Single umbilical artery and perinatal outcome

Abstract

A major role in the pregnancy routine ultrasound examination is played by the investigation of the umbilical cord (the identification of the number of vessels). The detection of a single umbilical artery (SUA) is a marker for aneuploidy, low birth weight and congenital anomalies. The presence of this anomaly can be associated with adverse perinatal outcome, compared to fetuses with normal cord thus making imperative the proper antepartum ultrasound examination. In our study we presented a review of epidemiology, pathogenesis and current diagnostic of SUA syndrome with predilection on 4 cases of SUA complicated with intrauterine growth restriction and 12 cases with isolated SUA. The 16 cases were evaluated in our Clinical Hospital of Obstetrics and Gynecology "Dr. I.A. Sbarcea" Brasov from Romania. It was observed that SUA and isolated SUA increase the risk for adverse perinatal outcomes. Therefore the detection of SUA is important for the prenatal diagnosis of congenital defects and aneuploidy. To improve the adverse perinatal outcomes, the surveillance of fetuses with isolated SUA has a major role. Even if a SUA is a relatively rare finding, when is detected, a serious search for associated malformation needs to be undertaken.
Keywords: *single umbilical artery, intrauterine growth restriction, perinatal outcome*

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Introduction

In the normal umbilical cord three vessels can be identified: one umbilical vein and two umbilical arteries. In case of an abnormal cord with single umbilical artery (SUA) there are only one umbilical artery and one umbilical vein. The arterial system is formed during the 4th and 5th week of the embryonic development. Three theories describing the pathogenesis of an absent umbilical artery are described in the literature: primary agenesis, secondary atrophy or atresia of the previously normal developed vessel, and original allantoic artery persistence[1].

The incidence of SUA, in fetuses with anomalies and even in fetuses without anomalies is 0.2%-1.6% in euploid fetuses, and 9-11% in aneuploidy fetuses. In different studies the association with different congenital anomalies and also the increased perinatal morbidity of the newborn with SUA had been investigated[2].

SUA is an isolated anomaly in >80% of cases, in rest of the cases (~20%) being associated with other anomalies (i.e. heart, urogenital system)[3]. In urogenital anomalies or renal agenesis, the anomaly is found on the side on which the artery is missing[3,4]. In case of fetuses with SUA, aneuploidy and intrauterine growth restriction (IUGR) are more often detected[5].

The association of SUA with malformations of the cardiovascular, gastrointestinal and urogenital system is well known, being noted as early as 1960[6,7]. Chromosomal abnormalities are reported in approximately 8-11% of the cases of fetuses with SUA, the incidence being higher in case of associated pathology, such as trisomy 13 and 18.

The best data, however, came from a 1998's meta-analysis of 37 reported studies[8]. The information from this study is derived from 2 types of studies: those that collected data from pregnancy losses, abortion and stillborn fetuses, and those that collected data from live-born fetuses. Among the first group, they found an incidence of SUA of 2.1% and a rate of congenital malformations of 66.3%. In the second group of live-born fetuses, they found SUA in 0.55% of the cases and congenital malformation rate at 27%. This malformation rate is considerably above the baseline rate of 2% to 3% (Figure 1).

In a study conducted by Sepulveda and contributors, they identified a compensatory increase in the diameter of the artery which leads to a vein/artery ratio ≤2 in case of fetuses with SUA, condition that is not occurring in fetuses with normal cord. To confirm or exclude the diagnosis, color Doppler ultrasound can be used, the goal being the visualization of the arteries (one or both) on either side of the bladder. In the 1st trimester of pregnancy and also in situations with suboptimal resolution, color Doppler examination is valuable because it identifies the umbilical arteries near the fetal bladder, on both sides. From about 12 weeks of pregnancy, the umbilical arteries can be seen on high resolution transvaginal color Doppler[9-12].

In a review article, Sur and contributors evaluated 15 autopsies of fetuses with SUA, during 1 year. They discovered other malformations and syndromes, apart from the common one, which were not described previously. From the total cases, 5 of them identified uni/bilateral cystic renal dysplasia. In 2 of these cases it had been found posterior urethral valves, in 2 cases additional features of Potter's sequence and in 1 case the Meckel's syndrome. The pathogenesis of these malformations could have been resulted because of the obstruction to the urinary outflow (i.e. pathology that is known to determine cystic renal dysplasia) or may have appeared from the ischemia associated with single umbilical artery[12,13].

