

Determination of risk factors and perinatal outcomes of singleton pregnancies complicated by isolated single umbilical artery in Turkish population

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Abstract

Objective: To address the possible risk factors, eventual pregnancy outcomes, and probable troubles in follow-ups of pregnancies complicated by an isolated single umbilical artery and to provide data on Turkish cases in such an aspect that ethnic divergences may have influence.

Material and Methods: A total of 16568 singleton pregnancies that were delivered between May 2006 and May 2013 were retrospectively screened. Ninety-three fetuses were found to have an isolated single umbilical artery. One-hundred pregnancies that did not show any structural or chromosomal abnormalities were randomly selected from the rest of the cases to establish the control group. IBM SPSS Statistics 20.0 software was utilized for statistical analysis. Non-parametric data were analyzed with Mann-Whitney U test and were presented as means±standard deviations. P values less than 0.05 were statistically significant. For the adjustment of confounding factors, odds ratios (ORs) and 95% confidence intervals (CIs) were estimated by multiple logistic regression analysis.

Results: The incidence of small for gestational age (SGA) fetuses and hypertensive disorders in pregnancy was found to be significantly higher in cases with an isolated single umbilical artery ($p<0.001$ and $p=0.022$, respectively). Maternal smoking was found to be independently associated with the occurrence of an isolated single umbilical artery (OR: 3.556; 95% CI: 1.104-11.45). The risk of preterm birth was not higher in the study group (OR: 0.538; 95% CI: 0.576-2.873). The incidence of cases who underwent cesarean delivery because of non-reassuring fetal heart trace was similar in the study and control groups ($p=0.499$).

Conclusion: Attention should be paid to the development of hypertensive disorders in cases with a diagnosis of an isolated single umbilical artery, and parents should be counseled properly, including the information on increased risk of SGA. Strict follow-up of pregnancies complicated with an isolated single umbilical artery in terms of preterm birth seems unfeasible except in cases with accompanying risk factors for preterm labor. (J Turk Ger Gynecol Assoc 2015; 16: 21-4)

Keywords: Isolated single umbilical artery, SGA, pregnancy outcome, hypertensive disorders, preterm birth

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Introduction

A single umbilical artery is a malformation where the umbilical cord carries one artery and one vein instead of two arteries and one vein. A two-vessel umbilical cord or single umbilical artery is seen in approximately 0.5%-1% of all deliveries, and it is the most common anomaly of the umbilical cord (1). Many risk factors have been suggested in previous studies, including maternal age, maternal smoking status, ethnicity, multiparity, and multiple gestations (2). Some studies have also indicated that risks of some adverse pregnancy outcomes such as intra-uterine growth restriction, low birth weight, preterm delivery, and hypertensive disorders in pregnancy could be increased in cases with a single umbilical artery (3, 4).

A single umbilical artery is known to be associated with fetal chromosomal and structural abnormalities particularly neural tube, musculoskeletal, genitourinary, and cardiac anomalies (5, 6). The prognoses of fetuses with a single umbilical artery

largely depend on the severity of the coexisting anomaly. In the absence of these additional chromosomal or structural abnormalities, a single umbilical artery is considered to be isolated. The clinical importance of a diagnosed isolated single umbilical artery is still controversial (7). Moreover, there is a meager amount of data obtained from Turkish cases in literature on the issue that divergences in ethnicity may have a significant impact (8-11). Furthermore, most of these studies were conducted on single umbilical artery cases with additional anomalies (9-11). This retrospective cohort study was conducted to evaluate the pregnancy outcomes and possible risk factors associated with an isolated single umbilical artery in a Turkish population.

Material and Methods

This retrospective cohort study was conducted in the Department of Obstetrics and Gynecology of Ankara University

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Table 1. Demographic characteristics of study and control groups

	Isolated single umbilical artery group (n=93)	Control group (n=100)	p value
Maternal age (years)	27.1±5.37	27.4±5.28	0.623
Body Mass Index (kg/m ²)	28.3±4.28	28.3±3.38	0.628
Maternal gravidity	3.91±1.96	3.84±1.04	0.653
Maternal parity	2.1±0.98	2.3±1.2	0.886
Values are compared by Mann-Whitney U test and are presented as means±standard deviations. P<0.05 is considered statistically significant			

Table 2. Multiple logistic regression analysis for variables independently associated with the occurrence of an isolated single umbilical artery

