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The Incidence of Isolated Single Umbilical Artery in Twins And Adverse Pregnancy Outcomes

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Abstract

Objectives—To estimate the incidence of single umbilical artery (SUA) in twin pregnancies and to investigate whether SUA in twin gestations is associated with adverse obstetric outcomes.

Methods—Retrospective cohort study of consecutive twin pregnancies over 17 years at a tertiary care hospital. Primary exposure was SUA in one or both twins documented at routine second trimester anatomic survey. Adverse obstetric outcomes included small for gestational age (SGA), placental abruption, and preterm birth, evaluated in univariable and multivariable analyses. Analysis was performed both at the pregnancy level and at the fetal level using paired analyses to account for the non-independence of twin pairs.

Results—Of 2,378 twin pregnancies without major anatomic abnormalities, 1.7% (n=40) had SUA. Only 1 pregnancy (one monochorionic twin pair) was complicated by both twins having SUA. Twin fetuses with SUA are at increased risk for SGA (aOR 2.1 (1.2-4.1), p=0.03) after adjusting for pertinent confounding factors, similar to the findings of previous studies in singleton pregnancies. In addition, twins with SUA may be at increased risk for preterm delivery before 28 weeks compared to twin pregnancies with normal three-vessel umbilical cords (aOR 3.2 (1.3-7.89.4), p=0.01).

Conclusions—The incidence of SUA in twin gestations in this cohort is significantly less than recently published data. Similar to reports in singleton gestations, SUA appears to be associated with an increased risk for SGA in twins.

Keywords

Twin pregnancies; Single Umbilical Artery; Fetal anomaly

Introduction

Normal umbilical artery anatomy includes two umbilical arteries and one umbilical vein. The incidence of single umbilical artery (SUA) in liveborn singleton infants is approximately 0.5-1%¹⁻⁴. Several studies have suggested that SUA in singletons is associated with adverse obstetric outcomes including growth abnormalities, preterm delivery, fetal death and congenital anomalies^{1, 2, 4, 5}. A singleton cohort from our institution detected a two-fold increase of small for gestational age growth in the setting of SUA, even after excluding pregnancies with other congenital anomalies¹.

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Two recent publications reported incidences of SUA in twin gestations of 4.6% and 9.8%, significantly higher than the typically reported incidence of 1% in singleton pregnancies^{2, 6}. Given that twin pregnancies are already at increased risk for growth abnormalities relative to singletons, and recent studies suggest a high incidence of SUA in twins, we aimed to confirm the incidence of SUA in a large cohort of twin gestations. In addition we aimed to evaluate whether twin gestations with SUA are at risk for adverse obstetric outcomes compared to those with normal umbilical cord anatomy.

Methods

We performed a retrospective cohort study of all consecutive twin pregnancies undergoing routine second trimester ultrasound between 17-22 weeks, from 1990-2008, at a large tertiary care center. This analysis was performed using the institutional perinatal database and was approved by the Washington University School of Medicine human studies review board.

Diagnosis of SUA in one or both twins was made at the anatomic survey ultrasound, performed by dedicated, certified obstetric and gynecologic sonographers and confirmed by a Maternal Fetal Medicine attending physician. Umbilical cord anatomy is routinely examined at two locations: 1) at the umbilical cord insert on the fetal abdomen in a transverse plane and 2) at the level of the fetal bladder to demonstrate 2 umbilical arteries, one on each side of the bladder⁷. Color Doppler is used to confirm the normal anatomy of 2 arteries bifurcating around the fetal bladder. Data on maternal medical and obstetric history, as well as socio-demographic characteristics were obtained from the patient and medical chart review and was entered into the perinatal database by dedicated obstetric outcome research coordinators. Obstetric outcomes were collected prospectively as the pregnancies progressed during the study period. For patients who delivered within our institution, outcome information was obtained from the medical record. To maximize follow-up information for patients who delivered outside of our institution, both the patient and the referring physician were contacted to obtain pregnancy outcome information. Gestational age was determined by the best data available from last menstrual period (LMP) consistent with ultrasound dating (± 5 days in the first trimester or ± 14 days in the second trimester). If LMP was unknown or ultrasound dating was inconsistent, the patient was dated according to the earliest ultrasound available.

