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Original Research

Single umbilical artery: a continuous dilemma and challenge in obstetric management

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Background: The single umbilical artery (SUA), an entity with almost unknown etiology, is still subject to discussion regarding its clinical significance, especially when it is an isolated discovery (iSUA). *Methods*: This retrospective study focused on the evaluation of fetuses with ultrasound proven SUA during second trimester screening. These fetuses were carefully investigated for other malformations. The respective pregnancies were attentively followed up and the newborns were evaluated confirming SUA. *Results*: The incidence of SUA was 0.57%, with 34.6% of these fetuses having associated abnormalities being 19.2% cardiovascular, 15.3% gastrointestinal, 11.5% cerebral, 7.6% osteomuscular and 3.8% urogenital. Aneuploidy was present in 8% of these infants. These rates were significantly greater compared with those noticed in "normal" three vessels umbilical cord (TVC) fetuses (control group) ($p < 0.001$). Similar relations were found for the rates of IUGR and/or SGA, polyhydramnios and oligohydramnios ($p < 0.001$). Interestingly, in iSUA group (65.4% of all SUA cases), only the rate of oligohydramnios was significantly increased compared with the control group ($p = 0.038$). Furthermore, in a dichorionic diamniotic twin pregnancy, with only one fetus revealing iSUA, the "affected" fetus paradoxically weighted more than the "healthy" one. *Conclusion*: We concluded that SUA is an important finding during morphological ultrasound examination. When associated with other anomalies, a fetal karyotype is mandatory due to the increased risk of aneuploidy. Furthermore, the pregnancy should be meticulously monitored in order to promptly diagnose other developmental anomalies associated with abnormalities of the amniotic fluid volume and to detect any anatomical anomalies missed at the initial prenatal evaluation. Finally, we concluded that diabetes mellitus represents a strong favoring condition for SUA with first pregnancy also being a contributor.

Keywords

Single umbilical artery (SUA); Malformation; Aneuploidy; Trisomy; Oligohydramnios; Polyhydramnios

1. Introduction

The single umbilical artery (SUA) is the most common cord anomaly [1]. Its clinical significance is strongly associated with other fetal abnormalities. Fetuses presenting SUA as a unique finding have a significantly better outcome compared with those with other malformations and/or genetic anomalies [2–5].

Factors that have been proposed to be involved in the genesis of SUA include maternal smoking, diabetes mellitus, ethnicity and maternal age [6], but its specific etiology remains unknown.

The present study was focused on the identification and quantification of other fetal abnormalities (genetic or not) associated with SUA and on the eventual impact of SUA on pregnancy outcome. Because the repercussions of an isolated SUA (iSUA) on fetal and/or pregnancy outcome is still disputed [2, 6–10], we compared the characteristics of our iSUA cases with a "normal" cohort of fetuses and pregnancies.

2. Method

This is a retrospective study on all second trimester ultrasound screenings performed between January 2013 and December 2019 in the Department of Obstetrics and Gynecology, Clinical Emergency County Hospital of Craiova, Romania (Institutional Ethical Approval 897/2020).

The assessment of the number of vessels in the umbilical cord is routine during the ultrasound examination at this gestational age as it has been recommended by numerous clinical guidelines [2, 11].

The SUA was detected through common method where a transverse view of the fetal pelvis showed a single umbilical

artery coursing the fetal bladder. Color or power Doppler ultrasound was utilized to confirm the diagnosis.

All documented SUA cases were further investigated for other fetoplacental abnormalities and, if considered necessary, further genetic investigations were recommended.

All maternal and historical data were carefully investigated and recorded.

The patients were advised to follow up their pregnancies in the same unit by a specialist in pregnancy ultrasound and to deliver in our Department.

We recorded all data obtained during the remainder of the pregnancy as well as all delivery data.

For comparing the rate, the characteristics and the evolution of the eventual abnormal aspects in SUA cases with those within the "normal" population, we used a control group (three vessels umbilical cord fetuses—TVC group), consisting of all delivered fetuses registered in our medical unit during 2019 (n = 2.718).

