Single Umbilical Artery Risk Factors and Pregnancy Outcomes

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OBJECTIVE: To identify risk factors for fetuses and neonates with single umbilical artery and isolated single umbilical artery (single umbilical artery in the absence of chromosomal abnormalities and structural abnormalities) and to assess whether there is an increased risk for complications during pregnancy, labor, and delivery, and for perinatal morbidity and mortality.

METHODS: A population-based retrospective cohort analysis of deliveries in Nova Scotia, Canada, between 1980 and 2002 was conducted using the Nova Scotia Atlee Perinatal Database. Risk factors and outcomes for single umbilical artery and isolated single umbilical artery pregnancies were compared with three-vessel-cord pregnancies. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated for each outcome using multiple logistic regression to adjust for confounding factors. Separate models were run for single umbilical artery and isolated single umbilical artery.

RESULTS: There were 203,240 fetuses and neonates available for analysis, with 885 (0.44%) having single umbilical artery and 725 (0.37%) having isolated single umbilical artery. Single umbilical artery fetuses and neonates had a 6.77 times greater risk of congenital anomalies and 15.35 times greater risk of chromosomal abnormalities. The most common congenital anomalies in chromosomally normal fetuses and neonates were genitourinary (6.48%), followed by cardiovascular (6.25%) and musculoskeletal (5.44%). For isolated single umbilical artery, placental abnormalities (OR 3.63, 95% CI 3.01–4.39), hydramnios (OR 2.80, 95% CI 1.42–5.49), and amniocentesis (OR 2.52, 95% CI 1.82–3.51) occurred more frequently than with three vessel cords. Neonates with single umbilical artery and isolated single umbilical artery had increased rates of prematurity, growth restriction, and adverse neonatal outcomes.

CONCLUSION: Fetuses and neonates with single umbilical artery and isolated single umbilical artery are at increased risk for adverse outcomes. Identification of single umbilical artery is important for prenatal diagnosis of congenital anomalies and aneuploidy. Increased surveillance with isolated single umbilical artery may improve pregnancy outcomes.

LEVEL OF EVIDENCE: II

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The human umbilical cord normally develops with two arteries and one vein. Single umbilical artery is a condition of the umbilical cord in which one artery is missing and the prevalence ranges from 0.2% to 11%, depending on the population studied.[1–5]

Numerous maternal and fetal risk factors and characteristics associated with single umbilical artery have been reported, including sex, multiple births, ethnicity, older maternal age, multiparity, and smoking, as well as the presence of maternal medical and pregnancy complications, such as preexisting diabetes, hypertension, preeclampsia, and epilepsy. Also reported are associations with maternal drug use (such as vitamin A, phenytoin, and levothyroxine), substance abuse, seasonal variations in conception, and placental abnormalities.[1,6–22]

Chromosomal abnormalities and congenital malformations are increased in fetuses with single umbilical artery.[1,2,5,7,8,12,23] Congenital malformations associated with single umbilical artery include neural tube and cardiac defects; respiratory, gastrointestinal, musculoskeletal, and genitourinary anomalies; and acar-

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diac twinning.[7,23–26] Among neonates with apparently isolated single umbilical artery, postnatally diagnosed congenital malformations are increased compared with the general population.[27] Increased rates of placental, cord, and amniotic fluid abnormalities have been found to be associated with single umbilical artery, including placental structural abnormalities, previa, abruption, abnormal cord length, and hydramnios and oligohydramnios.[1,13,14,17,22]

Although the prognosis for fetuses with single umbilical artery is mainly related to associated fetal structural or chromosomal anomalies, there remains an increased frequency of intrauterine or intrapartum fetal deaths among fetuses with isolated single umbilical artery.[1,28,29] The incidence of intrauterine growth restriction (IUGR) has been reported to be increased among fetuses with single umbilical artery and may be present without other congenital anomalies.[3,29] Another study found no increased rate of IUGR in anatomically normal single umbilical artery fetuses.[30]

Overall mortality rate for neonates with single umbilical artery is higher than that for neonates with three vessel cords, and this high mortality rate is attributable to several interrelated factors including prematurity, low birth weight, and associated lethal malformations and an increased incidence of structural malformations of the placenta.[22,31] With isolated single umbilical artery, higher rates of stillbirth, IUGR, prematurity, and neonatal mortality have been reported when compared with those fetuses and neonates with three vessel cords, events that cannot be explained by aneuploidy or chromosomal abnormalities.[3,14,17–19,26] Mode of delivery may be influenced by the presence of single umbilical artery, with a higher rate of cesarean delivery being reported for neonates with two vessel cords.[32]

