Prenatal Sonographic Diagnosis of Single Umbilical Artery: Evaluation of 23 Cases

Prenatal Sonografide Tek Umbilikal Arter Tanısı: 23 Olgunun Değerlendirilmesi

Mahmut Tuncay ÖZGÜN, MD,[a]
Çağdaş TÜRKYILMAZ, MD,[a]
Mustafa BAŞBUĞ, MD,[a]
Dilek KAYA, MD,[a]
Cem BATUKAN, MD[a]

[a]Department of Obstetrics and Gynecology, Erciyes University, Faculty of Medicine, Kayseri

Geliş Tarihi/*Received:* 13.10.2008
Kabul Tarihi/*Accepted:* 19.01.2009

This work was presented at the 6th Congress of the Turkish Society of Maternal Fetal Medicine and Perinatology, which was held on 29 October-2 November 2008, in Antalya, TURKEY.

Yazışma Adresi/*Correspondence:*
Mahmut Tuncay ÖZGÜN, MD
Erciyes University, Faculty of Medicine, Department of Obstetrics and Gynecology
Kayseri,
TÜRKİYE/TURKEY
mtozgun@erciyes.edu.tr

ABSTRACT Objective: Single umbilical artery (SUA) is associated with congenital anomalies, abnormal karyotypes and adverse perinatal outcome including intrauterine growth retardation (IUGR), low birth weight and prematurity. The aim of this study was to present perinatal results of cases with SUA. **Material and Methods:** This is a retrospective analysis of prenatally diagnosed 23 cases with SUA out of 3558 pregnancies between January 2004 and December 2007. **Results:** The gestational age at diagnosis varied between 14 and 34 weeks. The mean maternal age was 27.4 ± 4.7 (22-40) years. The median parity was 0 (range 0-4). Six of the 23 fetuses had additional congenital anomalies including bilateral renal agenesis (n= 1), unilateral renal agenesis (n= 2) or cardiac malformations (n= 3). IUGR was detected in one fetus. Eight fetuses had soft markers for chromosomal anomalies and SUA was isolated in 8 (35%) cases. The karyotype of all 11 fetuses with additional anomalies or soft markers was normal. One case was terminated at 18 weeks due to bilateral renal agenesis. Preterm delivery complicated five pregnancies. After birth, 6 fetuses were diagnosed to be small for gestational age. Three babies died after birth. All of these fetuses had a congenital anomaly along with SUA. **Conclusion:** A targeted ultrasound examination for detection of additional anomalies and soft markers should be performed in cases with SUA. Close surveillance is necessary for monitoring fetal growth and fetal well-being in cases with SUA.

Key Words: Umbilical arteries; ultrasonography, prenatal; umbilical cord

ÖZET Amaç: Tek umbilikal arter (TUA) konjenital anomaliler, kromozom anomalileri ve düşük doğum ağırlığı, prematürite ile intrauterin gelişme geriliği gibi olumsuz perinatal akıbet ile birlikte olabilir. Bu çalışmanın amacı TUA saptanan olguların perinatal sonuçlarını sunmaktır. **Gereç ve Yöntemler:** Bu retrospektif çalışmaya Ocak 2004 ile Aralık 2007 tarihleri arasında arasında değerlendirilen 3558 gebelikten TUA saptanan 23 olgu dahil edildi. **Bulgular:** Fetuslara 14 ile 34 gebelik haftaları arasında tanı konuldu. Ortalama maternal yaş 27.4 ± 4.7 (22-40) yıl, median parite 0 (0-4 arasında) olarak bulundu. Altı fetusta ek anomali saptandı ve bunlar, bilateral renal agenezi (n= 1), tek taraflı renal agenezi (n= 2), ve kardiyak anomali (n= 3) şeklinde idi. Bir fetusta ise intrauterin gelişme geriliği saptandı. Sekiz fetusta kromozom anomalisi ile ilişkili "soft marker" izlenirken, 8 (%35) olguda ise izole TUA saptandı. Ek anomali veya "soft marker" saptanan 11 olguda karyotip analizi yapıldı ve bunların hepsinde normal karyotip saptandı. Bilateral renal agenezi saptanan bir olguda gebelik 18. haftada sonlandırıldı. Beş olguda erken doğum oldu, 6 olguda ise doğum sonrası bebeklerin gebelik haftasına göre düşük doğum ağırlıklı oldukları saptandı. Doğum sonrası ek anomalileri olan 3 bebek kaybedildi. **Sonuç:** TUA saptanan olgularda ek anomaliler ve "soft marker" olup olmadığının araştırılması için detaylı ultrason incelemesi yapılmaldır. Bu hastalarda fetal gelişimin ve fetal iyilik halinin takibi gereklidir.