Umbilical cords with SUA present a number of morphological differences in comparison to three-vessel umbilical cords[14,15]. The study of Raio et al.[14] has demonstrated that umbilical cords with SUA are characterized not only by an adaptive dilatation of the artery, as previously

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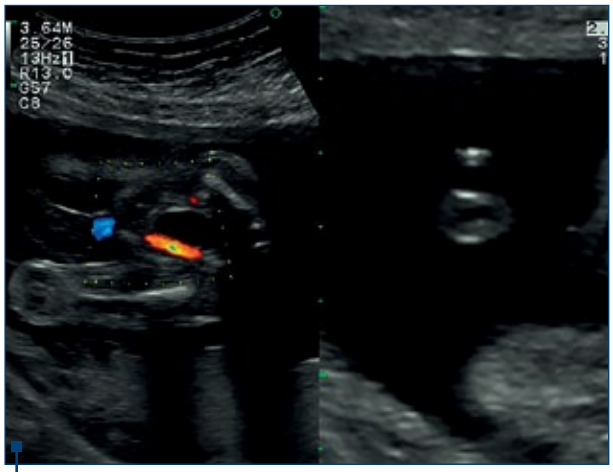

Figure 1. SUA identified by color Doppler examination, transverse scan of urinary bladder that shows SUA (in the left), transverse section of umbilical cord showing two vessels: one artery and one vein (in the right)

reported by others[12], but also by an increased caliber of the vein. This is in concordance with a previous study conducted by the same authors on a different population, in which 11 of 22 fetuses with SUA had an umbilical vein area >2 SD[16]. Another study performed by Lacro et al.[17], concluded that umbilical cord with SUA has lower number of vascular coils. Reynolds[18] investigated and also concluded that when measuring the blood flow, the central role is played by the presence/absence of the vascular coils. This was also the conclusion from the study made by Di Naro et al.[19], who identified a correlation between the index of umbilical coiling and the volume of the blood flow and also the velocity blood flow in the umbilical vein. Bäz et al.[20] identified also an abnormal A-wave of the blood flow in the ductus venosus. The velocity of the ductus venosus during the atrial contraction (i.e. A-wave) is correlated to the intensity of hypoxemia and acydemia in fetuses with IUGR)[21,22], and it was under the 5th centile in a higher proportion of healthy fetuses with single umbilical artery in the study of Raio. This suggests that, in fetuses with single umbilical artery, the hemodynamic characteristics are different from those of fetuses with normal cord[16].

Methods

This paper aims to study the effect of a SUA on infant prognosis. The role of correct ultrasound examinations realized antepartum along with amniocentesis and normal family histories provide important information so that a favorable prognostic can be expected even in a SUA pregnancy.

During 2 years, SUA was suspected on antenatal ultrasound scan in 16 cases examined at our Clinical Hospital of Obstetrics and Gynecology "Dr. I.A. Sbarcea" Brasov from Romania. The mean gestational age at delivery date was 38.2±2.4 weeks and the mean birth weight was 3203.12±835.8 g. All patients underwent genetic amniocentesis, and fetuses had a normal karyotype. SUA was detected using color-flow Doppler.

Results

The patients' personal and family histories were reviewed, including any previous pregnancy complications, medication or teratogen exposure, other children with congenital anomalies and any genetic disorders in the maternal and paternal families. A targeted ultrasound anatomic survey was performed and no other anomalies were identified. Amniocentesis was performed and the fetuses had a normal karyotype.

Serial ultrasound examination was made in order to identify signs of IUGR. The sonography parameters of fetus development were in normal ranges in 12 cases and modified in 4 cases (IUGR) (Table 1).

The modality of delivery was vaginal for the 12 cases without any complications and caesarian section for the 4 cases with IUGR (i.e. the fetus had an altered Doppler velocimetry) (Table 2).

Previous studies showed that SUA may occur as a single feature or associated to other malformations. The cases studied were not associated with any chromosomal structural abnormalities, the perinatal outcome was good in all the 16 cases, 4 cases were associated with IUGR, but no other abnormality was found following accurate investigation.

In the absence of additional ultrasound detectable malformations, an isolated SUA does not seem to affect the outcome, thus should not affect the routine obstetric assessment. An early intervention and appropriate termination of pregnancy allowed delivery of live premature newborn with good postpartum adaptation and good prognosis.