The long-term consequences of isolated single umbilical artery have not been studied extensively, but there is some evidence to suggest that there are long-term sequelae as a result of this malformation.[33–35] In a large collaborative study, most children were found to be healthy and developing normally in early childhood, which shows that the majority of children born with isolated single umbilical artery show normal cognitive and physical development.[20] Some studies suggest that inguinal hernias may be more common in the single umbilical artery population.[3,14,35]

This study explores the risk factors for development of single umbilical artery as well as the relationship between single umbilical artery and pregnancy and neonatal outcomes using a large, population-based birth cohort over a 22-year period.

MATERIALS AND METHODS

This was a population-based retrospective cohort study of deliveries of residents of‘ Nova Scotia, Canada, between 1980 and 2002. This study included all deliveries to residents of Nova Scotia, Canada, between 1988 and 2002 and all deliveries occurring in Halifax County between 1980 and 1987. All deliveries at 20 weeks of gestation or more or weighing 500 g or more were included in the study. Data for this study were obtained from the population-based Nova Scotia Atlee Perinatal Database. The Atlee Perinatal Database is administered by the Nova Scotia Reproductive Care Program and contains variables related to maternal characteristics, medical conditions, labor, and delivery, and neonatal outcomes on all births at 20 or more weeks of gestation, and weighing more than 500 g, born in the province of Nova Scotia, as well as for births to Nova Scotia residents who deliver in the province of New Brunswick. Follow-up information on death and cause of death in the first year after birth is included. Data for the Nova Scotia Atlee database are abstracted by trained coders from standardized clinical forms and hospital records. In addition to information abstracted from the prenatal and delivery admission records, information pertaining to all antepartum admissions during pregnancy is also recorded in the database.

For the purpose of this study, single umbilical artery was defined as the absence of either the left or right umbilical artery and the presence of an umbilical vein. For single umbilical artery to have been recorded as present in the Atlee Perinatal Database, notation of single umbilical artery had to be present in one of the following: birth record, pathology report, or neonatal physical examination. Single umbilical artery was confirmed through gross or histologic examination of the placenta, examination of the neonate, or autopsy. Therefore, a neonate who was not noted to have a single umbilical artery in these records was assumed to have three vessel cords.

Number of fetuses was defined as those carried through to delivery. For multiples, twin type was defined as dichorionic and monochorionic, in which monochorionic also included monoamniotic and conjoined twins. For twins and multiples, each fetus or neonate was analyzed separately in calculating the rate of single umbilical artery and outcomes.

Maternal characteristics including age, obstetric history, maternal medical conditions, and medications were examined as potential risk factors. Potential fetal factors examined as potential risk factors

included phenotypic sex, number of fetuses carried to delivery, and twin type.

The relationship between single umbilical artery and the following outcomes was explored: maternal pregnancy complications, need for invasive testing, fetal anomalies and chromosomal abnormalities, placental abnormalities, amniotic fluid abnormalities, intrauterine growth restriction and small for gestational age, labor and delivery, perinatal mortality, prematurity, and neonatal outcomes. Maternal pregnancy complications included pregnancy induced hypertension, eclampsia, hyperemesis, premature rupture of membranes, and gestational diabetes. Placental abnormalities included abruption, previa, villamentous cord insertion, circumvallate, amnionodosum, succenturiate, marginal cord insertion, and other miscellaneous placental abnormalities. Abnormalities of amniotic fluid were defined as oligohydramnios and hydramnios. Invasive testing assessed rates of chorionic villous sampling and amniocentesis. The presence of multiple anomalies was defined as two or more major anomalies. Chromosomal abnormalities included any aberration in chromosomes including trisomies, tetraploidy, deletions, translocations, triploidy, sex chromosome abnormalities, p and q abnormalities, and ring abnormalities. Outcomes of labor and delivery included induction of labor, fetal distress, meconium, mode of delivery, method of delivery, fetal position at delivery, and cesarean delivery because of fetal distress. Perinatal mortality was defined to include fetal or neonatal death. Preterm birth was defined as birth before 34 weeks or birth before 37 weeks of gestation. IUGR was defined as a birth weight at the third percentile or less, and small for gestational age as the 10th percentile or less.[36] Neonatal outcomes included 1-minute and 5-minute Apgar score, admission to special care nursery, arterial cord Ph, depression at birth (defined by neonate requiring intermittent positive pressure breathing), postasphyctic central nervous system depression, postasphyctic central nervous system excitation, postasphyctic increased intracranial pressure, postasphyctic central nervous system depression or excitation and related outcomes, intraventricular hemorrhage, and aspiration pneumonitis.