The results obtained were statistically analyzed using One-way ANOVA for numerical data. A p value < 0.05 was considered statistically significant and <0.001 was considered highly significant. Odds Ratio (OR) was calculated to compare the particular aspects in fetuses, in pregnancy outcomes and deliveries in SUA patients to those within the "normal" population with the accepted confidence interval (C.I.) being 95%.

3. Results

Between January 2013 and December 2019, 4561 singleton pregnancies between 18–24 weeks of gestation were screened in the Department of Obstetrics and Gynecology, Emergency Clinical County Hospital of Craiova, Romania.

This represented approximately 25% of all births registered in our Department during the study period with the majority of the delivering women arriving from the south-western region of Romania and who were assigned to this tertiary referral medical unit.

SUA was observed in 26 fetuses, representing an incidence of 0.57%.

Nine of these fetuses (34.6%) had other abnormal ultrasound findings (aSUA group): cardiac anomalies (right ventricular hypoplasia, ductal independent aortic coarctation, ventricular asymmetry, ventricular septal defect, atrial septal defect, left ventricular echogenic focus), cerebral anomalies (Dandy-Walker syndrome, cerebral ventriculomegaly, choroid plexus cysts), gastrointestinal anomalies (esophageal atresia, hyperechoic bowel), urogenital anomalies (Potter II sd.), other structural anomalies (cheilognathopalatoschisis and diaphragmatic hernia) and/or intrauterine growth-restriction (IUGR). The majority of these fetuses had multiple malformations and 2 of them proved to be aneuploidic; one case with trisomy 21 and one with trisomy 13. In both cases, the pregnancy was terminated at patient request. The same decision was taken for the fetus with diaphragmatic hernia and ventricular septal defect. The pregnancy with SUA and Potter II syndrome developed anhydramnios and an emergency C-section was done at 31 weeks with subsequent neonatal death (Table 1).

All anomalies discovered during the second trimester ultrasound screening were confirmed after birth. However, postpartum we found one case of imperforate anus and one case of bicuspid aortic valve which were missed at the US screening (Table 1).

The fetuses who demonstrated iSUA were born at term and with no complications except for one fetus who developed intrauterine growth restriction (IUGR) and a second with oligohydramnios. No further genetic investigation was considered (Table 1).

A dichorionic diamniotic twin pregnancy with one fetus missing the left umbilical artery was identified. The affected fetus weighed more than the other twin who had a "normal" three-vessels umbilical cord (Table 1).

The absent umbilical artery was the left one in 18/26 cases, corresponding to 69.2% from all fetuses with SUA, but in 7/9 from fetuses with associated malformations—77.7% (Table 1).

We found a significantly increased ponder of primiparity in SUA group as compared to the control group. The incidence of preconceptional diabetes mellitus (DM) was also significantly increased in the same group. Because we had few data on the smoking rate in the control group, we used as a control, a report about the smoking rate in pregnant women in US—10.3% in 2019 [12], which was similar with the incidence observed by us (Table 2).

The incidence of fetal malformations and fetal aneuploidies was significantly increased in SUA group when compared with the control group. As expected, in affected fetuses (aSUA group), the rates of IUGR and/or of the small for gestational age (<10th percentile) (SGA), low Apgar scores, small placentas (<10th percentile), polyhydramnios or oligohydramnios were significantly higher compared with the control group. However, in iSUA group (65.4% of all SUA cases) we noticed only a significantly increased rate of oligohydramnios compared with TVC fetuses. Except for the two medical abortions, there were no cases of intrauterine fetal death (IUFD) in the study group (Table 3).

4. Discussion

The incidence of SUA is around 0.5% of all second trimester pregnancy screenings [13], but it is discovered in 2.1% of fetal deaths, autopsies or aborted fetuses [7].