Ultrasound assessment was perfomed at 25, 32, 34, 36, 38 weeks of pregnancy. Estimated gestational age and estimated weight are represented in 16 fetuses with SUA. Four cases with SUA had IUGR and are represented in red.

Discussion

Scientific literature shows a direct correspondence between the existence of SUA and fetal malformations, especially when maternal risk factors exist[23,24]. In our group study the lack of existence of such factors correlates with pregnancies terminated with normal babies.

If we care to study those clinical signs that foresee the delivery of an infant with poor prognosis we should take note of the APGAR score, the cord length and the term.

The mean length of the cord in the pregnancies terminated through cesarean section is of 58.0875 cm. According to the study of Rayburn and contributors short and long cords are associated with the development of some intrapartum conditions such as meconium staining, fetal heart rate abnormalities, arrest of fetal descent and birth asphyxia[25]. Our medium cord length does not correlate with any of these entities. Moreover if we also analyze the study of Martinez-Frias et al. we can conclude that the shortening or the extension of the umbilical cord in SUA pregnancies appear with the same percentage as in normal pregnancies[26].

The Apgar score registered in our study group has a range value of 8.5 which is non-significant taking into

Table 1 Ultrasound assessment of fetuses with SUA from 25 weeks of pregnancy to birth

	25 Weeks		32 Weeks		34 Weeks		36 Weeks		Weeks	
	EW	GA	EW	GA	EW	GA	EW	GA	EW	GA
1	790 g	24w6d	2100 g	32w5d	2350 g	34w1d	2830 g	36w0d	3400 g	38w1d
2	814 g	25w2d	2050 g	32w4d	2300 g	33w6d	2810 g	35w6d	3360 g	37w6d
3	590 g	23w3d	1550 g	30w0d	1920 g	32w1d	2300 g	33w6d	2600 g	35w0d
4	823 g	25w3d	1980 g	32w3d	2400 g	34w3d	2880 g	36w1d	3450 g	38w4d
5	785 g	24w6d	1900 g	32w0d	2290 g	33w5d	2900 g	36w2d	3300 g	37w4d
6	772 g	24w5d	1950 g	32w2d	2330 g	34w0d	2790 g	35w5d	3410 g	38w1d
7	569 g	23w0d	1560 g	30w1d	1900 g	32w0d	2250 g	33w2d	2580 g	34w6d
8	820 g	25w2d	2150 g	33w1d	2380 g	34w2d	2850 g	36w1d	3500 g	39w0d
9	826 g	25w3d	2130 g	33w0d	2250 g	33w2d	2750 g	35w4d	3350 g	37w6d
10	770 g	24w5d	1920 g	32w1d	2350 g	34w1d	2810 g	35w6d	3410 g	38w1d
11	550 g	22w5d	1490 g	29w4d	1940 g	32w2d	2350 g	34w1d	2610 g	35w0d
12	795 g	25w0d	1930 g	32w1d	2320 g	34w0d	2830 g	36w0d	3430 g	38w3d
13	780 g	24w5d	1890 g	31w6d	2420 g	34w4d	2900 g	36w2d	3450 g	38w4d
14	810 g	25w1d	1850 g	31w4d	2300 g	33w6d	2870 g	36w2d	3400 g	38w1d
15	580 g	23w1d	1530 g	30w0d	1950 g	32w2d	2250 g	33w2d	2550 g	34w4d
16	800 g	25w0d	1940 g	32w2d	2370 g	34w2d	2810 g	35w2d	3450 g	38w4d

EW=estimated weight; GA=gestational age

account the fact that at birth the clinical examination showed no specific pathology.

When analyzing the gestational age at delivery we can easily observe that the pregnancies were terminated through cesarean section at a mean term of 34.75 weeks, explaining thus the lower birth weights.

Unlike the study of Prucka et al.[27] where the incidence of smaller than gestational age babies was noticed, our study does not show small-for-gestational-age (SGA) cases. The four cases of cesarean section were realized for the IUGR excluding thus the SGA diagnostic.

Moreover, in contrast with the study of Prucka et al.[27] the study realized by Abuhamad et al. showed that the incidence of SGA fetuses does not appear increased in case of an isolated SUA, this having concordance to our study. The same study mentions the cytogenetic and complex fetal anomalies only when the left artery is absent[28].

