Prenatal Diagnosis of Single Umbilical Artery (SUA) and Postpartum Outcome

Tian-gang Li[1], Gang Wang[2], Fang Xie[2], Juan-min Yao[2], Lan Yang[2], Meng-lin Wang[1], Jian Wang[3], Lin Xing[3], and Fang Nie[4]

[1]Affiliation not available
[2] Gansu Provincial Maternity and Child-care Hospital
[3]Gansu Provincial Maternity and Child-care Hospital
[4]Lanzhou University Second Hospital

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Abstract

Objectives: To investigate the incidence of single umbilical artery (SUA), malformation, and postpartum outcomes in a retrospective analysis of 781 fetuses with SUA. Methods: A retrospective analysis of 781 pregnant women with singleton fetuses with SUA were diagnosed in the Gansu Provincial Maternal and Child-care Hospital from 2013 to 2019. Detailed data on maternal and fetal characteristics and postpartum outcomes were obtained. Results: A total of 624 (79.9%) fetuses were diagnosed with isolated SUA, whereas 157 (20.1%) fetuses had SUA with other structural and/or chromosomal abnormalities. The highest incidence of malformations was found in the urinary system, followed by the cardiovascular system and the digestive system. The incidence of SUA on the right side was 59.1% and life side was 40.9% respectively. Fetuses with SUA and other abnormalities showed a trend to be small for gestational age (3061 g vs 3201 g, $p < 0.01$) but not be delivered preterm. Conclusions: After a diagnosis of SUA, structural observation of the fetus is required. The urinary, cardiovascular, and digestive systems should be the focus of observation. If relevant malformations are found, genetic testing must be performed. With isolated SUA, it is recommended to dynamically monitor biological indicators to be alert for SGA, but genetic testing is not recommended.

Introduction

A normal umbilical cord contains two umbilical arteries and an umbilical vein. In cases with single umbilical artery (SUA), there is only one umbilical artery in the fetal umbilical cord.[1,2] SUA is one of the most common fetal abnormalities identified during prenatal screening, with an incidence of approximately 0.5% to 5%.[3,4] Maternal risk factors for SUA include smoking, metabolic disease, advanced age, pregnancy achieved through reproductive technology, and multiple births.[5-8] In multiple pregnancies, the incidence of SUA is 3 to 4 times higher than that of singleton pregnancies.[9] SUA is also associated with fetal structural malformations,[10] fetal aneuploidy,[11] and increased risk of intrauterine growth restriction.[12] About 80% of SUA cases have isolated SUA,[13-14] which is a soft indicator of fetal chromosomal abnormalities, congenital malformations, and premature birth. In addition, isolated SUA often causes certain obstetric complications, such as increased perinatal mortality and increased incidence of fetal growth restriction.[15-17] This study evaluated maternal characteristics, fetal complications, and perinatal outcomes among 781 women with singleton pregnancies who received a prenatal diagnosis of SUA between 2013 and 2019. The goal of this study is to provide a better basis for counseling of affected pregnant women.

Methods

Study design. Between November 2013 and March 2019, we retrospectively analyzed the characteristics of 781 fetuses with SUAs and their mothers at Gansu Provincial Maternity and Child-care Hospital. Pregnant

mothers with multiple gestations were excluded from the study.

The diagnosis of SUA was confirmed using two-dimensional imaging of the umbilical cord in cross section (UA; Figure 1) or color blood flow at the level of fetal abdominal cord insertion (Figure 2). We confirmed the diagnosis of isolated SUAs by postnatal pathological examination, and all neonates were found to be anatomically normal. We collected data on maternal characteristics, results of ultrasound examinations, and postnatal outcomes (Table 1). We calculated gestational age based on the first day of the last menstrual period, which was confirmed by crown-rump length measurement at the first trimester ultrasound examination. A small-for-gestational-age (SGA) fetus was diagnosed when the birth weight of the newborn was less than 5th percentile for gestational age.

