	Z	*p*-value	Z - adjusted	*p*-value	Valid N - Group 1	Valid N - Group 2	2*1sided - exact *p*-value
Umbilical cord diameter	1835.5	2629.5	845.5	-1.92465	0.049	-1.92545	0.054174	86	50	0.053518

Mann-Whitney U Test. By variable groups marked tests are significant at $p<0.05$

Tab. 2. Values of the diameter of the umbilical vein in the control group (Group 2) and the whole IUGR group (Group 1).

	Rank Sum - Group 1	Rank Sum - Group 2	U	Z	*p*-value	Z - adjusted	*p*-value	Valid N - Group 1	Valid N - Group 2	2*1sided - exact *p*-value
Umbilical vein diameter	1805.500	2659.500	815.5000	-2.15197	0.031401	-2.15312	0.031310	86	50	0.030645

Mann-Whitney U Test. By variable groups marked tests are significant at $p<0.05$

Tab. 3. Values of the diameter of the umbilical artery in the control group (Group 2) and the whole IUGR group (Group 1).

	Max Neg - Differnc	Max Pos - Differnc	*p*-value	Mean - Group 1	Mean - Group 2	Std.Dev. - Group 1	Std.Dev. - Group 2	Valid N - Group 1	Valid N - Group 2
Umbilical artery dimeter	-0.082791	0.091163	>0.10	3.693023	3.708800	0.904327	0.988358	86	50

Kolmogorov-Smirnov Test. By variable groups marked tests are significant at $p<0.05$

Tab. 4. Values of the area of Wharton's jelly in the control group (Group 2) and the whole IUGR group (Group 1).

	Max Neg - Differnc	Max Pos - Differnc	*p*-value	Mean - Group 1	Mean - Group 2	Std.Dev. - Group 1	Std.Dev. - Group 2	Valid N - Group 1	Valid N - Group 2
Area of the jelly	-0.227669	0.00	>0.10	62.57255	85.33704	50.81401	54.03023	86	50

Kolmogorov-Smirnov Test. By variable groups marked tests are significant at $p<0.05$

Tab. 5. Values of the length of the uncoiled section in the control group (Group 2) and the whole IUGR group (Group 1).

	Max Neg - Differnc	Max Pos - Differnc	*p*-value	Mean - Group 1	Mean - Group 2	Std.Dev. - Group 1	Std.Dev. - Group 2	Valid N - Group 1	Valid N - Group 2
Uncoiled section lenght	-0.169697	0.026263	>0.10	32.54545	36.30889	10.02029	13.13226	86	50

Kolmogorov-Smirnov Test. By variable groups marked tests are significant at $p<0.05$

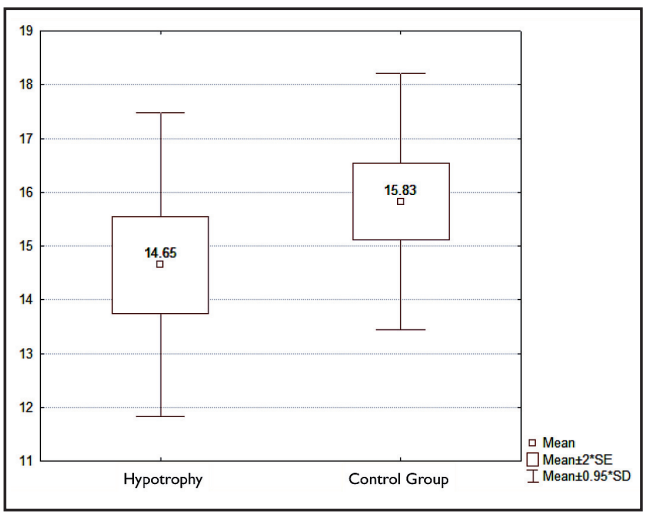

Fig. 1. Mean values and standard deviations of the diameter of the umbilical cord in the control group and the whole IUGR group.