Initially, the rates of single umbilical artery and isolated single umbilical artery were calculated. For isolated single umbilical artery, those fetuses and neonates with chromosomal abnormalities and congenital anomalies were removed from the overall baseline single umbilical artery population. Fetuses and neonates with chromosomal abnormalities and congenital anomalies were also removed from the comparison group without single umbilical artery. For the risk factor analyses, unadjusted odds ratios (ORs) and 95% confidence intervals (CIs) were calculated for each potential risk factor. Multiple logistic regression was then used to determine the best-fit model for risk factors associated with single umbilical artery using a backward regression approach. Multiple logistic regression was then used to determine the best-fit model for risk factors for isolated single umbilical artery.

For the outcomes analyses, univariable analysis was used to calculate unadjusted ORs and 95% CIs expressing the relationship of single umbilical artery, isolated single umbilical artery, and each outcome. Adjusted ORs and 95% CIs were then calculated for those outcomes statistically significant in the univariable analysis. Potential confounders of the relationship between single umbilical artery and outcomes were identified for both groups using stepwise logistic regression of fetal and maternal risk factors for single umbilical artery, and those risk factors with $P<.1$ from the univariable analysis were included in the model as potential confounders. Potential confounding factors for single umbilical artery were entered into a logistic regression model with each outcome and with single umbilical artery and isolated single umbilical artery as the principal independent variables of interest. Potential confounders included multiple pregnancy, maternal antibodies, maternal drug use, neurologic illness, pulmonary disease, maternal prepregnancy diabetes, chronic hypertensive disease, and maternal smoking. Observations for women with more than one delivery during the study period may not be independent (eg, a pregnancy outcome for a woman may be more or less likely to occur because of her outcome from a previous delivery). To adjust for this nonindependence, general estimating equations were used.

To determine the final model for each outcome, the following process was used: The potential confounder with the highest *P* value was removed and the degree of change in the point estimate for single umbilical artery was evaluated. If removing the factor did not change the point estimate for single umbilical artery by greater than 5%, the factor was eliminated and the process repeated until the final model was established. All analysis was conducted with SAS 8.2 software. This study received approval from the Isaac Walton Killam Health Centre Research Ethics Board.

RESULTS

There were 203,240 fetuses and neonates available for analysis between 1980 and 2002 with 885 fetuses and neonates (0.44%) having single umbilical artery. For

isolated single umbilical artery, there were 196,752 fetuses and neonates available for analysis with 725 (0.37%) having an isolated single umbilical artery. All fetuses or neonates had the number of cord vessels recorded.

For isolated single umbilical artery, in the univariable risk factor analysis, smoking, drug use, presence of maternal antibodies, neurologic disease, pulmonary disease, preexisting diabetes, and chronic hypertension were associated with an increased risk for single umbilical artery. For fetal risk factors, twins and higher order multiples were associated with an increased risk for single umbilical artery. Following the stepwise modeling procedure, four variables remained in the final adjusted model for single umbilical artery (Table 1). The factors in the final model for isolated single umbilical artery included smoking (OR 1.71, 95% CI 1.46–2.01), previous child with low birth weight (OR 1.56, 95% CI 1.10–2.21), preexisting maternal neurological disease (OR 2.75, 95% CI 1.55–4.88), and twins and higher multiples (OR 2.73, CI 1.88–3.97).

