Isolated Single Umbilical Artery: Implications For Pregnancy

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ABSTRACT

This study aimed to evaluate whether the presence of an isolated single umbilical artery (iSUA) is associated with adverse perinatal outcomes.

Fifty-one patients with iSUA and 54 controls were enrolled in the case-control study. Demographic characteristics and perinatal outcomes were recorded.

All patients had normal umbilical artery (UMA) Doppler findings, and their detailed ultrasound weeks were between 18 and 23 weeks. The birth weights of the babies in the iSUA group were significantly lower than the control group (2898.82±434.56 g vs 3143.70±419.09 g, p=0.004). In the iSUA group, oligohydramnios (7.8% vs 0%) , preterm premature rupture of membranes (PPROM) (3.9% vs 0%), preterm delivery (9.8% vs 3.7%), small for gestational age (SGA) (11.8% vs 3.7%) and neonatal intensive care unit (NICU) (2% vs 0%) admission rates were higher than control group, but there was no statistical significance (p>0.05). But the total adverse pregnancy outcomes were observed in 35.3% (18/51) of cases with iSUA is higher than controls 7.4% (4/54) (p=0.001).

In our study, iSUA is found to be associated with low newborn weight. In the iSUA group, oligohydramnios, PPROM, preterm delivery, SGA, and NICU admission rates were high, but there was no statistical significance. But the total adverse pregnancy outcomes were higher in the iSUA group. These results indicate that close follow-up is essential to prevent and manage adverse perinatal outcomes in iSUA patients.

Key Words: Pregnancy, isolated single umbilical artery, perinatal outcomes

Introduction

The development of the blood vessels and fetal circulation begins by the fourth week of embryonic life. At the commencement of pregnancy, the umbilical cord involves two umbilical arteries and two umbilical veins that the right umbilical vein regresses. Consequently, the umbilical cord consists of two arteries and one vein enclosed by Wharton gel. The umbilical artery pair carrying the deoxygenated blood is drained into the placenta's chorionic vessels by passing through the connecting stalk, which will then become the umbilical cord (1).

A single umbilical artery (SUA) is described as the absence of one of the two umbilical arteries. SUA is the most frequently occurring abnormality of the umbilical cord (2). The frequency of SUA is 0,3-1% (3,4). The exact pathogenesis of SUA is still unclear, yet there are two potential explanations: primary agenesis or thrombotic atrophy of one umbilical artery (5). The majority of umbilical cord abnormalities can be recognized by ultrasound (6). Umbilical cord abnormalities are typically associated with fetal chromosomal, structural abnormalities, and adverse perinatal outcomes (7-9).

When SUA is detected, it is necessary to exclude possible pathological conditions by using a detailed ultrasonographic (US) evaluation in the second trimester. SUA is called isolated SUA (iSUA) in the lack of extra structural and chromosomal abnormalities. 65-80% of SUA cases are isolated (10).

Previous studies have identified numerous possible risk factors for iSUA, such as maternal age, ethnicity, multiparity, maternal smoking, and multiple pregnancies (11-14). However, there is not enough evidence to confirm these results.

iSUA is related to adverse perinatal outcomes including oligohydramnios, preterm premature rupture of membranes (PPROM), preterm birth, small for gestational age (SGA), and low placental weight. Postnatal studies have shown that iSUA pregnancies are significantly lower in birth weight compared to control group pregnancies (11,15,16,17).

In the current study, we aimed to evaluate whether an isolated single umbilical artery (iSUA) is associated with adverse perinatal outcomes.