We found an incidence of 0.57% for SUA. In 65.4% of cases, the SUA was the only finding. Ebbing [8] and Hua [13] reported the incidence of iSUA to be around 70–85%, which is similar to our findings.

The left umbilical artery was missing in 69.2% of the cases, a value concordant with other reports [14].

The impact of iSUA on pregnancy and fetal outcome is still disputed. Ebbing [8] reported a rate of iSUA as being 0.41% in a sixteen-year study. Among maternal causes, he found a

Table 1. Details of the cases with single umbilical artery (SUA) associating structural and evolutive abnormalities. Also presented is the single twin case.

Case	Maternal characteristics			Placenta	Artery missing	Fetal characteristics							
	Age (years)	Parity	Conditions			GA (LMP) (weeks)	Weight (g)	Apgar	Birth events	Morphology	Delivery	Sex	Genetics
1	36	I	—	<10% percentile	left	22	340	—	No	Dandy Walker sd.; Right ventricular hypoplasia; Cheilognato-palatoskisis; Hyperechoic bowel	Medical abortion	F	47,XX, +13
2	24	I	No	Normal	left	38	3280	7	No	Ductal independent aortic coartaction; Ventricular asymmetry (TIII); Bicuspidic aortic valve*	CS	F	na
3	21	I	Smoker	<10% percentile	left	37	2460	8	No	Esophageal atresia; Polyhydramnios; IUGR	Vaginal delivery	F	na
4	38	II	No	<10% percentile	left	31	1100	0 (Neonatal death)	No	Potter II sd.; Early severe oligohydramnios; IUGR	CS	M	46,XY
5	21	I	No	normal	left	18	160	—	—	Choroid plexus cyst; Hyperechogenic bowel	Medical abortion	M	47,XY, +21
6	18	I	No	<10% percentile	left	37	2680	8	No	Atrial septal defect; Polyhydramnios; IUGR; Imperforate anus*	CS	M	46,XY
7	24	II	No	Normal	right	39	3540	7	No	Borderline lateral cerebral ventriculomegaly	CS	M	46,XY
8	29	I	No	Normal	left	38	3080	8	No	Echogenic left ventricular focus	Vaginal delivery	F	na
9	26	I	No	Normal	right	21	320	—	—	Diaphragmatic hernia; Ventricular septal defect	Medical abortion	M	46,XY
10	32	I	No	Normal	left	35	1750	9	No	**IUGR	Vaginal	M	na
11	28	II	No	Normal	left	37	2840	8	No	**Olygohydramnios	Vaginal	M	na
12	22	I	No	Dichorionic diamniotic	I. SUA, left II. TVC	37	I. 2720 II. 2460	I. 8 II. 7	No	I. Normal II. Normal	CS	F F	na na

Abbreviations: SUA, single uterine artery; CS, cesarean-section; IUGR, intrauterine growth-restriction; TCV, three vessels umbilical cord (*discovered at birth; **SUA was initially discovered as an isolated finding (iSUA); sd., syndrome; na, not available).

Table 2. The mothers' clinical characteristics.

Parameter		Study group	Control	Statistics	
		(n = 26)	(n = 2.718)	p	Test's value
Patient's age (years)	Mean ± SD	27 ± 5	26 ± 2	0.593	f-r: 0.286
	Interval	19–38	13–44	—	—
Parity	Mean ± SD	1.3 ± 0.5	1.6 ± 0.8	0.072	f-r: 3.286
	I para	76.9% (20)	54%	0.025	OR: 2.5 (1.1–7.1)
	II para	19.2% (5)	32%	0.173	OR: 0.5 (0.2–1.3)
	III para	3.8% (1)	11%	0.269	OR: 0.3 (0.02–2.1)
	>III para	0.0% (0)	4%	0.730	OR: 0.6 (0.03–10.1)
Smoker		11.5% (3)	[10.3%]#	0.835	OR: 1.1 (0.2–5.3)
DM		3.8% (1)	0.18%	0.005	OR: 21.7 (2.4–192.5)
Other maternal condition		0.0% (0)	1.5%	0.891	OR: 1.2 (0.07–20.3)
Twins		3.8% (1)	1.8%	0.449	OR: 2.1 (0.2–16.4)