Adjusted ORs for each of the outcomes for fetuses and neonates affected by single umbilical artery indicate that this group has increased risk of adverse outcomes. Of note is that fetuses and neonates with a two-vessel cord had a 15.35-fold greater risk of being affected with a chromosomal abnormality (OR 15.35, CI 9.90–23.81) and a 6.77-fold risk of having one or more major congenital anomaly (OR 6.77, CI 5.69–8.06), and a further increased risk of 18.7 times of having two or more major anomalies (OR18.18, CI 14.66–22.55). The most common congenital anomalies in the single umbilical artery fetuses and neonates without chromosomal abnormalities were genitourinary (6.48%) followed by cardiovascular (6.25%) and musculoskeletal (5.44%).

Table 1. Adjusted Odds Ratios and 95% Confidence Intervals for Risk Factors for Isolated Single Umbilical Artery

Variable and Category	Odds Ratio (95% CI)
Number of fetuses	
1	1.0
2 or more	2.73 (1.88–3.97)
Neurologic disease	
No	1.0
Yes	2.75 (1.55–4.88)
Smoking	
No	1.0
Yes	1.71 (1.46–2.01)
Previous low birth weight	
No	1.0
Yes	1.56 (1.10–2.21)

CI, confidence interval.

Table 2 shows the adjusted ORs for each of the outcomes for fetuses and neonates affected by isolated single umbilical artery. Hydramnios (OR 2.80, CI 1.42–5.49) and placental abnormalities (OR 3.63, CI 3.01–4.39) were significantly higher in pregnancies affected by isolated single umbilical artery when compared with three-vessel cord pregnancies. With regard to invasive testing, pregnancies with fetuses with isolated single umbilical artery had higher rates of amniocentesis (OR 2.52, CI 1.82–3.51) compared with pregnancies with three-vessel cord fetuses. For maternal medical conditions of pregnancy, pregnancy-induced hypertension (OR 1.36, CI 1.09–1.70), premature rupture of membranes (OR 1.34, CI 1.12–1.62), and gestational diabetes (OR 1.90, CI 1.34–2.68) were all increased in women with pregnancies with isolated two-vessel cords when compared with three-vessel cord pregnancies.

With respect to intrauterine growth problems, fetuses and neonates with isolated single umbilical artery were more likely to experience growth restriction with an OR of 2.23 (CI 1.84–2.69) for the 10th percentile or less and an OR of 2.46 (CI 1.89–3.22) for the 3rd percentile or less, respectively, when compared with those with three-vessel cords. Rates of prematurity were also significantly higher for less than 37 weeks of gestation (OR 2.48, CI 1.91–3.23) and less than 34 weeks of gestation (OR 3.05, CI 2.05–4.53), respectively, for fetuses and neonates with isolated single umbilical artery. For outcomes of labor and delivery, fetuses and neonates with isolated single umbilical artery had increased rates of induction (OR 1.75, CI 1.35–2.27), cesarean delivery (OR 1.52, CI 1.33–1.74), and cesarean delivery for fetal distress (OR 3.22, CI 2.43–4.28).

For neonatal outcomes, after adjusting for multiples, both 1-minute (OR 1.87, CI 1.37–2.55) and 5-minute Apgar scores (OR 2.54, CI 1.66–3.88) were significantly lower for newborns with isolated single umbilical artery compared with those with three-vessel cords. There were significantly more isolated single umbilical artery neonates with depression at birth (OR 1.59, CI 1.21–2.10). Special care nursery admissions (OR 2.66, CI 2.23–3.18) were higher for neonates with isolated single umbilical artery. For perinatal mortality, after adjusting for multiple pregnancies, the odds ratios for fetal deaths (OR 3.50, CI 2.12–5.82), neonatal deaths (OR 2.21, CI 0.88–5.53), perinatal deaths (OR 3.11, CI 1.97–4.94), and deaths up to 1 year of age (OR 2.70, CI 1.22–5.94) were all

Table 2. Adjusted Outcomes for Isolated Single Umbilical Artery Between 1980 and 2002