Anahtar Kelimeler: Umbilikal arterler; ultrasonografi, prenatal; umbilikal kord

Turkiye Klinikleri J Gynecol Obst 2009;19(2):75-80

The umbilical cord normally consists of three vessels, two arteries and one vein. The absence of one umbilical artery is described as SUA which has been associated with some adverse perinatal events, such as low birth weight, prematurity, perinatal mortality, IUGR and congenital malformations including central nervous system, cardiovascular, gastrointestinal and renal systems.[1-4] The incidence of SUA is about 1% in singleton pregnancies and approximately 5% in twins, umbilical cord should be evaluated routinely in second trimester ultrasonographic examinations.[5] If SUA is diagnosed, a detailed sonographic examination is necessary to rule out associated abnormalities. Isolated single umbilical artery has a perfect perinatal outcome. However, when additional anomalies or ultrasonographic markers related to chromosomal abnormalities are present, fetal karyotyping to rule out any chromosomal abnormalities may be necessary.[6] In the absence of additional anomalies or soft markers related to abnormal karyotypes, isolated SUA is not an indication for karyotyping.

We report a retrospective study of prenatally diagnosed 23 cases with single umbilical artery at our tertiary referral center over a period of 3 years. The associated anomalies, karyotypes and neonatal outcomes were also documented.

MATERIAL AND METHODS

A total of 23 fetuses with SUA, diagnosed by prenatal ultrasound examination at the University of Erciyes, Faculty of Medicine, Department of Obstetrics and Gynecology, between January 2004 and December 2007, were included in this retrospective analysis. Ultrasound examinations were carried out on a heterogeneous population that includes both low- and high-risk patients. Fifteen cases were diagnosed during routine antenatal examination in our unit. The other 8 cases were referred from other institutions for suspected SUA or suspected congenital anomalies detected during fetal ultrasound examination at various scans during pregnancy. Indications of targeted sonographic examinations were summarized in Table 1. Gestational age was calculated from the last menstrual period or determined from standard fetal biometric measurements. We diagnosed single umbilical artery when a cross-sectional image of the umbilical cord demonstrated only 2 vessels and/or an oblique transverse section of the lower fetal abdomen, including the fetal bladder, was first obtained and color flow mapping was then used to visualize the both umbilical arteries on either side of the bladder (Figure 1). In the absence of one of them, SUA was confirmed (Figure 2). All of these fetuses underwent a detailed second-level ultrasonographic examination. All targeted ultrasound examinations were performed transabdominally by using Logiq 500 Pro (3.5-MHz linear-array transducer) or GE Voluson 730 Pro (4.5-7.5 MHz linear-array transducer). The finding of a SUA was confirmed after delivery in all newborns, and on pathological examination of an aborted fetus. Karyotyping was offered to all patients where additional fetal anomalies or soft markers were identified. Fetal karyotype was available in 11 cases. The outcome data concerning the presence or absence any other structural and chromosomal abnormalities were determined by a variety of methods, including review of hospital records, postnatal chart reviews and contact with the families. Small for gestational age (SGA) fetuses were diagnosed if their birth weight was below the 10th centile for gestational age. After birth, complete physical examination was performed by a pediatrician.