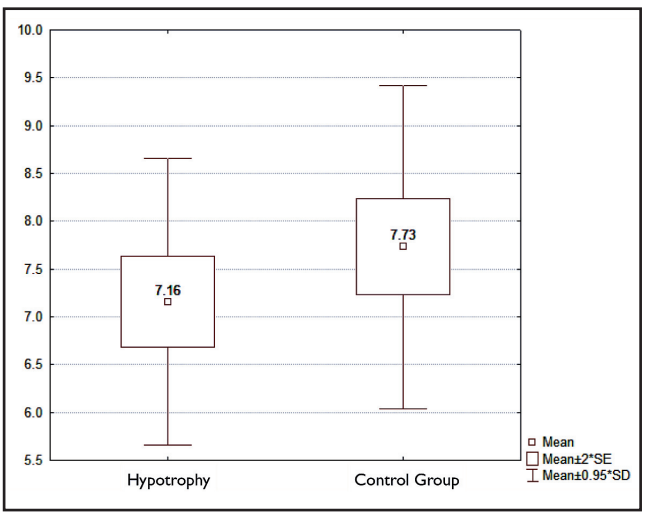

Fig. 2. Mean values and standard deviations of the diameter of the umbilical vein in the control group and the whole IUGR group.

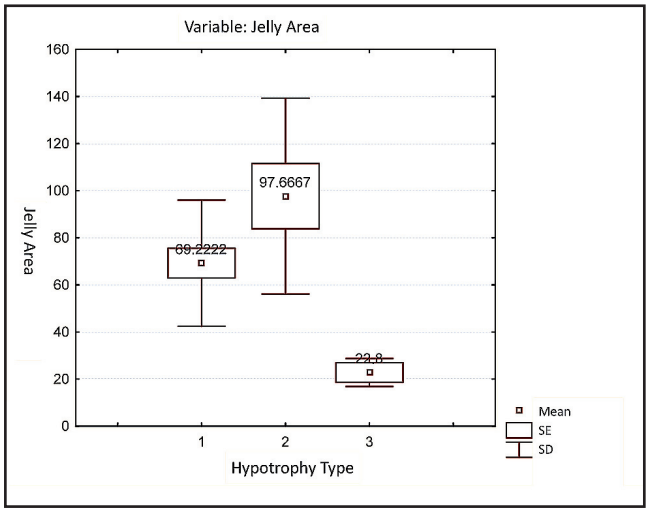

Fig. 3. Mean values and standard deviations of the area of Wharton's jelly (1 – Idiopathic Hypotrophy Group, 2- Smokers Group, 3- PIH).

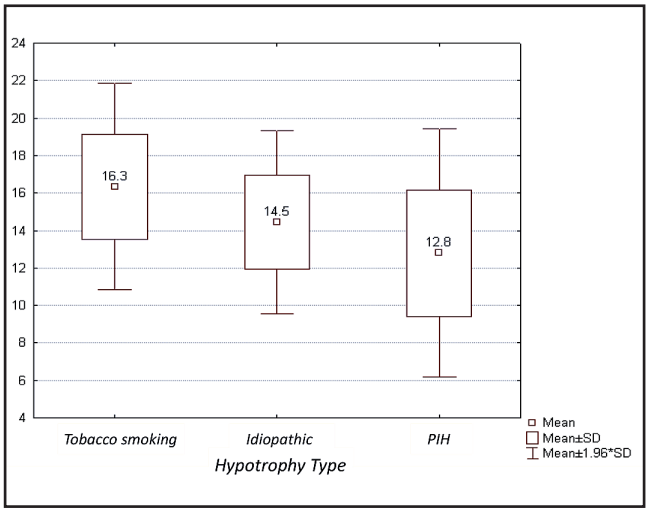

Fig. 4. Mean values and standard deviations of the diameter of the umbilical cord in IUGR subgroups.