Abbreviations: DM, diabetes mellitus (#data from literature [12]; SD, standard deviation; f-r, f-ratio in One-way ANOVA test; OR, Odds ratio (95% confidence interval).

slight increase of iSUA incidence in smoking mothers, multiparity (>3) and a previous cesarean delivery. The iSUA was associated with increased rates of intrauterine and perinatal death, preterm birth and 5 min Apgar score <7. The incidence of SGA (below the 5th percentile) was significantly increased in iSUA, compared with cases with three vessel umbilical cord (TVC). The rate of preeclampsia and of the pregnancy-induced hypertension (PIH) was not increased. The rate of associate anomalies of the cord and placenta were significantly increased in iSUA compared with TVC. Finally, he found that a pregnancy with a SUA increases the risk of SUA in the subsequent pregnancy with higher incidence of anomalous cord insertion.

Our data failed to show any correlation between iSUA and the mean fetal weight, GA(LMP) and lower Apgar scores at delivery. This was a similar to the observation of Tulek [2], who found that the Doppler flow in the unique umbilical artery was in normal range. The incidence of oligyhydramnios but not the polyhydramnios was significantly increased in iSUA group compared with the control. Furthermore, the GA(LMP) was significantly reduced in the control group as compared to iSUA group. This apparent paradox was probably the result of our National guidelines, which advise that all pregnancies with estimated delivery before 37 weeks should be sent to the regional third referral medical unit which includes our department (Table 3).

It is accepted that approximately 15–30% of SUA are associated with different fetal abnormalities.

In our group, the rate of malformed fetuses was 34.6% (9/26). This value, which was highly significant greater compared with the incidence of malformations in TVC group, demonstrates the very high risk of structural and/or genetic abnormalities in SUA fetuses. The incidence of different anomalies was 19.2% cardiovascular, 15.3% gastrointestinal, 11.5% cerebral, osteomuscular 7.6% and urogenital 3.8%. The majority of the fetuses had multiple malformations. Friebe-Hofman [15] found an incidence of 9.0% for cardiovascular, 3.5% for urogenital, 2.9% for musculoskeletal, 3.0% for gastrointestinal and 2.1% for cerebral abnormalities in SUA fetuses. The rate of aneuploidy was 8%. This value was significantly increased compared with the control and is concordant with other reports [8]. All fetuses with aneuploidy were missing the left umbilical artery. Similar findings by Geipel [14] and Abuhamad [16] who reported that up to 90% of aneuploidies associated with SUA are in cases where the left umbilical artery is absent.

As expected, contrary to iSUA group, the aSUA group showed significantly or even highly significant increased rates of IUGR and/or SGA, small placentas, polyhydramnios, olygohydramnios (noticed also in iSUA group) and lower mean fetal weight at delivery, compared with the control group. The incidence of an Apgar score <7 and severe prematurity were four and six times increased in aSUA group vs the control, but this difference was not significant probably due to limited number of cases with these characteristics, since the mean Apgar scores was significantly reduced in aSUA vs TVC fetuses.

Overall, in SUA group, beside the incidence of structural and/or genetic abnormalities, we noticed a highly significant increased rate of IUGR and/or SGA, polyhydramnios and oligohydramnios.

We registered no cases of hypertensive disorders in the study group. Previously, Tulek [2] found a four to five times increased rate of preeclampsia and pregnancy-induced hypertension in pregnancies with SUA compared with the control.

We registered no intrauterine fetal deaths (IUFD). Voskamp [7] also failed to find a correlation between SUA and perinatal death.