RESULTS

SUA was identified in 23 fetuses out of 3558 pregnancies that had a detailed second-level ultrasonographic examination, thus representing a prevalence of 0.6%. Twenty one of the fetuses with SUA were singletons. In two sets of twins the fetuses were discordant for SUA. In the study period, 3355 singletons, 177 twin and 26 triplet pregnancies underwent a detailed sonographic evaluation. The prevalence of SUA was 0.6% for singletons and about 1% for multifetal pregnancies. Only one woman reported a previous malformed delivery, whereas the obstetric histories were unremarkable in the remaining women. The gestational age at the time of diagnosis varied between 14 and 34 weeks. The mean maternal age was 27.4 ± 4.7 years (22-40). The median parity was 0 (range 0-4). The ma-

TABLE 1: Indications for sonography, presence of additional ultrasound findings, and outcomes of the fetuses with single umbilical artery (SUA).

Case	Gestational age at diagnosis (week)	Indication for ultrasound examination	Additional sonographic findings	Karyotyping	Gestational age at delivery (week)	Outcome
1	14	SUA+NT↑	Yes	Yes	40	Live birth
2	16	Screening	Yes	Yes	40	Live birth
3	16	Anhydramnios	Yes	-	18	TOP
4	19	SUA+hydronephrosis	Yes	Yes	38	Live birth
5	20	CPC	Yes	Yes	36	Live birth
6	20	Abdominal cyst	Yes	Yes	40	Neonatal death, SGA
7	20	Cardiac anomaly	Yes	Yes	40	Neonatal death
8	20	MS-AFP↑	Yes	Yes	36	Live birth, SGA
9	20	Renal anomaly+advanced maternal age	Yes	Yes	39	Live birth
10	21	Screening	Yes	Yes	39	Live birth
11	21	Screening	-	-	37	Live birth
12	22	Screening	-	-	34	Live birth, SGA
13	22	SUA	-	-	40	Live birth
14	23	Screening	-	-	40	Live birth, SGA
15	23	SUA	Yes	Yes	39	Live birth
16	24	SUA+pyelectasis	Yes	Yes	37	Live birth
17	24	SUA	-	-	40	Live birth
18	24	Screening	-	-	40	Live birth
19	24	SUA	-	-	40	Live birth
20	26	SUA	-	-	38	Live birth
21	28	IUGR	Yes	-	32	Live birth, SGA
22	29	Anhydramnios	Yes	-	33	Neonatal death, SGA
23	34	Short femur	Yes	-	40	Live birth

IUGR, intrauterine growth retardation; CPC, choroid plexus cyst; NT, nuchal translucency; MS-AFP, maternal serum alpha-fetoprotein;; TOP, termination of pregnancy.

le to female ratio of the babies was 0.8:1. Presence of additional ultrasound findings, indications for sonography, fetal karyotype and perinatal outcome of the fetuses were summarized in Table 1. Six of the 23 fetuses had additional congenital anomalies. These anomalies included bilateral renal agenesis (n= 1), unilateral renal agenesis (n= 2), double outlet right ventricle and bilateral hydronephrosis (n= 1), primum type ASD (n= 1), and cardiomegaly (n= 1). Intrauterine growth retardation was detected in one fetus. Eight fetuses had soft markers belong to chromosomal anomalies. These soft markers included hypoplastic nasal bone (n= 1), bilateral choroid plexus cyst (n= 2), nuchal edema (n= 1), pyelectasis (n= 1), hyperechogenic bowel together with an abdominal cyst (n= 1), increased fetal nuchal translucency (n= 1) and hydronephrosis (n= 1).

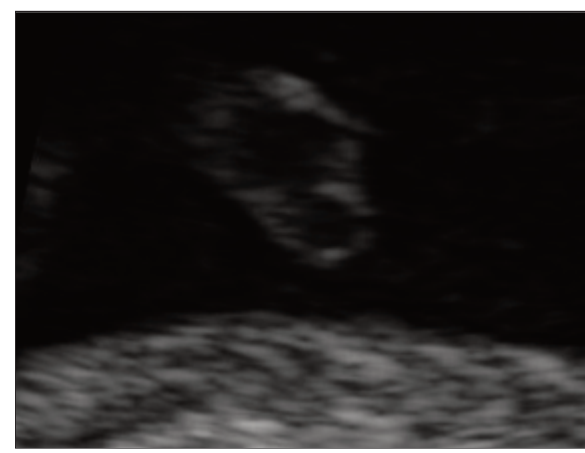

FIGURE 1: Cross section of the umbilical cord showing only two vessels corresponding to single umbilical artery.