Regarding the mean maternal age on the moment of cesarean section, our group study has a mean value of 26.25 years ranging from 30 to 23 years thus demonstrating that the advanced age has no correlation to the IUGR incidence, results similar to the scientific literature regarding cases of SUA[27].

All of the cases involved in our study have been monitored by ultrasound anatomic surveys thus being able to find the four cases of abnormal development (IUGR). In the study of Chow et al. assessment of anomalies in fetuses was also performed using sonography. In their study, when selecting the isolated SUA cases we can notice that only 7% proved to have anomalies at birth. In our group

Table 2 Outcome of patients with SUA

Name	Age	Gestational age	Newborn weight (g)	Birth modality	Outcome Apgar Score	Placental weight (g)	Cord length (cm)
A.S.	23	38w1d	3400 g	Vaginal delivery	Newborn- alive/ IA - 9	465.3	61.5
P.I.	25	37w6d	3360 g	Vaginal delivery	Newborn- alive/ IA - 9	441.2	60.8
S.P.	29	35w0d	2600 g	Caesarian section	NN alive/IA - 8	412.2	48.4
S.D.	21	38w4d	3450 g	Vaginal delivery	Newborn- alive/ IA - 9	462.1	61.1
F.C.	25	37w4d	3300 g	Vaginal delivery	Newborn- alive/ IA - 9	452.2	59.7
C.F.	31	38w1d	3410 g	Vaginal delivery	Newborn- alive/ IA - 9	466.3	61.2
A.M.	23	34w6d	2580 g	Caesarian section	Newborn-alive/ IA-8	405.9	46.3
D.A.	26	39w0d	3500 g	Vaginal delivery	Newborn- alive/ IA - 9	470.2	61.8
M.I.	28	37w6d	3350 g	Vaginal delivery	Newborn alive/ IA - 8	436.8	60.2
P.M.	34	38w1d	3410 g	Vaginal delivery	Newborn- alive/ IA - 9	469.2	61.0
B.O.	23	35w0d	2610 g	Caesarian section	Newborn alive/ IA - 8	409.3	47.0
I.F	27	38w3d	3430 g	Vaginal delivery	Newborn- alive/ IA - 9	471.3	62.4
L.A	23	38w4d	3450 g	Vaginal delivery	Newborn- alive/ IA - 8	473.1	63.7
P.A	29	38w1d	3400 g	Vaginal delivery	Newborn- alive/ IA - 9	465.6	61.2
G.I.	30	34w4d	2550 g	Caesarian section	Newborn-alive/ IA-7	410.3	49.5
V.C	24	38w4d	3450 g	Vaginal delivery	Newborn- alive/ IA - 8	475.7	63.6

study, none of the cases presented with anomalies at birth, results matching the normal parameters of the fetuses monitored by ultrasound examination periodically[6].

Another study designed by Cristina et al. examined the pregnant women by ultrasound examination at 20 weeks of pregnancy. Their results state that in pregnancies where the ultrasound scan at 20 weeks showed no other associated abnormalities, in which aneuploidies was not found[29]. In our group, both amniocentesis and periodic ultrasound examination were performed. The amniocentesis showed normal karyotype to all the fetuses and the ultrasound examination only appeared modified in 4 of the cases. Prenatally, the diagnostic of those 4 cases was not different than that of normal pregnancies with normal fetuses in development, fact also sustained by the postnatal examinations. The perinatal mortality rate was 0 among the fetuses with SUA in contrast to the study of Cristina et al. where the registered value of perinatal mortality was 5%, an incidence that represents a mortality rate higher than the overall rate among the total patients[29].

Discovering a singular umbilical artery does not increase the risk for trisomy 21. On the other side, a single umbilical artery is associated with a 7-fold increase in the risk of trisomy 18. An increased number of fetuses with trisomy 18 have other major malformations that can be identified at the 11-14 week ultrasound examination and different

other malformations that are identified only during the 16-20 weeks screening. Thus, because of this anomalies, the ultrasound examination needs to be performed more detailed, because of the early detection of other anomalies (i.e. overlapping fingers, cardiac anomalies, facial cleft or spine bifida), that usually are not identified at a routine examination at 11 week of pregnancy.