Instruments and methods. We used E10 and E8 (GE Healthcare, USA) ultrasound systems to perform fetal biometric measurements. The abdominal probe frequency was set to 3.0 to 5.0 MHz. All ultrasound images were preprocessed by a routine setting. The Doppler energy was set to $<$100 mW/cm^2. SUAs were confirmed during the second or third trimesters. All fetuses with SUA underwent detailed ultrasound examination, and karyotyping was performed based on the findings of the prenatal examination. The results of the ultrasound examinations were evaluated by three specialized sonographers. The study protocol was approved by the Medical Ethics Committee of Gansu Provincial Maternity and Child-care Hospital and pregnant mothers provided their written informed consent.

Statistical analysis. We performed data analysis using IBM SPSS Statistics for Windows version 23.0 (IBM Corp., Armonk, NY, USA). Continuous variables are presented as mean ± SD as appropriate. The nonparametric Mann-Whitney U test was used to compare continuous variables between groups. Data from categorical variables were analyzed using relative and absolute frequencies, and chi-square test or Fisher's exact test was used to analyze categorical variables. All of the statistical tests results were two-tailed, and p [?] 0.05 was considered to indicate statistical significance.

Results

Between November 2013 and March 2019, 1328 pregnancies with SUAs fetuses were diagnosed in 369,372 pregnant women using prenatal ultrasound; the incidence of SUA was 0.36%. There were 781 cases with complete information for further analysis. We performed a comparison of maternal characteristics and pregnancy-related parameters of fetuses with isolated SUA and fetuses with SUA and other (structural and/or chromosomal) abnormalities (Table 1). The median age of the pregnant women was 28.6 years (range, 15-46 years). Ultrasound examination findings showed a minimum gestational age of 12 weeks, maximum gestational age of 41 weeks, and mean gestational age of 29 weeks. Of the women, 112 (14.3%) were determined to be smokers or passive smokers. Thirty-two (4.1%) cases used assisted reproductive technology to achieve pregnancy. Two hundred fifty-four (19.7%) pregnant women had previously delivered a fetus or had a history of abortion. There were no significant differences in maternal characteristics between the two groups, including maternal age, body mass index, or the rate of passive smoking ($p > 0.05$; Table 1).

Information on the absence of an umbilical artery based on ultrasound examination was available for 318 cases: 188 (59.1%) fetuses lacked the left umbilical artery, whereas 130 (40.9%) fetuses lacked the right umbilical artery. The placenta was mainly located in the anterior or posterior wall, and there were no significant differences in placental position between the two groups ($p > 0.05$; Table 2).

Among the 781 fetuses with SUAs, 709 live births were recorded, 3 (0.52%) of 624 isolated SUA fetuses had intrauterine deaths, and 2 neonates died after birth (0.34%). Among the 157 fetuses with SUA and other abnormalities, 5 (3.27%) died intrauterinely, 3 (2.23%) died postnatally, and 59 (36.6%) pregnancies were voluntarily terminated because of malformations. There were 709 (86.7%) of live births, of which 486 (68.55%) underwent vaginal delivery and 223 (31.45%) underwent cesarean delivery. The median gestational age at delivery of a solitary SUA fetus was 38^{+6}W (range, 28^{+2}-42^{+1}W), and the median birth weight was 3201 g (range, 970-4300 g). Ninety fetuses (12.69%) with other abnormalities had a median gestational age at delivery of 38^{+5}W (range, 25^{+4}-41^{+5}W) and an average birth weight of 3060 g (range, 520-4300 g).

Thirty-seven SGA infants were born with isolated SUA, and 11 SGA newborns had SUA with abnormalities (Table 3). The incidence of SUA with abnormalities was higher than that of isolated SUA (5.98% vs 12.22%, $p < 0.05$). Fetuses with additional abnormalities were less likely to be born (57.32% vs 99.20%), and the incidence of intrauterine deaths and terminations was higher among SUA fetuses with abnormalities (Table 3). A chromosome examination was performed for 252 fetuses, among which 6 were found to have chromosomal abnormalities. All of the fetuses with chromosomal abnormalities had at least one organ system abnormality, Three cases had congenital heart disease, and 3 cases had multiple system abnormalities.