It is generally accepted that ultrasound has an accuracy for SUA detection of almost 100% [17] and when a single umbilical artery is present, it is usually larger in caliber approaching the diameter of the umbilical vein [18]. Pierce [17] found that the sensitivity of echographic detection and characterization of associated fetal malformations is about 85%, a value corresponding with our results with two anomalies being observed at delivery: a bicuspid aortic valve and a case of imperforate

Table 3. The rates of fetal malformations and genetic anomalies; the pregnancy evolution and the fetal state at delivery.

Fetus/newborn			SUA	Control	Statistics	
					p	Test's value
APGAR	Mean ± SD	iSUA	8.2 ± 0.6	8.2 ± 1.5	0.755	*f*-r: 0.097
		aSUA[a]	6.3 ± 2	8.2 ± 1.5	<0.001	*f*-r: 12.533
		tSUA[a]	7.8 ± 1	8.2 ± 1.5	0.047	*f*-r: 3.978
	<7	iSUA	0.0% (0/17)	5.1%	0.649	OR: 0.5 (0.03–8.6)
		aSUA[a]	16.6% (1/6)	5.1%	0.238	OR: 3.6 (0.4–31.4)
		tSUA[a]	4.3% (1/23)	5.1%	0.662	OR: 0.8 (0.01–6.2)
Newborn weight (g)	Mean ± SD	iSUA	3183 ± 421	3007 ± 322	0.057	*f*-r: 0.363
		aSUA[a]	2690 ± 796	3007 ± 322	0.029	*f*-r: 4.809
		tSUA[a]	3043 ± 594	3007 ± 322	0.729	*f*-r: 0.125
	Interval	iSUA	1750–3620	1290–4310	—	—
		aSUA[a]	1100–3540	1290–4310	—	—
		tSUA[a]	1100–3620	1290–4310	—	—
Small placenta (<10th percentile)		iSUA	0.0% (0/17)	3.8%	0.614	OR: 0.4 (0.02–8.0)
		aSUA[b]	44.4% (4/9)	3.8%	<0.001	OR: 20.7 (5.4–78.3)
		tSUA[b]	15.3% (4/26)	3.8%	0.005	OR: 4.7 (1.5–13.9)
GA(LMP) at delivery (weeks) Mean ± SD		iSUA	37.9 ± 1.4	36.3 ± 1.7	<0.001	*f*-r: 15.320
		aSUA[a]	36.6 ± 2.6	36.3 ± 1.7	0.791	*f*-r: 0.069
		tSUA[a]	37.5 ± 1.9	36.3 ± 1.7	<0.001	*f*-r: 11.257
IUGR/SGA		iSUA	5.8% (1/17)	3.1%	0.516	OR: 1.9 (0.2–14.9)
		aSUA[b]	33.3.% (3/9)	3.1%	<0.001	OR: 15.6 (3.8–63.7)
		tSUA[b]	15.3% (4/26)	3.1%	0.001	OR: 5.7 (1.9–16.9)
IUFD		iSUA	0.0% (0/17)	0.3%	0.153	OR: 8.1 (0.4–145.4)
		aSUA[b]	0.0% (0/9)	0.3%	0.039	OR: 21.9 (1.1–417.5)
		tSUA[b]	0.0% (0/26)	0.3%	0.250	OR: 5.3 (0.3–94.8)
Polyhydramnios		iSUA	0.0% (0/17)	0.2%	0.077	OR: 14.0 (0.7–264.7)
		aSUA[b]	22.2% (2/9)	0.2%	<0.001	OR: 271.3 (40.1–1833.4)
		tSUA[b]	7.6% (2/26)	0.2%	<0.001	OR: 45.2 (8.3–244.6)
Oligohydramnios		iSUA	5.8% (1/17)	0.7%	0.038	OR: 8.9 (1.1–70.6)
		aSUA[b]	11.1% (1/9)	0.7%	0.002	OR: 28.5 (3.1–255.8)
		tSUA[b]	7.6% (2/26)	0.7%	0.001	OR: 11.8 (2.6–53.6)
Other complications during pregnancy		iSUA	0.0% (0/17)	1.5%	0.671	OR: 1.8 (0.1–31.1)
		aSUA[b]	0.0% (0/9)	1.5%	0.277	OR: 4.9 (0.2–89.5)
		tSUA[b]	0.0% (0/26)	1.5%	0.167	OR: 1.2 (0.07–21.2)
Fetal malformations		tSUA[b]	34.6% (9/26)	1.5%	<0.001	OR: 32.9 (13.9–78.0)
Genetic anomalies		tSUA[b]	7.8% (2/26)	0.2%	<0.001	OR: 45.3 (8.3–245.1)