In almost 89% of cases, the ultrasound examination will identify a correct antenatal diagnosis of singular umbilical artery, but as in any exam the diagnosis can be false-positive, even in the most experienced investigators. In 66% of the cases scanned at 16-17 weeks and in 97% at 18-19 weeks of gestation, the umbilical cords can be examined with gray-scale ultrasound examination. Of course, many factors like maternal wall thickness, gestational age, and presence of lower abdominal scar, amniotic fluid amount, scanning experience, or fetal position and equipment can be involved in the correct diagnosis of a SUA. Also, varying degrees of umbilical artery fusion that can appear near the placenta may complicate the correct diagnosis of SUA[27].

SUA pathology can be also associated with rare cases of cystic renal dysplasia, Meckel's syndrome or Potter's sequence, apart from the well-known associations with malformations of the cardiovascular, urogenital tract, muscular-skeletal, gastrointestinal tract, central nervous system and also limb reduction malformations. These malformations may have resulted because of the obstruction to the urinary outflow or because the ischemia. It is possible that the single umbilical artery is playing a major role in the development of these pathologies, because the ethio-pathogenesis in these defects is multi-factorial[28].

Fetuses and newborn with SUA and isolated SUA are at high risk for adverse perinatal outcomes. The detection of SUA is important for the prenatal diagnosis of congenital defects and aneuploidy. To improve the adverse perinatal outcomes, the surveillance of fetuses with isolated SUA has a major role. Even if a SUA is a relatively rare finding, when is detected, a serious search for associated malformation may be undertaken. Pregnancies that were identified having fetuses with associated malformations should be indicated an amniocentesis. Pregnancies with isolated SUA have to be carefully investigated[29].

Conclusions

If SUA is detected prenatally, detailed series of ultrasound examinations should be performed to rule out associated malformations. There are recommended invasive techniques for karyotyping only in cases selected, if at the ultrasound scan there were detected anomalies. A major role in the management of these cases is played by the postnatal follow-up of the newborn.

SUA and isolated SUA increase the risk for adverse perinatal outcomes, therefore the detection of SUA it is important for the prenatal diagnosis of congenital defects and aneuploidy.

In the absence of additional ultrasound detectable malformations, an isolated SUA does not seem to affect the outcome, thus should not affect the routine obstetric assessment nor the choice of vaginal delivery. To improve the adverse perinatal outcomes, the surveillance of fetuses with isolated SUA has a major role. Even if a SUA is relatively a rare finding, when is detected, a serious search for associated malformation needs to be undertaken. ■