There were 624 cases of isolated SUAs, resulting in an incidence of 79.9%; 157 of the cases of abnormal fetuses had at least 1 additional structure, and 6 had chromosomal abnormalities. There were 209 abnormal organ systems found in 157 fetuses, including 115 cases with one abnormal organ system, 33 cases with two abnormal organ systems, 8 cases with three abnormal organ systems, and 1 case with four abnormal organ systems. The highest proportion of abnormal organ systems was determined to urinary (n = 53, 25.4%), followed by the cardiovascular and digestive systems, accounting for 23.4% (n = 49) and 13.9% (n = 29), respectively (Table4).

discussion

With the application of modern ultrasound technology, the evaluation for SUA is now performed as a routine ultrasound examination, and the diagnosis of SUA is increasing. SUA can be diagnosed by color Doppler blood flow or umbilical cord cross section as early as the nuchal translucency examination during early pregnancy.[18] In our study, the incidence of SUA was 0.35%, which is consistent previous studies.[3] SUA is considered to be a soft marker for congenital abnormalities. When an SUA is detected, it is important to carry out a detailed examination of the structure. If structural abnormalities are found, invasive diagnostic tests should be performed.[19] We analyzed 781 pregnant women diagnosed with SUA by prenatal ultrasound and found a single right umbilical artery in 59.1% of cases and a single left umbilical artery in 40.9% of cases, similar to previous studies.[18] Compared with the reported SUA incidence of 13% to 50% in the literature, the abnormality rate (structural and/or chromosomal) of our SUA fetus was 20.1%, similar to that reported by some studies.[20,21]

Among the 157 SUA fetuses with 209 organ abnormal systems, we found that the incidence of urinary system abnormalities was highest, followed by cardiovascular structural abnormalities and digestive system abnormalities, which is inconsistent with the results of previous studies. Studies often report that SUA is most often associated with congenital heart disease.[4,5] The reasons for this may be due to the absence of a unilateral UA in the embryo of the SUA fetus, which affects the development of the yolk duct, and the yolk duct is closely related to the development of the fetal urinary system. Therefore, the author believes that in future work, once SUA is determined by ultrasound, a detailed ultrasound examination of the urinary system structure should be performed. Earlier studies estimated the incidence of nephropathy in children with SUA to be as high as 16%.[22] Therefore, routine monitoring of kidney structure and function in SUA fetuses after birth should allow early detection and treatment of kidney diseases.

In this study, the highest proportion of abnormal amniotic fluid occurred in SUA fetuses with nonstructural anomalies. UAs come from the internal iliac arteries, and the blood vessels of the lower limbs in fetuses may be influenced by the loss of one umbilical artery. This may lead to a change in abdominal aorta blood flow in SUA fetuses, resulting in a change in fetal renal arterial hemodynamics and renal function that may affect amniotic fluid production. In our study, in cases of fetal simple amniotic fluid abnormality, there were more cases with reduced amniotic fluid than too much amniotic fluid, indicating that SUAs fetuses may have a potential risk of changes in fetal kidney function. Therefore, the author believes that in future work, once SUA is determined by ultrasound, a detailed ultrasound examination of the fetal amniotic fluid should be performed.

In addition, there were 152 cases of fetuses with only one soft index, such as ventricular bright spots, enhanced bowel echo, pelvic separation, and all of neonates had a good prognosis. This indicates that combining a single soft index with SUA has no significant effect on the fetus's prognosis, and routine chromosomal examination in

cases of isolated SUA is not required. In our study, 6 fetuses were found to have chromosomal abnormalities: 3 cases had congenital heart disease, and 3 cases had multiple system abnormalities. Therefore, when structural abnormalities are present in the SUA fetus, invasive diagnostic tests and echocardiogram should be performed for the diagnosis of congenital heart disease.

The incidence of chromosomal abnormalities in SUAs fetuses is reported to be between 1.3% and 15.3%.[14] In our study, only 0.8% of fetuses were found to have chromosomal abnormalities. This low percentage of chromosomal abnormalities may be due to the ability of modern ultrasound to observe severe structural abnormalities during early pregnancy or in the second trimester, resulting in a higher proportion of voluntary terminations. However, most of the fetuses with severe structural abnormalities did not undergo relevant chromosomal examinations, resulting in a lower incidence of chromosomal abnormalities in our study. In addition, whether invasive diagnostic tests for isolated SUA should be part of the prenatal diagnosis is a controversial issue. Because the possibility of chromosomal abnormalities in neonates with isolated SUAs is very small, some scholars do not recommend invasive prenatal diagnosis of isolated SUA.[19] In our study, there were no cases of chromosomal abnormalities detected in isolated SUA fetuses. This indicates that once SUAs are detected and other structural abnormalities are excluded, the probability of chromosomal abnormalities is very low. We suggest that conventional chromosomal examinations can be performed for elderly pregnant women with isolated SUAs.