Materials and Methods

Fifty-one patients with iSUA and fifty-four controls were enrolled in the retrospective case-control study at the Department of Obstetrics and Gynecology, Suleymaniye Maternity Education and Research Hospital, Health Sciences University, Istanbul Turkey; Department of Obstetrics and Gynecology, Diyarbakir Gazi Yasargil Education and Research Hospital, and the Health Sciences University in Diyarbakir, Turkey between March 2010 and February 2018. The ethical review committee of Gazi Yasargil Training and Research Hospital approved the study. The patients found to have two-vessel umbilical cords without any additional structural or chromosomal abnormalities were selected. Participants in control groups were single pregnancy with the normal three-vessel cord and without any additional structural or chromosomal abnormalities. Gestational age was measured by the first day of the woman's last menstrual period and/or first-trimester ultrasound measurements. We diagnosed SUA in the second trimester when a cross-sectional picture of the umbilical cord proved only two vessels and/or in the oblique transverse section using color flow mapping to envision one of two umbilical arteries at nearby to the fetal bladder. A detailed ultrasonographic examination was performed in all fetuses with SUA by an experienced ultrasonographer or perinatologist. All patients underwent prenatal screening tests. However, fetal karyotyping was not performed because there is no evidence of an increased risk of chromosomal abnormalities in iSUA cases in prenatal screening tests (18).

We defined oligohydramnios as an amniotic fluid index ≤ 5 cm. The preterm premature rupture of membranes (PPROM) was defined as amniotic fluid leakage before the 37th week. We described preterm delivery as delivery before the 37th week. We defined small for gestational age (SGA) as birth weight less than the gestational weeks 10th percentile. The total adverse pregnancy outcomes were defined as the presence of at least one of the following: oligohydramnios, preterm premature rupture of membrane, preterm delivery, SGA, and neonatal intensive care unit admission.

Delivery mode, gender, newborn weight, and 1st and 5th minute Apgar scores were noted. Demographic characteristics and ultrasonographic findings were pointed out in the first examination. We obtained pregnancy outcomes from hospital documentation. We confirmed the diagnosis of SUA by macroscopic examination of the newborn. Paediatrician performed a physical exam of all babies.

Statistical Analysis: IBM SPSS 21.0 for Windows (SPSS Inc., Chicago, IL, USA) statistical package program was used for statistical evaluation of our research data. Shapiro Wilks test was used to determine whether the numerical data matched the normality distribution. Student's t-test was used to compare quantitative data between groups and the Mann-Whitney U test was used to compare non-normal distribution parameters. The chi-square test, Fisher's exact test and Yates's continuity correction were used to compare the qualitative data. Significance was evaluated at P-value <0.05.

Results

The mean maternal age was 26.51±3.54 in the iSUA group and 26.98±4.33 in the control group. There was no statistically significant difference between the groups in terms of median age and parity numbers (p>0.05; Table 1). All patients had normal umbilical artery (UMA), and Doppler screenings were made between 18 and 23 weeks (Table 1). There was no significant difference between groups in terms of delivery type, gestational age, gender, APGAR scores (p> 0.05, Table 2). None of the prenatal screening tests of patients with iSUA had a high risk for a chromosomal abnormality, and no patient was advised to undergo invasive prenatal tests, including amniocentesis and cordocentesis.

The birth weights of the babies in the iSUA group were significantly lower than the control group (2898.82±434.56 g and 3143.70±419.09 g, respectively, p=0.004, Table 2).

Table 1. Maternal and antenatal demographics in the iSUA and Controls groups

Parameters	iSUA n:51	Controls n:54	p-value
Maternal age, mean±sd	26.51±3.54	26.98±4.33	[1]0.544
Parity, median (min-max)	1 (0-3)	0 (0-4)	[2]0.306
Detailed ultrasound week	18-23 weeks	18-23 weeks	-