Primary outcomes were incidence of isolated SUA as well as risk of small for gestational age growth (defined as birth weight less than the 10th percentile for gestational age by the Alexander growth standard⁸) in the setting of SUA. We also estimated the risks of placental abruption (defined clinically by the obstetric provider in the medical record), NICU admission, and preterm delivery at less than 24, 28, and 34 weeks for any indication in the setting of SUA. Pregnancies complicated by major fetal anomalies other than SUA were excluded.

Descriptive statistics were used to evaluate baseline demographic characteristics of the two study groups. The incidence of isolated SUA was calculated for the entire cohort and was further estimated stratified by chorionicity. The analysis of adverse obstetric outcomes was first performed at the level of the pregnancy, using each mother as an individual observation and comparing pregnancies with one or both babies having SUA to twin pregnancies where both fetuses had normal 3VC. Univariable analysis was performed using χ^2 or Fischer-exact for categorical variables, as appropriate. Relative risk and 95% confidence intervals were calculated for each of the outcomes of interest. Backward stepwise logistic regression was used to control for pertinent confounding variables. The likelihood ratio test was used to assess the impact of removing covariates of the model. If there were fewer than 10

observations for any cell, multivariable logistic regression was not performed to avoid overfitting and the potential for erroneous estimates of risk.

Comparisons at the fetal level were performed comparing fetuses with SUA to unaffected fetuses clustered by the maternal identifier to account for the non-independence of twin pairs. Fetal level analyses were performed only for small for gestational age growth, given that preterm birth is a pregnancy level outcome and delayed interval deliveries are not routinely performed at our institution. All statistical analyses were performed using STATA 10.0 (special edition, Stat-Corp, College Station, TX).

Results

Of 2,445 twin pregnancies, 67 pregnancies were excluded for major fetal anomalies in one or both twins, leaving 2,378 pregnancies for this analysis. The pregnancy incidence of isolated SUA was 1.7% (n=40). Only 1 pregnancy was complicated by both twins having SUA. All other pregnancies consisted of 1 twin with SUA and 1 twin with normal 3VC anatomy. Maternal obesity (defined as BMI > 30), smoking, and maternal medical problems including preeclampsia were not significantly different in pregnancies with SUA compared to those with normal 3VC. However, women with pregnancies complicated by SUA were more likely to be of advanced maternal age and less likely to be black (Table 1).

Incidence of SUA was examined by chorionicity. Of the full cohort, 77.1% of pregnancies were dichorionic and 22.9% were monochorionic. SUA occurred in 2.4% of monochorionic pregnancies and 1.8 % of dichorionic pregnancies (Table 2). The risk of having a fetus with SUA was not significantly different in monochorionic compared to dichorionic pregnancies (RR 1.2 95%CI 0.6-2.5, p=0.6).

Small for gestational age growth was increased in pregnancies complicated by SUA relative to those with 3VC (Table 3). In the paired analysis, small for gestational age growth remained significantly increased in fetuses with SUA compared to fetuses without SUA. This finding remained significant even after adjusting for advanced maternal age and chorionicity and excluding pregnancies with intrauterine fetal death (48.6% vs 26.3%, aOR 2.1 95%CI 1.2-4.1, p=0.03).

Adverse obstetric outcomes according to pregnancy-level analysis were compared between study groups and are reported in Table 4. Twin pregnancies with SUA delivered on average 1 week earlier than twin pregnancies without SUA (33.0 ± 4.4 weeks vs. 34.7 ± 4.7 weeks, p=0.04). Preterm delivery at less than 34 weeks (37.0% vs. 22.3% aOR 2.1 95% CI 1.0-4.1, p=0.04) and 28 weeks (14.8% vs. 5.1%, aOR 3.2 95% CI 1.3-7.8, p=0.01) was increased in pregnancies with SUA even after controlling for prior preterm birth and monochorionicity. However risk for preterm birth at less than 24 weeks (3.7% vs 2.7% aOR 1.4, 95% CI 0.2-9.2, p=0.7) did not differ in twin pregnancies with SUA compared to those without. Placental abruption did not differ between study groups. Neonatal intensive care unit (NICU) admission did not differ between study groups (31.4% of twins with SUA as compared to 19.6% of twins without SUA (p<0.06)). Furthermore, after controlling for gestational age at delivery, the trend toward a difference in NICU admission between study groups did not remain.