Although some authors found no significant difference in the development of fetuses with isolated SUA compared with normal fetuses,[5,20] some scholars suggest that routine dynamic measurement of fetal biological parameters and Doppler ultrasound assessment should be performed to identify possible intrauterine growth restriction in fetuses with isolated SUA.[23-25] In our study, the proportion of SGA with isolated SUA was high, reaching 6.0%, and we may support the latter suggestion based on our findings. The reason why isolated SUA does not affect the growth and development of the fetus may be that the diameter of the artery is compensatorily increased compared with a normal arterial diameter.

Because this was a retrospective study, there are some limitations to our findings. First, the gestational week may have a certain impact on the detection of fetal malformations. In this study, SUA cases were found from early pregnancy to the third trimester. For example, some malformations during early pregnancy cannot be accurately detected, resulting in a low positive rate of structural abnormalities during this period, which could affect the statistical results. In addition, the perinatal results of the analyzed fetuses may be biased by limited follow-up data. In 2013, Voskamp et al.[26] published a meta-analysis of fetuses with isolated SUA and concluded that the overall minority of cases did not ensure large-scale prospective cohort studies to draw further conclusions. Overall, although this was a descriptive retrospective single-center study, the importance of our study is emphasized by the data presented from 781 fetuses with SUA, including 573 fetuses with isolated SUA.

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Author Contributions

TL and FN carried out image acquisition and drafted the manuscript. GW, FX and JY participated in the design of the study and performed the image analysis. LY and MW analyzed the patient data and examined the fetues. JW and LX performed the statistical analysis. All authors read and approved the final manuscript.

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Conflict of interest:

The authors have no conflicts of interest.

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Availability of data and materials

The data and material in the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

The study protocol was approved by the Medical Ethics Committee of Gansu Provincial Maternity and Child-care Hospital (Approval number 2017-14).

References

1.Araujo Junior E1, Palma-Dias R, Martins WP, Reidy K, da Silva Costa F. Congenital heart disease and adverse perinatal outcome in fetuses with confirmed isolated single functioning umbilical artery. J Obstet Gynecol. 2015;35(1):85–87.

2 Bugatto F, Quintero-Prado R, Melero-Jimenez V. Ultrasound pre-dictors of birth weight in euploid fetuses with isolated sisingleum-bilical artery.Ultrasound Obstet Gynecol. 2010; 36(6):724-727.

3. Gornall AS, Kurinczuk JJ, Konje JC. Antenatal detection of a single umbilical artery: does it matter? Prenat Diagn. 2003; 23(2):117–123.

4. Hua M, Odibo AO, Macones GA, Roehl KA, Crane JP, Cahill AG. Single umbilical artery and its associated findings. Obstet Gynecol. 2010; 115(5):930–934.

5. Friebe-Hoffmann U, Hiltmann A, Friedl TWP, Lato K, Hammer R, Janni W, et al. Prenatally Diagnosed Single Umbilical Artery (SUA) - Retrospective Analysis of 1169 Fetuses. Pranatal diagnostizierte singulare Nabelschnurarterie (SUA) – retrospektive Analyse von 1169 Feten. Ultraschall Med. 2019; 40(2):221–229.

6. Burshtein S, Levy A, Holcberg G, Zlotnik A, Sheiner E. Is single umbilical artery an independent risk factor for perinatal mortality? Arch Gynecol Obstet. 2011; 283(2):191–194

7. Lilja GM. Single umbilical artery and maternal smoking. BMJ. 1991; 302(6776):569–570

8. Leung AK, Robson WLM. Single umbilical artery. A report of 159 cases. Am J Dis Child 1989; 143(1):108–111

9. Volpe G, Volpe P, Boscia FM, Volpe N, Buonadonna AL, Gentile M. 'Isolated' single umbilical artery: incidence, cytogenetic abnormalities, malformation and perinatal outcome. Minerva Ginecol. 2005; 57(2):189–198.