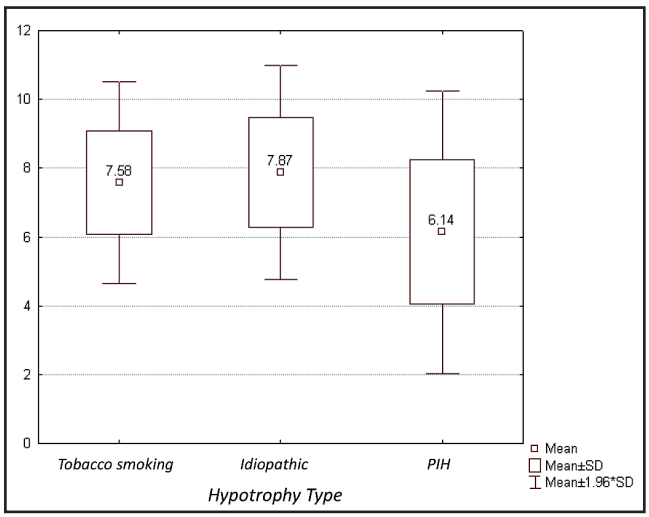

Fig. 5. Mean values and standard deviations of the diameter of the umbilical vein in IUGR subgroups.

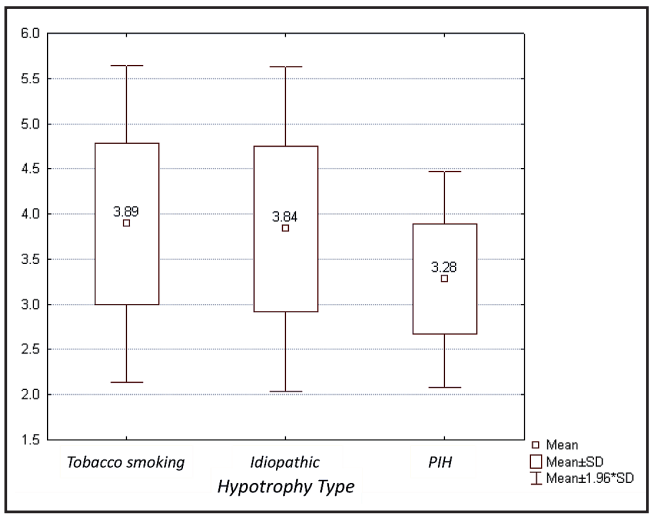

Fig. 6. Mean values and standard deviations of the diameter of the umbilical artery in IUGR subgroups.

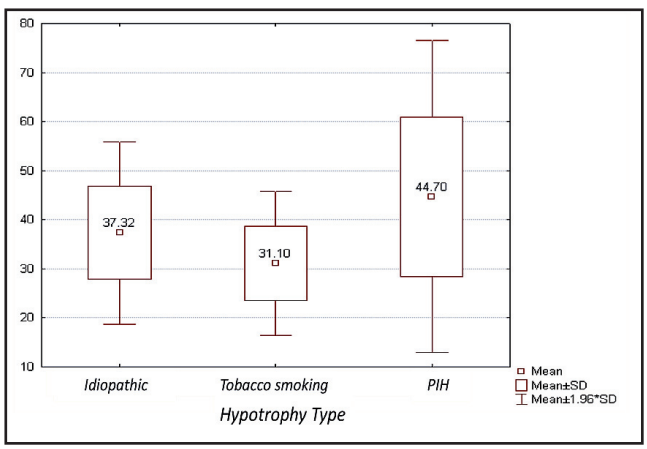

Fig. 7. Mean values and standard deviations of the length of the uncoiled section in IUGR subgroups.

9. The diameter of the vein is the longest in the idiopathic IUGR group, slightly shorter in the smokers group and significantly shorter in the PIH group (Figure 5).
10. The diameter of the artery is significantly longer in smokers than in idiopathic IUGR type and much longer than in the PIH group (the thinnest artery) – p=0.0323 (Figure 6).
11. A statistically significant difference in the length of the uncoiled section among the IUGR subgroups – p=0.01831 (Figure 7).

In our paper we analyzed the relationship between parameters of umbilical cord and duration of pregnancy and we found that not exactly the duration of pregnancy had the role but the estimated weight of

Tab. 6. Correlation coefficients between each of the umbilical cord parameters and the neonate's birth weight for control group and IUGR group.

	Total	IUGR			Control
Umbilical cord diameter	0.55	0.65			0.18
Vein diameter	0.54	0.57			0.27
Artery diameter	0.51	0.52			0.51
Jelly area	0.38	0.38			0.05
Length of uncoiled section	0.36	0.31			0.54
		Cigarettes	Idiophatic	PIH	
		-0.04	0.29	0.99	

fetus. In the control group parameters were correlated with the duration of pregnancy but in IUGR – no. The rate of growth was other. In what way the parameters was related to fetal weight we show above.