Conclusion

In our large cohort of consecutive twin pregnancies, we found a 1.7% incidence of isolated SUA, significantly less than recently published literature reporting an incidence of SUA in twins of 4-10%^{6,9}. The vast difference from previously reported incidence of 4-10% may be due to specific accrual or referral biases in those cohorts, artificially inflating the

incidence. Given the incidence of SUA in singletons is approximately 0.5-1%^{1, 2, 4}, a 1.7% rate of SUA noted in this cohort of twin pregnancies is consistent with what would be expected; approximately double the opportunity for abnormalities in umbilical cord structure to occur in twin pregnancies. A prior cohort study including both singletons and twins reported an odds ratio of 2 for isolated SUA in multiple gestations relative to singletons, consistent with the results we report in this cohort⁴.

Several studies, including a singleton cohort from our institution, have suggested an increased risk of growth abnormalities in fetuses with single umbilical artery^{1, 4, 5}. Because twin pregnancies are already at increased risk for growth abnormalities relative to singletons, the suggestion of growth abnormalities associated with SUA could potentially augment the risk already present in twins. The analysis of pregnancies with one twin having SUA compared to twin pregnancies with both fetuses demonstrating normal umbilical cord anatomy suggests an increase in small for gestational age growth in pregnancies where one twin has SUA. The fetal-level analyses confirmed the pregnancy-level findings, suggesting that twin fetuses with SUA are at increased risk for decreased fetal growth above the background risk associated with twin pregnancy. To explore the timing of growth abnormalities we analyzed the association between SUA and IUGR at the time of study ultrasound (anatomic survey). Although nearly 30% of fetuses with SUA demonstrated IUGR at the time of anatomic survey, the incidence of SGA by birthweight was nearly 50% suggesting that although growth abnormalities may be detected early, a significant proportion of twins will exhibit suboptimal growth later in pregnancy.

Pregnancy level outcomes of preterm birth were slightly increased in pregnancies complicated by SUA. Preterm birth at less than 34 weeks and less than 28 weeks were marginally increased in twin pregnancies with SUA however, this finding did not persist in the less than 24 week strata. The lack of significance in the 24 week group could result from the manifestation of growth abnormalities and other indications for iatrogenic preterm delivery evolving after 24 weeks. Women with pregnancies with SUA were overall similar in baseline characteristics to those with normal umbilical cords in both twins. However, women with SUA were less likely to be black. Given known racial disparities in adverse pregnancy outcomes, this difference could have biased results toward the null, yet significant differences in study groups were still noted. NICU admission did not differ between twins with SUA compared to those without. Analysis controlling for gestational age suggested the risk for intensive nursery care admission is driven predominantly by gestational age at delivery and not by the presence or absence of SUA.

This study represents, to our knowledge, the largest cohort of twin pregnancies evaluating obstetric outcomes associated with SUA. The prior reported incidences of nearly 10% for SUA in twins was concerning given the possible association of growth abnormalities with SUA. However, this large cohort of twin pregnancies suggests an incidence greater than that in singletons, but much more modest than recent reports suggested. Nonetheless, twin pregnancies fetuses with SUA are at increased risk for growth abnormalities when compared to other twin fetuses. Another strength of this study is the ability to analyze outcomes both at the pregnancy level as well as the fetal level, and being able to account for chorionicity. Patients carrying twin pregnancies in which one or both babies has an SUA may have questions about their risk for complications in the pregnancy overall, and also may inquire about the risk of complications specifically in the twin with the SUA. The two analyses performed in this cohort allowed for addressing both sets of questions.

One potential limitation of our study is that we do not have histopathologic confirmation of SUA. A recent study by Lamberty et al. used the gold standard of placental histopathology and reported a sensitivity and specificity of 86% and 99% respectively for the ultrasound

diagnosis of SUA diagnosis in the second trimester¹⁰. One patient was misclassified as having SUA and another was misclassified as normal suggesting that the diagnostic error occurs in both directions and thus may not contribute to systematic bias. Furthermore, we would offer that ultrasound diagnosis is most clinically relevant as it is what care-givers have at the time of counseling and management decisions, thus adding generalizability.