Outcome	No Single Umbilical Artery (n=196,027)	Single Umbilical Artery (n=725)
Death by 1 y of age		
n* (%)	635 (0.36)	7 (1.10)
Adjusted OR† (95% CI)	1.0	2.70 (1.22–5.94)
Perinatal death		
n* (%)	1,675 (0.93)	22 (3.35)
Adjusted OR‡ (95% CI)	1.0	3.11 (1.97–4.94)
Neonatal death		
n* (%)	480 (0.27)	5 (0.78)
Adjusted OR‡ (95% CI)	1.0	2.21 (0.88–5.34)
Fetal death		
n* (%)	1,195 (0.66)	17 (2.59)
Adjusted OR‡ (95% CI)	1.0	3.50 (2.12–5.82)
Estimated gestational age less than 37 wk		
n* (%)	9,234 (6.03)	91 (16.25)
Adjusted OR† (95% CI)	1.0	2.48 (1.91–3.23)
Estimated gestational age less than 34 wk		
n* (%)	2,819 (1.84)	36 (6.43)
Adjusted OR† (95% CI)	1.0	3.05 (2.05–4.53)
Birth weight less than third percentile		
n* (%)	7,111 (3.70)	79 (11.10)
Adjusted OR† (95% CI)	1.0	2.46 (1.89–3.22)
Birth weight less than 10th percentile		
n* (%)	20,981 (10.92)	178 (25.00)
Adjusted OR† (95% CI)	1.0	2.23 (1.84–2.69)
1-min Apgar score 3 or lower		
n* (%)	6,880 (3.51)	47 (6.48)
Adjusted OR† (95% CI)	1.0	1.87 (1.37–2.55)
5-min Apgar score 3 or lower		
n* (%)	2,566 (1.31)	24 (3.31)
Adjusted OR† (95% CI)	1.0	2.54 (1.66–3.88)
Admitted to special care nursery		
n* (%)	20,193 (10.30)	185 (25.52)
Adjusted OR‡ (95% CI)	1.0	2.66 (2.23–3.18)
Birth depression		
n* (%)	10,036 (5.12)	58 (8.00)
Adjusted OR† (95% CI)	1.0	1.59 (1.21–2.10)
Induction		
n* (%)	10,018 (5.47)	61 (9.20)
Adjusted OR (95% CI)	1.0	1.75 (1.35–2.27)
Cesarean delivery		
n* (%)	38,906 (19.85)	218 (30.07)
Adjusted OR‡ (95% CI)	1.0	1.52 (1.33–1.74)
Cesarean delivery because of fetal distress		
n* (%)	4,656 (2.38)	54 (7.45)
Adjusted OR (95% CI)	1.0	3.22 (2.43–4.28)
Placental abnormalities		
n* (%)	11,741 (5.99)	137 (18.90)
Adjusted OR (95% CI)	1.0	3.63 (3.01–4.39)
Polyhydramnios		
n* (%)	880 (0.45)	10 (1.38)
Adjusted OR† (95% CI)	1.0	2.80 (1.42–5.49)
Amniocentesis		
n* (%)	4,276 (2.18)	42(5.79)
Adjusted OR‖ (95% CI)	1.0	2.52 (1.82–3.51)
Pregnancy-induced hypertension		
n* (%)	19,117 (9.75)	97 (13.38)
Adjusted OR¶ (95% CI)	1.0	1.36 (1.09–1.70)

(*continued*)

Table 2. Adjusted Outcomes for Isolated Single Umbilical Artery between 1980 and 2002 (*continued*)

Outcome	No Single Umbilical Artery (n=196,027)	Single Umbilical Artery (n=725)
Premature rupture of membranes		
n* (%)	29,535 (15.07)	142 (19.59)
Adjusted OR (95% CI)	1.0	1.34 (1.12–1.62)
Gestational diabetes		
n* (%)	4,390 (2.25)	33 (4.60)
Adjusted OR (95% CI)	1.0	1.90 (1.34–2.68)

OR, odds ratio; CI, confidence interval.
* Participants with missing information excluded.
† Adjusted for two or more fetuses and maternal smoking.
‡ Adjusted for two or more fetuses.
§ Adjusted for maternal smoking.
‖ Adjusted for preexisting diabetes.
¶ Adjusted for two or more fetuses, maternal smoking, and medication use.

higher in fetuses and neonates with isolated single umbilical artery.

DISCUSSION

The overall birth prevalence of single umbilical artery was 0.44%, and the birth prevalence of isolated single umbilical artery was 0.37%, which are both in keeping with previous reported rates.[1–5] Our study found similar rates of chromosomal abnormalities and congenital anomalies as reported in earlier studies.[1,2,5,7,8,12,23] For the development of single umbilical artery and isolated single umbilical artery, smoking was the only modifiable risk factor after adjustment. It is likely that the prevalence of smoking is higher among women who have spontaneous abortions (ie, delivery at less than 500 g) compared with women who deliver neonates weighing 500 g or more.[37] A higher prevalence of smokers among the missing data (neonates born weighing less than 500 g) would likely have the effect of our OR estimate for smoking to be conservative. As well, it is important to recognize that the observed association between maternal smoking and single umbilical artery may not be causal and that further prospective studies, which capture early pregnancy losses, are necessary to fully understand the relationship between smoking and single umbilical artery.