10. Chow JS, Benson CB, Doubilet PM. Frequency and nature of structural anomalies in fetuses with single umbilical arteries. J Ultrasound Med. 1998; 17(12):765–768

11. Persutte WH, Hobbins J. Single umbilical artery: a clinical enigma in modern prenatal diagnosis. Ultrasound Obstet Gynecol. 1995; 6(3):216–229

12. Catanzarite VA, Hendricks SK, Maida C, Westbrook C, Cousins L, Schrimmer D. Prenatal diagnosis of the two-vessel cord: implications for patient counselling and obstetric management. Ultrasound Obstet Gynecol. 1995; 5(2):98–105

13. Martinez-Payo C, Gaitero A, Tamarit I, Garcia-Espantaleon M, Iglesias Goy E. Perinatal results following the prenatal ultrasound diagnosis of single umbilical artery. Acta Obstet Gynecol Scand. 2005; 84(11):1068-74

14. Chetty-John S, Zhang J, Chen Z, Albert P, Sun L, Klebanoff M, Grewal U, et al. Long-term physical and neurologic development in newborn infants with isolated single umbilical artery. Am J Obstet Gynecol 2010;203(4):368.e1–368.e3687.

15. De Catte L, Burrini D, Mares C, Waterschoot T. Single umbilical artery: analysis of Doppler flow indices and arterial diameters in normal and small-for-gestational age fetuses. Ultrasound Obstet Gynecol 1996; 8(1):27–30.

16. Martinez-Payo C, Gaitero A, Tamarit I, Garcia-Espantaleon M, Iglesias Goy E. Perinatal results following the prenatal ultrasound diagnosis of single umbilical artery. Acta Obstet Gynecol Scand 2005; 84(11): 1068–1074.

17. Horton AL, Barroilhet L, Wolfe HM. Perinatal outcomes in isolated single umbilical artery. Am J Perinatol 2010; 27(4): 321–324.

18. Geipel A, Germer U, Welp T, Schwinger E, Gembruch U. Prenatal diagnosis of single umbilical artery: determination of the absent side, associated anomalies, Doppler findings and perinatal outcome. Ultrasound Obstet Gynecol. 2000; 15(2):114–117

19. Van den Hof MC, Wilson RD. Diagnostic Imaging Committee, Society of Obstetricians and Gynaecologists of Canada; Genetics Committee, Society of Obstetricians and Gynaecologists of Canada. Fetal soft markers in obstetric ultrasound. J Obstet Gynaecol Can 2005; 27(6): 592–636

20. Blazer S, Sujov P, Escholi Z, Itai BH, Bronshtein M. Single umbilical artery–right or left? Does it matter? Prenat Diagn. 1997; 17(1):5–8.

21. Jauniaux E. The single artery umbilical cord: it is worth screening for antenatally? Ultrasound Obstet Gynecol. 1995; 5(2):75–76.

22. Thummala MR, Raju TN, Langenberg PJ. Isolated single umbilical artery anomaly and the risk for congenital malformations: a meta-analysis. Pediatr Surg. 1998; 33(4): 580–585.

23. 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(3):149–152.

24. Murphy-Kaulbeck L, Dodds L, Joseph KS, Van den Hof, M. Single umbilical artery risk factors and pregnancy outcomes. Obstet Gynecol. 2010; 116(4):843–850.

25. Ashwal E, Melamed N, Hiersch L, Edel S, Bardin R, Wiznitzer A, Yogev Y. The impact of isolated single umbilical artery on labor and delivery outcome. Prenat Diagn. 2014; 34(6):581–585.

26. Voskamp BJ, Fleurke-Rozema H, Oude-Rengerink K, Snijders RJ, Bilardo CM, Mol BW, et al. Relationship of isolated single umbilical artery to fetal growth, aneuploidy and perinatal mortality: systematic review and meta-analysis. Ultrasound Obstet Gynecol. 2013;42(6):622–628.