Isolated SUA was diagnosed in 8 (35%) cases. As invasive testing was not offered in these cases, fetal karyotype was available in 11 cases showing

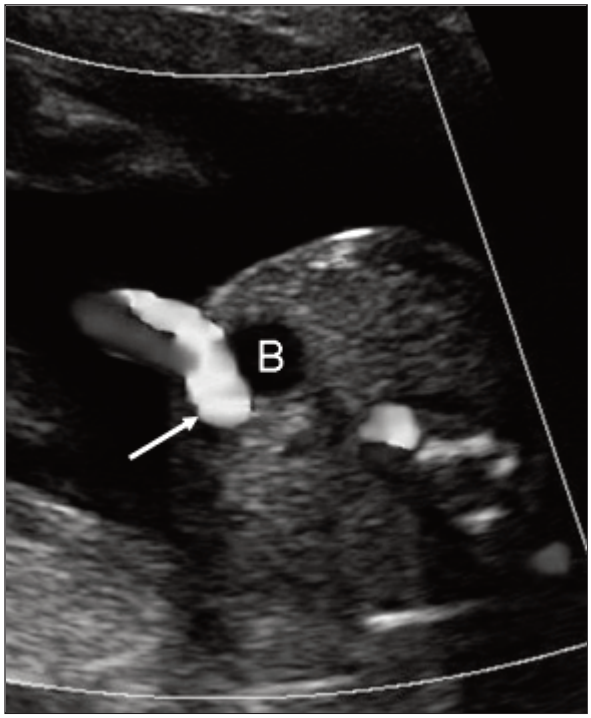

FIGURE 2: Color Doppler ultrasound confirms a single umbilical artery (arrow) coursing around the urinary bladder (B).

additional anomalies or soft markers together with SUA on prenatal ultrasound. All of these fetuses carried a normal karyotype. Premature delivery complicated 5 pregnancies. Six newborns were SGA. One case with bilateral renal agenesis was terminated at 18 weeks and the diagnosis was confirmed with postmortem pathological examination. The remaining 22 pregnancies resulted in live birth. However, three babies died after birth. All of them had an additional congenital anomaly along with SUA (Table 1). Meconium peritonitis was diagnosed in one newborn, which had hyperechogenic bowel together with an abdominal cyst on prenatal ultrasound and this baby underwent a laparatomy and died after operation due to infecion. Double outlet right ventricle was confirmed by echocardiography in one newborn and this baby died 2 monts after delivery. Cardiac failure due to dilatated cardiomyopathy was diagnosed by echocardiography in one newborn, which had cardiomegaly on prenatal ultrasound and this baby died one day after delivery. The families denied autopsy in this 3 cases. Unilateral renal agenesis in 2 fetuses and bilateral renal agenesis in one fetus were confirmed after birth.

DISCUSSION

SUA is the most frequent malformation of the umbilical cord. The presence of a SUA occurs in 1% of all live-born infants. As in the present study, the incidence of SUA is higher in twin pregnancies. Additionally, SUA was found to be more frequent in twins originating from assisted reproduction.[7] SUA may accompany other abnormalities or occur as an isolated defect. There are three theories regarding the pathogenic mechanism resulting in SUA: It may result from primary agenesis of one umbilical artery (1), secondary atrophy of a previously normal umbilical artery (2) or persistence of the original allantoic artery of the body stalk.[8] It is believed that atrophy is the most frequent mechanism. Since the umbilical cord can be easily seen prenatally by ultrasound, the presence of a single umbilical artery should be readily detectable in most pregnancies, even as early as 12 weeks of gestation.[9] The evaluation of the umbilical cord has become an integral part of the routine obstetric ultrasound examination and the number of vessels should be identified whenever possible.