[1]*Student's t-test*
[2]*Mann-Whitney U Test*

Table 2. Perinatal outcomes in the iSUA and Controls groups

Parameters	iSUA n:51	Controls n:54	p-value
Gestational age at delivery (weeks), mean±sd	38.21±2.01	38.80±1.17	[1]0.077
Delivery mode n (%)			
Vaginal	20 (39.2%)	30 (55.6%)	[2]0.894
Cesarean sectio	31 (60.8%)	24 (44.4%)	
APGAR score, median (min-max)			
1.minute	8 (6-9)	8 (7-9)	[3]0.861
5. minute	10 (7-10)	9 (8-10)	[3]0.183
Gendern (%)			
Female	30 (58.8%)	29 (53.7%)	[2]0.597
Male	21 (41.2%)	25 (46.3%)	
Newborn weight (g), mean±sd	2898.82±434.56	3143.70±419.09	[1]**0.004***
Perinatal outcomesn (%)			
Oligohydramniosis	4 (7.8%)	0 (0%)	[4]0.052
Preterm premature rupture of membrane	2 (3.9%)	0 (0%)	[4]0.234
Preterm delivery	5 (9.8%)	2 (3.7%)	[4]0.261
Small for gestational age	6 (11.8%)	2 (3.7%)	[4]0.153
Neonatal intensive care unit admission	1 (2%)	0 (0%)	[4]0.486
Total adverse perinatal outcomes	18 (35.3%)	4 (7.4%)	[5]**0.001***

[1]Student's t-test
[2]Chi-squared Test
[3]Mann-Whitney U Test
[4]Fisher's Exact Test
[5]Yates' continuity correction
* p<0.05

The incidence of oligohydramnios in infants within the iSUA group (7.8%) was higher than that in the control group (0%), but this difference was not statistically significant (p=0.052; Table 2). PPROM, preterm birth, SGA and neonatal intensive care unit (NICU) admission rates were high in the iSUA group, but there was no significant statistical difference (p>0.05, Table 2). Nevertheless, the total adverse pregnancy outcomes observed in 35.3% (18/51) of cases with iSUA were higher than in 7.4% (4/54) of the control group (p=0.001; Table 2).

Discussion

In our study, the birth weights of the neonates in the iSUA group ((2898.82±434.56 g) were significantly lower than the control group (3143.70±419.09 g, p= 0.004). In the iSUA group, oligohydramnios (7.8% vs 0%) , preterm premature rupture of membranes (PPROM) (3.9% vs 0%), preterm delivery (9.8% vs 3.7%), small for gestational age (SGA) (11.8% vs 3.7%) and neonatal intensive care unit (NICU) (2% vs 0%) admission rates were higher than control group,

but there was no statistical significance (p>0.05). However, the total adverse pregnancy outcomes were observed in 35.3% (18/51) of cases with iSUA is higher than in 7.4% (4/54) of controls (p=0.001).

SUA patients with additional congenital anomalies have a high risk of adverse perinatal outcomes. However, it remains unclear in iSUA cases. In numerous studies, iSUA has been associated with oligohydramnios, polyhydramnios, preterm birth, PPROM, SGA, low placental weight, gestational diabetes mellitus (GDM) and perinatal mortality (19-21).

Mu et al. investigated the perinatal outcomes of asymptomatic iSUA patients. They were stated that the sample size was comparatively small in their study. Still, the incidence of SGA was significantly higher in iSUA patients (35%) than the control group (3.6%, p=0.011) (21). In a study Horton et al., the birth weight of iSUA neonates was significantly lower than the control group (3279±404 g, and 3423±374 g, respectively, p=0.016) (12). Also, the duration in the NICU was significantly longer in iSUA group (1.25±2.2 days) than the controls (0.48±1.25 days, p=0.023) (12). Numerous studies confirmed that SUA is associated with an increased risk of preterm labor (2,13,15,17).

In our study, birth weight was low in iSUA patients. Preterm delivery, PPROM, oligohydramnios, and NICU hospitalization rates increased but were not statistically significant. However, the total adverse pregnancy outcomes observed in 35.3% (18/51) of cases with iSUA is higher than in7.4% (4/54) of the control group (p=0.001).

In some studies, iSUA was reported as no increased risk for preterm birth (13,14), intrauterine growth restriction (IUGR) (22), SGA, or prenatal morbidity and mortality (3).