	Wald	OR (95% CI)	p value
Positive smoking status	4.519	3.556 (1.104-11.45)	0.034
Assisted reproduction	2.540	3.76 (0.738-19.168)	0.11
Rhesus incompatibility	0.993	1.73 (0.589-5.081)	0.31
Maternal age	0.965	0.972(0.919-1.029)	0.326
Body Mass Index (kg/m ²)	0.158	1.016(0.941-1.097)	0.691
Constant	1.268	0.844	0.26
CI: Confidence interval OR: Odd ratio			

in Ankara, Turkey. The records of women who gave birth between May 2006 and May 2013 were screened. This study was structured via retrospective data assessment and neither ethics committee approval nor patients' informed consents were obtained. The medical history and other necessary information were obtained from the patient records and by phone calls if required. The records of detailed ultrasonographic examinations and birth charts were investigated. Only singleton pregnancies were evaluated. The cases that were found to have two-vessel umbilical cords without any additional structural or chromosomal abnormalities were selected. Single umbilical arteries were diagnosed by the visualization of only one umbilical artery in the color flow mapping of the fetal pelvis as a standard component of routine detailed obstetric ultrasound examination. Detailed obstetric ultrasound examinations were performed between the 18th and 21st gestational weeks by three certified obstetric sonographers. Siemens Sonoline G50 ultrasound, Voluson E6, and Logiq 5P (GE Healthcare Company, Little Chalfont, United Kingdom) with 3.5 and 5 MHz transducers were used for the detailed obstetric ultrasound examination.

Small for gestational age (SGA) is defined as an infant that weighs below the 10th percentile because of local curves (12) and that do not have any abnormal parameters on Doppler studies. Pregnancies complicated with preeclampsia, eclampsia, or gestational hypertension were described as hypertensive disorders in pregnancy.

In our institution, non-reassuring fetal heart trace was described as a fetal heart rate pattern that was classified as either Category II (without achieving adequate reassurance) or Category III, according to National Institute of Child Health and Human Development workshop report (13). However, the retrospective nature of this study prevented us from further standardizing the term "non-reassuring fetal heart trace" and eliminating inter-physician divergences in interpretation.

Ninety-three cases of an isolated single umbilical artery were found to be diagnosed, and 100 women randomly selected among singleton pregnancies that were demonstrated to have chromosomal or structural abnormalities and that were delivered within the selected study period.

Data analysis was performed with IBM SPSS Statistics 20.0 software (IBM Corporation Software Group, New York, United States of America).

Categorical variables were expressed as numbers and percentages. Non-parametric data were compared by Mann-Whitney U test and were presented as means±standard deviations. P values less than 0.05 were considered statistically significant. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated using multiple logistic regression analysis to adjust for confounding factors.

Results

A total of 17987 birth charts were screened, and 16568 of them were singleton pregnancies. Among these pregnancies, 93 fetuses (0.34%) were diagnosed to have two-vessel umbilical cords without any chromosomal or structural abnormalities, including genitourinary, cardiac, or musculoskeletal anomalies. Maternal demographic characteristics were similar in the isolated single umbilical artery and control groups in terms of maternal age, body mass index (BMI), maternal gravidity, and maternal parity (Table 1).

Through multiple logistic regression analysis, maternal smoking was found to increase the risk of occurrence of an isolated single umbilical artery (OR 4.15; 95% CI 1.104-11.45), whereas rhesus incompatibility, maternal age, maternal BMI, and assisted reproduction were unlikely to be associated with an increased risk for occurrence of a single umbilical artery (Table 2).

The mean birth weight of infants with an isolated single umbilical artery was found to be lower than infants with normal umbilical cords despite the difference not having reached statistical significance ($p=0.591$) after adjustment for maternal smoking status and gestational age at birth (Table 3). Both total cesarean rate and cesarean rate because of non-reassuring fetal heart trace were found to be similar between the groups ($p=0.241$ and $p=0.499$, respectively). There were 24 cases (25.8%) of SGA infants in the single umbilical artery group, whereas there were only four cases (4%) of SGA in the control group. Incidence of SGA infants was higher in the isolated single umbilical artery group even after adjusted for maternal smoking status ($p<0.001$). The incidence of hypertensive disorders was also higher in cases with two-vessel umbilical cords ($p=0.022$). No significant differences were observed between the study and control groups in terms of pregnancies

Table 3. Comparison of pregnancy outcomes in control and isolated single umbilical artery groups

	Isolated single umbilical artery group (n=93)	Control group (n=100)	P value
Mean birth weight (kg) ^{a,b}	2981.2±679.5	3195.7±2592.2	0.591
Cesarean section (n)	51 (56.9%)	46 (46%)	0.241
Cesarean section because of non-reassuring fetal heart trace (n)	20 (21.5%)	15 (15%)	0.499
Small for gestational age (n) ^a	24 (25.8%)	4 (4%)	<0.001
Hypertensive disorder in pregnancy (n) ^a	9 (9%)	2 (2%)	0.022
Oligohydramnion (n)	4 (4.3%)	3 (3%)	0.713
Preterm premature rupture of membranes (n)	3 (3.2%)	2 (2%)	0.673
Preterm delivery (n) ^a	15 (16.1%)	13 (13%)	0.537
Mean APGAR score at 1 st minute	8.1±1.2	8.9±1.9	0.812
Mean APGAR score at 5 th minute	9.2±1.1	9.8±1.0	0.523

Values are compared by Mann-Whitney U test. Categorical variables are expressed as numbers and percentages. Continuous variables are presented as means±standard deviations. P<0.05 is considered statistically significant
^aAdjusted for maternal smoking status. ^bAdjusted for gestational age at birth

complicated by oligohydramnios, preterm premature rupture of membranes, and preterm deliveries (Table 3). The mean APGAR scores of infants at the 1st and 5th minutes were found to be similar between the groups.