References

1. Bombrys AE, Neiger R, Hawkins S. et al. Pregnancy outcome in isolate single umbilical artery. Am J Perinatol 2008, 25, 239-42.
2. Wiegand S, McKenna DS, Croom C, Ventolini G, Sonek JD, Neiger R. Serial sonographic growth assessment in pregnancies complicated by an isolated single umbilical artery. Am J Perinatol 2008, 25, 149-52.
3. Deshpande SA, Jog S, Watson H, Gomall A. Do babieswithisolated single umbilical artery need routine postnatal renal ultrasonography? Arch Dis Child Fetal Neonatal Ed 2009, 94(4), F265-7.
4. Doornebal N, de Vries TW, Bos AF. et al. Screening infants with an isolated single umbilical artery for renal anomalies: nonsense? Early Human Dev 2007, 83(9), 567-70.
5. Martinez-Frias ML, Bermejo E, Rodriguez-Pinilla E, et al. Does single umbilical artery (SUA) predict any type of congenital defect ? Clinical-epidemiological analysis of a large consecutive series of malformates infants. Am J Med Genet A 2008, 1(146) 15-25.
6. Chow JS, Benson CB, Doubilet PM. Frequency and nature of structural anomalies in fetuses with single umbilical arteries. J Ultrasound Med 1998, 17, 7658.
7. Lyon FA. Fetal abnormalities associated with umbilical cords containing only one umbilical artery and one umbilical vein. Obstet Gynecol 1960, 16, 719-21.
8. Thummala MR, Raju TN, Langenberg P. Isolated single umbilical artery anomaly and the risk for congenital malformations: a meta-analysis. J Pediatr Surg 1998, 33, 580-5.
9. Predanic M, Perni SC, Friedman A, Chervenak FA, Chasen ST. Fetal growth assessment and neonatal birth weight in fetuses with an isolated single umbilical artery. Obstet Gynecol 2005, 105, 1093-7.
10. Csécsei K, Kovács T, Hinchliffe SA, Papp Z. Incidence and associations of single umbilical artery in prenatally diagnosed malformed, midtrimester fetuses: a review of 62 cases. Am J Med Genet 1992, 43(3), 524-30.
11. Burshtein S, Levy A, Holcberg G. Is single umbilical artery an independent risk factor for perinatal mortality? Arch Gynecol Obstet 2011, 283(2), 191-4.
12. Sepulveda W, Peek MJ, Hassan J, Hollingsworth J.Umbilical vein to artery ratio in fetuses with single umbilical artery. Ultrasound ObstetGynecol1996, 8, 236.
13. Sur M, Nayler SJ, Muc RS. Association Of Single Umbilical Artery With Common And Rare Congenital Malformations . Internet J Pediatr Neonatol 2004, 4(1).
14. Raio, L., Ghezzi, F., Di Naro, E., Cromi, A., Buttarelli, M., Sonnenschein, M. and Dürig, P. (2003), Ductus venosus blood flow velocity characteristics of fetuses with single umbilical artery. Ultrasound Obstet Gynecol 22, 252-6.
15. Heifetz SA. Single umbilical artery. A statistical analysis of 237 autopsy cases and review of the literature. Perspect Pediatr Pathos1984, 8, 345-87.
16. Raio L, Ghezzi F, Di Naro E, Franchi M, Brühwiler H, Lüscher KP. Prenatal assessment of Wharton's jelly in umbilical cords with single artery. Ultrasound ObstetGynecol1999; 14: 42–46.
17. Lacro RV, Jones KL, Benirschke K. The umbilical cord twist: origin, direction and relevance. Am J Obstet Gynecol 1987,157, 933-8.
18. Reynolds SRM. Mechanisms of placentofetal blood flow. Obstet Gynecol 1978, 51, 245-8.
19. Di Naro E, Raio L, Ghezzi F, Franchi M, Romano F, Addario VD. Longitudinal umbilical vein blood flow changes in normal and growth-retarded fetuses. Acta Obstet Gynecol Scand 2002, 81, 527-33.
20. Bäz E, Zikuling L, Hackelöer BJ, Hecher K. Abnormal ductus venosus blood flow: a clue to umbilical cord complication. Ultrasound Obstet Gynecol 1999, 13, 204-6.
21. Rizzo G, Capponi A, Talone PE, Arduini D, Romanini C. Doppler indices from inferior vena cava and ductus venosus in predicting pH and oxygen tension in umbilical blood at cordocentesis in growth-retarded fetuses. Ultrasound Obstet Gynecol 1996, 7, 401-10.
22. Murphy-Kaulbeck L, Dodds L, Joseph KS, Van den Hof M. Single umbilical artery risk factors and pregnancy outcomes. Obstet Gynecol 2010,116(4), 843-50.
23. Hua M, Odibo AO, Macones GA, Roehl KA, Crane JP, Cahill AG. Single umbilical artery and its associated findings. Obstet Gynecol 2010,115(5), 930-4.
24. Blache G, Garba A, Frairot P, Vancina S, Gaja R. Prognostic value of a single umbilical artery. 87 cases. J Gynecol Obstet Biol Reprod (Paris) 1995, 24(5), 522-8.
25. Rayburn WF, Beynen A, Brinkman DL. Umbilical cord length and intrapartum complications. Obstet Gynecol 1981, 57(4), 450-2.
26. Martinez-Frias ML, Bermejo-Sanchez E, Rodriguez-Pinilla E, Prieto-Merino D, Grupo de Periferico del ECEMC. Characterstics of neonates with and without a single umbilical artery. Analysis of two consecutive series of neonates with and without congenital defects. An Pediatr (Barc) 2006, 65(6), 541-50.
27. Prucka S, Clemens M, Craven C, McPherson E. What does it mean for the fetus? A case-control analysis of pathologically ascertained cases. Genet Med 2004. 6:54-57;
28. Abuhamad AZ, Shaffer W, Mari G, Copel JA. Single umbilical artery: does it matter which artery is missing? Am J Obstet Gynecol 1995, 173(3 Pt 1), 728-32.
29. Cristina MP, Ana G, Inés T, Manuel GE, Enrique IG. Perinatal results following the prenatal ultrasound diagnosis of single umbilical artery. Acta Obstet Gynecol Scand 2005, 84(11), 1068-74.