Figure legends

Figure 1.

a. Two-dimensional images of normal fetal umbilical cord cross section.

b. Two-dimensional images of SUA fetal umbilical cord cross section.

Figure 2.

a. Normal fetal umbilical cord color blood flow shows two umbilical arteries.

b. SUA fetal umbilical cord color blood flow shows only one umbilical artery.

Table 1. Comparison of maternal characteristics between fetuses with isolated SUAs and fetuses with SUAs and anomalies and/or chromosomal abnormalities.

	Total(781)	Isolated SUA(n=624)
Body mass index (kg/m^2)	23.2±3.4	23.6±3.5
Maternal age (years)	28.6±4.7	28.7±4.5
Passive smoking		
Yes	112	85
No	649	527
Unknown	20	12
Type of conception		
Spontaneous	726	629
Assisted reproduction	32	23
Unknown	23	17
Parity	781	624
0	527	410
1 or higher	254	214
1 Mann-Whitney U test; 2 Chi-square test.	1 Mann-Whitney U test; 2 Chi-square test.	1 Mann-Whitney U test; 2 Chi

Table 2. Comparison of results of ultrasound examination between fetuses with isolated SUAs and fetuses with SUAs and anomalies and/or chromosomal abnormalities.

	Total(781)	Isolated SUA(n=624)	SUA with anomalies (n=157)	t-value/ χ-value	p-value
Placental location				0.593	0.414[2]
Front wall	327	261	66		
Back wall	298	246	52		
Side walls	116	95	21		
Uterine floor	40	22	18		
Low placenta	3	2	1		
Placental structure	781	624	157	0.581	0.347[3]
Normal	775	620	155		
Racket shaped	3	2	1		
Sail shaped	3	2	1		
Amniotic fluid	781	624	157	20.392	0.000[2]
Normal	746(95.52%)	607(97.28%)	139(88.54%)		
Reduced	22(2.82%)	10(1.60%)	12(7.64%)		
Increased	13(1.66%)	7(1.12%)	6(3.82%)		
2 Chi-square test; 3 Fisher's exact test.	2 Chi-square test; 3 Fisher's exact test.	2 Chi-square test; 3 Fisher's exact test.	2 Chi-square test; 3 Fisher's exact test.	2 Chi-square test; 3 Fisher's exact test.	2 Chi-square test; 3 Fisher's exact test.

Table 3. Comparison of postnatal outcomes between fetuses with isolated SUAs and fetuses with SUAs and anomalies and/or chromosomal abnormalities.

	Total(781)	Isolated SUA(n=624)	SUA with anomalies (n=157)	t-value/ χ-value	p-value
Outcome				257.83	0.000[2]
Live birth	709(90.78)	619(99.20%)	90(57.32%)		
Intrauterine demise	8(1.02%)	3(0.05%)	5(3.57%)		
Death after birth	5(0.64%)	2(0.03%)	3(2.23%)		
Termination	59(7.55)	0	59(%)		
Gestational week (weeks)	38.87±1.39	38.89±1.327	38.67±1.79	1.209	0.227[1]
SGA (weight [?]5th percentile)	48(6.77%)	37(5.98%)	11 (12.22%)	4.848	0.03[2]
Fetal weigh	3.18±0.402	3.201±0.366	3.060±0.577	2.656	0.008[1]
1 Mann-Whitney U test; 2 Chi-square test.	1 Mann-Whitney U test; 2 Chi-square test.	1 Mann-Whitney U test; 2 Chi-square test.	1 Mann-Whitney U test; 2 Chi-square test.	1 Mann-Whitney U test; 2 Chi-square test.	1 Mann-Whitney U test; 2 Chi-square test.

Table 4. Abnormal organ systems involved in 871 fetuses with SUA (157 fetuses with 209 abnormal organ systems with at least one structural abnormality).

	One organ system abnormal (n = 115)	Two organ system abnormal (n = 33)	Three organ system abn
Urinary	33	16	4
Cardiovascular	31	13	4
Digestive	18	6	4
Nervous	8	11	5
Skeletal	8	13	3
Face and body	10	5	2
Other	7	2	2
Total	115	66	24