DISCUSSION

Cromi *et al.* (2007) and Ghezzi *et al.* (2000) demonstrated that in the group of healthy pregnant women and pregnant women with diabetes the measurements of umbilical cords after the 34th week were a very sensitive marker of macrosomia and that the cross-sectional area of the umbilical cord is positively correlated with fetal weight. According to Togni *et al.* (2006), not only the cross-sectional area of the umbilical cord, but also such parameters as the cross-section of the vessels and the area of Wharton's jelly increased with the growth of the fetus in healthy pregnancies.

Ghezzii *et al.* (2000) also observed that in pregnancies before 32nd week the increase of Wharton's jelly is directly proportional to the age of the pregnancy, diameter of the umbilical cord and fetal weight.

Our observations demonstrate that the diameter of the umbilical cord, the vein and the artery increase together with the weight of the fetus. This correlation was also observed for the area of Wharton's jelly. When separating the control group and IUGR group, the most evident dependence of the diameter of the umbilical cord on the fetal weight was observed in pregnancies complicated by IUGR. The diameter of the umbilical cord was also significantly smaller in the IUGR group than in the control group. Di Naro *et al.* (2000) made similar observations. In the IUGR group the umbilical cord is the thinnest in the case of PIH, and the thickest, although still thinner than in the control group, in case of tobacco smokers. We have observed that Wharton's jelly is significantly larger in the group of tobacco smokers. This is possibly correlated to a different level of collagen binding in smokers, and, thereby, a different helicity of the umbilical cord (Sekhon *et al.* 2004). In our study, the hyper-coiled umbilical cord is most explicit in smokers, what is more, the coiling index in this group was independent of the weight of the fetus. According to Kaplan *et al.* (2009) coiling is the most important anatomical feature of the umbilical cord that affects the vitality and correct development of the fetus. It is proved that the pressure of the blood flowing in the umbilical cord artery grows with the increasing number of umbilical cord twists (Kaplan *et al.* 2009). Many authors revealed that hyper-coiled umbilical cord is positively correlated with fetal growth restriction (Degani *et al.* 2001; de Laat *et al.* 2005; Predanic *et al.* 2005). It is not clear, if the improper coiling is the reason for pathology or one of its after-effects or both (de Laat *et al.* 2005). Seeking the reason for abnormal coling – low coiling of the umbilical cord in fetuses with Down syndrom, Raio et al (2003) and Ghezzi *et al.* (2000) analyzed the microstructure of Wharton's jelly and observed changes in the amount of hyaluronan. It is not exactly known what is the cause for the thinnest umbilical cord with the smallest Wharton's jelly content and the thinnest vessels, and at the same time a higher coiling index in IUGR pregnancies with PIH compared to IUGR pregnancies in case of tobacco smoking. It remains unresolved how the impaired trophoblast cell migration in PIH pregnancies affects the morphological parameters of the umbilical cord (Peker *et al.* 2006). Two completely different umbilical cord morphological models – tightly hyper-coiled with a wide Wharton's jelly of a smoker and a very thin one with a modest content of Wharton's jelly and thin vessels of PIH patients show how assessment of the umbilical cord morphology can be an important and useful marker to assess the background of IUGR. This is also stressed by many authors (de Laat *et al.* 2007; El Behery *et al.* 2009; Kaplan *et al.* 2009; Phaloprakarn *et al.* 2004; Singh *et al.* 2003). The assessment of umbilical cord coiling should become the integral part of fetal assessment in high risk pregnancies according to de Laat *et al.* (2005). This is also confirmed by our observations.

CONCLUSIONS

1. The umbilical cord in IUGR and concomitant tobacco smoking is hyper-coiled with coiling index independent of fetal weight and high content of Wharton's jelly.
2. The umbilical cord in IUGR and concomitant PIH is thinnest with thinnest vessels and the smallest content of Wharton's jelly.
3. The assessment of umbilical cord morphology should become an integral part of ultrasound exam in pregnancies complicated by IUGR.

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