The results of this study indicate that pregnancies affected by single umbilical artery have higher rates of adverse pregnancy outcome. An important component of this study is that it supports the existence of an increased risk of perinatal mortality for fetuses and neonates with isolated single umbilical artery.[4,32] This study supports previous studies showing that isolated single umbilical artery is a risk factor for poor pregnancy outcome, and based on this finding, increased surveillance may be warranted for these pregnancies.[4,23]

It is unclear why fetuses and neonates with isolated single umbilical artery are at increased risk for poor perinatal and neonatal outcomes. This study and previous studies have shown an increased risk for placental abnormalities with isolated single umbilical artery that may further compound risk to the fetus.[13,14] This does not necessarily explain the increased rates of poor postnatal outcomes that were also found in this study. It is possible that the underlying cause of single umbilical artery may also convey further risk to the fetus in the intrapartum and neonatal periods. With regard to an increased risk for poor perinatal and neonatal outcomes, consideration of the placental abnormality needs to be considered as a possible cause for, or contributing factor to, this increased risk.

A strength of this study is that infant deaths were followed until 1 year of age. Previous studies assessing outcomes in the isolated single umbilical artery population did not include infant deaths up to 1 year of age and therefore may not accurately reflect the true prognosis and outcomes in fetuses and neonates with isolated single umbilical artery.[28,29] Important questions to be answered with regard isolated single umbilical artery are the long-term outcomes such as survival beyond 1 year and developmental outcome. This is a difficult question to answer with regard to isolated single umbilical artery owing to the lack of long-term follow-up.

One of the limitations of this study is that only pregnancies at 20 or more weeks of gestation and weighing 500 g or more are included in the Atlee perinatal database. Terminations for fetal anomalies at less than 20 weeks of gestation or fetuses weighing less than 500 g were not included in this study. In Nova Scotia, a Fetal Anomaly Database captures all fetuses and neonates who have defined abnormalities, including all terminations of pregnancy as well as live

and still births. This database was started in 1992. Reviewing the Fetal Anomaly database, all fetuses terminated at less than an estimated 20 weeks of gestation with single umbilical artery had other associated anomalies or a chromosomal abnormality present. Therefore, the rate of isolated single umbilical artery in this study would not be affected by these terminations.

Although this is one of the largest studies assessing outcomes of single umbilical artery, the power of this study was limited for many of the outcomes studied as they are rare events, such as death up to 1 year of age and neonatal death. Compounding this limitation is that for some outcomes, such as cord artery pH and chorionic villous sampling, no data were recorded for a large proportion of the cohort, and therefore, analysis was not possible. The presence of single umbilical artery was determined by birth record, pathology report, or neonatal physical examination. Use of birth records and physical examination may underestimate the incidence of single umbilical artery. A previous study suggests that pathologic examination of the cord and placenta as well as gross examination after fixation increase the rate of detection for single umbilical artery.[1]

Our study supports previous studies on single umbilical artery that recommend further evaluation and consultation for pregnancies with suspected single umbilical artery.[30,38] The Society of Obstetricians and Gynaecologists of Canada recommend a detailed review of fetal anatomy with single umbilical artery and follow-up assessment of fetal growth given clinical concerns.[39] This study supports a targeted anatomic survey owing to the increased risk of chromosomal and congenital abnormalities. Prospective parents should be counseled with regard to the increased risk for poor perinatal outcome and that increased surveillance may be required. According to this study's findings, the risk of intrauterine growth restriction is increased, and repeated ultrasound examination with Doppler assessment and testing for fetal well-being may be necessary in later weeks of gestation. There is also an increased risk of preterm delivery with isolated single umbilical artery. Whether increased surveillance or cervical length assessment would be beneficial requires more study.

In summary, our study shows that single umbilical artery is a congenital abnormality of the umbilical artery associated with increased risk for poor perinatal outcomes, even in the absence of chromosomal abnormalities or major anomalies.

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