The prenatal sonographic identification of an SUA is usually made by examining the umbilical cord in longitudinal and transverse section on B-mode sonography. But, the number of umbilical arteries cannot be identified adequately with longitudinal and transverse sections in early pregnancy and in situations with suboptimal resolution, such as oligohydramnios and maternal obesity. In this situation, color Doppler ultrasound can be used to confirm or exclude the diagnosis by visualizing one or both arteries within the fetal abdomen on either side of the bladder.[10] The false-positive diagnosis rate of SUA has been reported between 20% and 6%.[11] There were not any false-positive cases in our series, which may be related to the use of color Doppler ultrasound and equipment with higher resolution. Sepulveda and coworkers observed a compensatory increase of the umbilical arterial diameter in SUA.[12] They suggested that an umbilical vein to umbilical artery dia-

meter ratio less than 2:1 is a good indicator for diagnosis of SUA. On the other hand, Perssutte and Leuke reported that transverse umbilical artery diameter measuring more than 4 mm between 20-36 weeks of gestation is useful prediction of diagnosis of SUA.[13]

SUA may be associated with many chromosomal abnormalities and congenital malformations.[6,14] However, SUA can also be seen as an isolated finding. The diagnosis of SUA necessitates searching for associated malformations such as facial cleft, cardiac anomalies, renal anomalies, spina bifida and soft markers related to chromosomal abnormalities that are detectable during the 18-22 week scan.

The incidence of congenital anomalies has been reported to be 20% in infants with SUA.[15] In our study, 26% of fetuses with SUA had major anomalies, similar to findings reported in previous studies.[12,13,15] However, there is no known malformation or syndrome that is invariably associated with SUA. It is not clear why SUA is linked to other fetal anomalies, The most frequent anomalies include genitourinary and cardiovascular systems, whereas the gastrointestinal and central nervous systems are affected less frequently.[5,16] Our results were in agreement with these data. We detected three cases with urogenital system abnormalities (unilateral-bilateral renal agenesis) and three cases with cardiac abnormalities (primum ASD, double outlet right ventricle, and cardiomegaly). Therefore, it should be emphasized that after the diagnosis of SUA, a detailed ultrasound examination is necessary to rule out concurrent anomalies, especially cardiac and renal abnormalities.

The incidence of cytogenetic abnormalities among fetuses with SUA approximates up to 17%, with nearly half of these fetuses having major anomalies.[15,17] However, we did not encounter any cytogenetic abnormality in our series. Lubusky et al reported 102 fetuses with SUA, 19 fetuses with additional abnormalities had abnormal karyotypes and no chromosomal anomalies were found in cases with isolated SUA.[6] Trisomy 18 is the most common aneuploidy associated with SUA with trisomy 13, Turner syndrome and triploidy being the next common ones. Trisomy 21 does not appear to be associated with this anomaly.[18] If a single umbilical artery is prenatally detected, targeted ultasonography should be performed in these patients for exclusion of associated anomalies.[19-21] We recommend fetal karyotyping only in cases with additional anomalies and with soft makers related to chromosomal abnormalities.

In accordance with previous reports, our study showed that fetuses with SUA have been found to have a significant risk for low birth weight, prematurity and perinatal and neonatal mortality. It is not clear why fetuses with SUA, even in isolated cases, are related to dismal perinatal outcome. It has been documented that these cords have a lower number of spirals and lesser amount of Wharton jelly, which make them vulnerable in situations of stress, such as compression of the umbilical cord during delivery. Therefore, serial ultasonography to assess fetal growth and development and fetal well-being tests should be performed in these patients. All newborns must receive a good physical examination and a careful follow-up during infancy.

In conclusion, we emphasize that umbilical cord examination should be an integral part of prenatal ultrasound studies. A detailed ultrasound examination for diagnosis of other anomalies should also be performed when SUA is diagnosed. SUA occurs to be an isolated anomaly in most of cases. In cases of apparently isolated SUA, there is no indication for fetal karyotyping because in this group there is no evidence of increased risk of chromosomal defects. The diagnosis of SUA should alert the obstetrician to search for associated malformations and markers of chromosomal defects. Fetal karyotyping may be necessary in the presence of associated anomalies or with the presence of soft markers. Close obstetric follow up is necessary in cases with SUA due to increased risk of IUGR, SGA, prematurity and neonatal mortality.

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