Logistic regression analysis demonstrated that the cases with an isolated single umbilical artery are more likely to be complicated by hypertensive disorders in pregnancy (OR 5.25; 95% CI 1.104-24.975) and SGA infants (OR 8.43; 95% CI 2.783-25.583). However, the increase in risks of preterm delivery (OR 1.287; 95% CI 0.576-2.873; p=0.538) and preterm premature rupture of membranes (OR 1.633 95% CI 0.267-10,000; p=0.592) were unlikely to be increased in cases with a single umbilical artery (Table 4).

Discussion

A single umbilical artery is found to be associated with genitourinary, cardiovascular and musculoskeletal system anomalies in 25% of cases, and these cases are accepted to carry a higher risk of chromosomal abnormalities (14, 15). The most commonly suggested theories on the development of a single umbilical artery are primary agenesis or secondary thrombotic

Table 4. Logistic regression analysis of pregnancy outcomes that are independently associated with isolated single umbilical artery

	Odds ratio	95% CI	p value
SGA	8.43	2.783-25.583	<0.001
Hypertensive disorder	5.250	1.104-24.975	0.018
Preterm delivery	1.287	0.576-2.873	0.538
PPROM	1.633	0.267-10.000	0.592

SGA: Small for gestational age; PPRM: preterm premature rupture of membranes

atrophy of one of the umbilical arteries (16). A single umbilical artery could be associated with some adverse perinatal outcomes such as growth restriction or higher fetal distress rates during the course of labor when it was described as an isolated finding. However, most studies were conducted in Western countries, and ethnic divergences may have a considerable impact on this issue. In this study, we endeavored to define the characteristics of isolated single umbilical artery cases in a Turkish population.

The results of this study indicated that fetuses with a single umbilical artery were more likely to be SGA infants. Although most of the studies indicate an association between SGA infants and an isolated single umbilical artery, this issue is not totally clarified yet (1, 4, 8, 17). A meta-analysis conducted by Voskamp et al. (17) demonstrated that larger studies on single umbilical arteries exhibited a weaker association between single umbilical artery and birth weight. Therefore, the authors indicated an evident relationship between birth weight and single umbilical artery in smaller sample-sized studies could be the results of publication biases. Our study indicates an evident association between SGA infants and single umbilical artery after adjusting for maternal smoking status. However, the mean birth weight of the single umbilical artery and control groups was not significantly different. It could be suggested that an isolated single umbilical artery leads to SGA in some infants and has no effect on the others. Bugatto et al. (18) demonstrated a correlation between uterine artery Doppler measurements and birth weights of fetuses with an isolated single umbilical artery and suggested that growth restriction in fetuses with an isolated single umbilical artery is a consequence of disorders in maternal-placental circulation rather than placental insufficiency.

Although we lack the data on uterine artery Doppler parameters, umbilical artery Doppler parameters were all within normal limits in all cases near term in this study. Thus, placental insufficiency is unlikely to be a cause of SGA in affected fetuses. SGA could be a result of the co-existence of other factor(s) that were not contributed in this study. Demonstrating these possible factors could explain the reason why an isolated single umbilical artery leads to SGA in some infants despite not having any effect on birth weight in others.

Maternal smoking is found to be independently associated with the development of a single umbilical artery (2), whereas assisted reproduction, maternal BMI, and maternal age demon-

strated have been demonstrated to not have any effect on the development of an isolated single umbilical artery.

Cesarean rates because of non-reassuring fetal heart trace is higher in cases with an isolated single umbilical artery in a majority of previous studies (4, 7), whereas other studies have failed to demonstrate any difference (19).

Our study demonstrated similar cesarean rates because of non-reassuring fetal heart trace. Different results in literature could be a consequence of subjectivities and inter-physician differences in the interpretation of non-reassuring fetal heart trace as well as personal differences in the threshold of cesarean decision. Future studies may include more objective criteria about this aspect to cope with the query of subjectivity.

The relation between preterm birth and an isolated single umbilical artery is also a controversial issue. Some studies have shown a higher risk of preterm birth in cases with isolated single umbilical arteries (2, 4) suggesting serial cervical length assessment in these cases (20) and others have demonstrated no association (7). The study conducted by Doğan et al. (8) demonstrated similar gestational ages at birth in isolated single umbilical artery and control cases. In our study, there was no association found between the increased risk of preterm delivery and isolated single umbilical artery after adjustment for maternal smoking status. Therefore, for the Turkish population, we do not suggest a strict monitoring of patients with an isolated single umbilical artery in terms of preterm birth unless there are no other existing risk factors.

Unlike previous reports, the results of this study also showed that cases with an isolated single umbilical artery are more likely to be complicated by hypertensive disorders in pregnancy.

In conclusion, one should be cautious about the development of hypertensive disorders and growth restriction in cases with a diagnosis of an isolated single umbilical artery. Parents should be counseled properly. A strict monitoring of pregnancies complicated with an isolated single umbilical artery for preterm birth seems unfeasible. However, prospective studies with larger sample sizes could be beneficial in the further clarification of these aspects.

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