Abbreviations: SUA, single umbilical artery; iSUA, isolated SUA (n, 17): aSUA, SUA associating other abnormalities (n, 9); tSUA, total cases with SUA (n, 26); [a], only live newborn; [b], including the three medical abortions; IUFD, intrauterine fetal death; IUGR, intrauterine growth restriction; SGA, small for gestational age; GA(LMP), gestational age (last menstrual period); SD, standard deviation; OR, Odds ratio (95% confidence interval); *f*-r, *f*-ratio in One-way ANOVA test); *only one of twins had a missing left umbilical artery.

anus which represents 11.1% (2/18) of all fetal anomalies detected.

We found a significantly increased risk of SUA in mothers with preconception diabetes mellitus, a similar finding of Xu [10]. Furthermore, the primiparity constitutes another condition with increased risk for SUA occurrence.

We found a slightly increased rate of male fetuses associated with SUA (57.6%). On the same parameter, Friebe-Hoffmann [15] reported a rate of 50.8% in female vs 49.2% in male fetuses.

No correlation between SUA incidence and maternal age or smoking was observed.

We noticed only one case of a dichorionic diamniotic twin pregnancy in our study group, with one fetus missing the left artery and the other with a "normal" three vessels cord. The SUA fetus was the heavier one. Klatt [19] found a greater than 10 times increased incidence of SUA in twin pregnancies—9.8% (8% in monochorionic and 11% in dichorionic pregnancies, respectively). But the incidence in twin fetuses is only 5.2%, a fact which supports that most commonly only one fetus presents SUA.

The physiopathogenesis of SUA is unknown, but Persute [20] proposed four mechanisms. The first suggests the agenesis of one umbilical artery and is always followed by a hy-

podevelopment on the side where the artery is missing. The second mechanism consists in the persistence of an allantoic artery. In this case, the SUA bifurcates in the fetal abdomen and communicates with both common iliac arteries. The third theory is the atresia or atrophy of a previous umbilical artery with this being the most accepted theory. The fourth proposal is a remaining of the vitelline artery and in association with sirenomelia.

5. Conclusions

The SUA constitutes an important finding and should be a target of the second trimester ultrasound screening, due to the very high rate of its association with fetal malformations and genetic anomalies. Furthermore, even in iSUA cases, the pregnancy should be meticulously monitored in order to diagnose other anatomical anomalies missed at the second trimester screening and to discover possible amniotic fluid abnormalities.

iSUA is a predictor factor for the presence of oligohydramnios, but differing from other studies, not for SGA and/or IUGR, or for low GA(LMP) and or Apgar scores at delivery.

Preconception DM is a strong favoring condition for SUA. Also, primiparity but not maternal age or the smoking increases the risk of SUA occurrence.

Author contributions

OST was responsible for conceptualization and, together with DC, VIT and VC, was responsible for ultrasound and for subsequent follow-up of pregnancies. AAT and IT wrote the manuscript. All authors equally contributed to this manuscript. All authors read and approved the final manuscript.

Ethics approval and consent to participate

All subjects gave their informed consent for inclusion before they participated in the study. The study was conducted in accordance with the Declaration of Helsinki, and the protocol was under approval of the Ethical Committee of the Emergency Clinical County Hospital of Craiova (approval number: 897/220).

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Conflict of interest

The authors declare no conflict of interest.

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