A study performed by Blum et al. (23) found increases in preterm birth, cord prolapse, placental abruption, non-reassuring fetal heart rates and cesarean birth rates in the iSUA group. Neonatal birth weight was significantly lower in the iSUA group (1988.0±697) than the control group (2388.3±481, p<0.001). 1st and 5th minute APGAR scores were significantly lower. Perinatal mortality was found to be significantly higher in the iSUA group. In the iSUA group, preterm delivery was individually associated with perinatal mortality (23). Naveiro-Fuentes et al. showed increased cesarean section rate, low birth weight

scores, and they reported altered cord pH values in the direction of acidosis in their studies (24).

Our study supports these studies' findings in terms of significant low birth weight in the iSUA group. However, there was no significant difference detected in terms of the delivery type, or 1st and 5th minute APGAR scores. The results of our study were similar to those of Chett Jonn et al. and Ashwal et al., who did not find any correlation between iSUA and APGAR scores (11,25).

A study by Burshtein et al. showed that iSUA patients (38.3±3.0 weeks) are related to one week earlier delivery when compared to patients without SUA (39.3±2.1 weeks, p<0.001) (17). However, in our study, we did not observe any significant difference between the two groups regarding the gestational week on delivery.

Increased NICU hospitalization rates, pregnancy-induced hypertension (PIH), and perinatal mortality rates have been reported in iSUA cases (10,17). The presence of ISUA was associated with a more than five times increased risk of intrauterine and perinatal death and with placental and cord complications (26).

In our study, one of the neonates needed NICU hospitalization due to the early preterm delivery. We did not encounter adverse outcomes such as perinatal mortality and PIH.

In one study, they reported an increased risk of renal anomalies in iSUA cases, but most of them were minor and self-limited (27). Therefore, extensive urologic radiographic studies are not recommended in asymptomatic newborns unless there are additional risk factors for malformations. In our study, no study was performed on renal anomalies since the newborns were asymptomatic.

In most studies and meta-analyzes, iSUA has been associated with increased adverse perinatal outcomes. In line with this evidence, iSUA cases should be evaluated as a high-risk pregnancy and followed up closely.

The incidence of chromosomal abnormalities is scarce in iSUA patients. Dagklis et al. stated an incidence of 0.7% in iSUA cases, yet found no evidence for an increased risk of chromosomal abnormalities in overt iSUA cases (18). We performed prenatal screening test in all cases, yet since there is no evidence for karyotyping in iSUA cases, it was not included in our study.

Joó et al. reported a male to female ratio of 1/17 in fetuses with SUA (28). In some studies, the dominance of the number of female babies was reported, but different from this rate, it may be

more or less (29-31). There was no significant difference between the gender ratio in the results of our study. Additional studies are needed to elucidate the role of the sex on chromosomal abnormalities, congenital anomalies, and adverse perinatal outcomes.

The role of environmental or genetic factors in the etiology of SUA remains unknown. The umbilical cord should be assessed by the US in the second trimester of pregnancy, as the vast majority of iSUA patients can be identified with a routine US examination (32). This detection is possible by 1st trimester (11-14 weeks) and the 2nd-trimester US examination (33,34). In our study group, the diagnosis of SUA was verified by the US at 18-23 weeks. Once SUA is detected, a detailed fetal evaluation should be performed with the US; possible abnormalities should be excluded. Pregnant women should be informed about possible adverse perinatal outcomes after the fetus is diagnosed as iSUA. Close follow up should be performed.

There are some limitations to this study. This study has been designed retrospectively and has the potential to contain limitations of such studies and a relatively low sample size. However, our study would shed light on future studies showing increased perinatal outcomes rates in the iSUA group.

In conclusion, we found a statistically significant low birth weight in the iSUA group. Although oligohydramnios, PPROM, preterm birth, SGA, and NICU admission rates were high, this increase did not reach statistical significance. However, the total adverse perinatal outcome increase was statistically significant. These results indicate that close follow-up is essential to prevent and manage adverse perinatal outcomes in iSUA patients.

Conflicts of interest statement: The authors have no conflicts of interest relevant to this article.

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