In conclusion, this cohort of twin pregnancies suggests an incidence of SUA of 1.7%, slightly above the incidence in singleton gestations, but significantly less than recent reports of up to 10%. The data in this cohort of twins is consistent with data in singleton cohorts suggesting an increased risk for growth abnormalities associated with SUA. We found that SUA in one or both twins is a marker of decreased fetal growth compared to twins without this finding. Multiple gestations often undergo ultrasound assessments of growth, but the presence of SUA indicated a greater risk for small for gestational age growth and the need for close evaluation. Based on these data we would suggest twin pregnancies with SUA undergo serial growth ultrasounds. A more complete understanding into the underlying mechanism of normal and abnormal umbilical cord development is needed to address the mechanism for the association of abnormal umbilical cord vessel anatomy with adverse pregnancy outcomes.

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What's Already Known About This Topic? Single umbilical artery in singleton gestations is associated with multiple adverse obstetric outcomes including small for gestational age birthweight.

What Does This Study Add? Because twin gestations are already at higher risk for adverse obstetric outcomes relative to singletons, this study aims to evaluate whether single umbilical artery in twins further increases the risk for obstetric complications, and specifically abnormal fetal growth.

Table 1

Baseline demographic characteristics of twin pregnancies complicated by single umbilical artery compared to three-vessel umbilical cord anatomy:

Characteristic	Single Umbilical Artery (n=40)	Three Vessel Cord (n=2378)	p-value
Advanced maternal age	40.0%	25.2%	0.03
Primiparous	36.2%	26.7%	0.14
Black Race	10.6%	23.3%	0.04
BMI ≥ 30	1.5%	2.1%	0.4
Smoking	8.5%	10.6%	0.6
Alcohol Use	17.0%	12.4%	0.3
Diabetes	2.1%	1.1%	0.5
Chronic hypertension	2.1%	3.0%	0.7
Preeclampsia	29.8%	19.7%	0.09

Table 2

Incidence of SUA in twin pregnancies.

Population	Incidence
Entire twin cohort	1.9%
Excluding anomalies (Isolated SUA)	1.7%
Dichorionic Pregnancies (nonanomalous)	1.8%
Monochorionic Pregnancies (nonanomalous)	2.4%

Table 3

Growth restriction according to pregnancy level and fetal level analyses.

Small for Gestational Age	Single Umbilical Artery	Three Vessel Cord	Relative Risk (95%CI)	Adjusted Odds Ratio (95%CI)	p-value
Pregnancy level Analysis(n=2378 pregnancies)	52.5%	35.8%	1.5 (1.1-2.0)	1.8 (1.0-3.1) *	0.03
Fetal level paired analysis (n=4756 fetuses)	48.6%	26.6%	2.6 (1.4-5.0)	2.1 (1.2-4.1) †	0.03

* Adjusted for advanced maternal age, tobacco use

† Adjusted for advanced maternal age, monochorionicity

Adverse pregnancy outcomes in twin pregnancies with single umbilical arteries compared to twin pregnancies with three-vessel umbilical cord anatomy:

Table 4

Outcomes	Single Umbilical Artery	Three Vessel Cord	Relative Risk (95%CI)	Adjusted Odds Ratio (95%CI)	p-value
Abruption (%) n=42	2.1%	1.9%	1.1 (0.2-8.0)	NA	0.9
Preterm Delivery <34 weeks (%) n=377	37.0%	22.3%	1.7 (1.0-2.7)	2.1 (1.0-4.1) *	0.04
Preterm Delivery <28 weeks (%) n=88	14.8%	5.1%	3.1 (1.1-7.3)	3.2 (1.3-7.9) *	0.01
Preterm Delivery <24 weeks (%) n=45	3.7%	2.7%	1.4 (0.2-9.7)	NA	0.7
NICU admission n=35	31.4%	19.1%	1.6 (1.0-2.7)	1.4 (0.6-2.9) †	0.4

* Adjusted for prior preterm birth and monochorionicity

† Adjusted for gestational age at delivery