International Journal of Women's Health

Dovepress
Taylor & Francis Group

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ORIGINAL RESEARCH

Risk Factors for Umbilical Artery Thrombosis in Pregnant Women: A Retrospective Study

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Purpose: Umbilical artery thrombosis (UAT) is a rare but potentially life-threatening complication in pregnancy. It shares ultrasonographic similarities with isolated single umbilical artery (iSUA), a relatively common condition with more favorable outcomes, highlighting the need for reliable differential markers. This study was performed to identify the risk factors for UAT in pregnant women. Also, we compared maternal and neonatal outcomes between UAT, iSUA, and normal controls with three umbilical vessels (NC).

Patients and Methods: This retrospective study was conducted at the Women's Hospital, Zhejiang University School of Medicine. A total of 195 participants were included between January 1, 2020, and December 31, 2024, including 65 of UAT, 65 of iSUA, and 65 of NC. The baseline information, laboratory data and relevant perinatal outcomes of all participants were collected and analyzed. Logistic regression models were employed to evaluate the association between antepartum findings and UAT in pregnant women.

Results: Compared with the iSUA group, the UAT group showed higher rates of abnormal fetal movement (p=0.006) and fetal heart rate (FHR) patterns (p<0.001), shorter prothrombin time (PT) (p=0.002) and lower high-density lipoprotein (HDL) levels (p=0.014). Doppler assessment demonstrated lower umbilical vascular indices in the preterm UAT participants (<37 weeks), including lower systolic/diastolic (S/D) ratios (p=0.037), pulsatility indices (PI) (p=0.005), and resistance indices (RI) (p=0.018), with two cases showing absent end-diastolic flow. Postpartum pathology revealed shorter cord length, smaller diameter, and higher hypercoiling prevalence in UAT. Multivariate analysis identified abnormal fetal movement, abnormal FHR patterns, prolonged activated partial thromboplastin time (APTT), and cord hypercoiling as the risk factors for UAT, while longer PT, higher HDL, higher umbilical vascular indices and favorable umbilical cord parameters served as the protective factors (all p<0.05). Critically, the UAT group was more likely to experience adverse maternal and neonatal outcomes than other two groups.

Conclusion: This study identifies distinct clinical, laboratory data, and sonographic markers that effectively differentiate UAT from iSUA, with abnormal fetal movement and FHR patterns, prolonged APTT, and umbilical cord hypercoiling as prominent risk factors for UAT.

Keywords: risk factors, umbilical artery thrombosis, antepartum findings, perinatal outcomes, isolated single umbilical artery

Introduction

Umbilical artery thrombosis (UAT) shows an incidence of 0.0025–0.045% in pregnancies and critically compromises fetal well-being by impairing oxygen and nutrients supply.[1,2] Notably, UAT presents without pathognomonic features, rendering prenatal diagnosis challenging. Although prenatal Doppler ultrasound is routinely employed to assess umbilical cord hemodynamics, its sensitivity for UAT detection remains limited, with studies reporting a detection rate as low as 37%.[3] Most cases are ultimately diagnosed through postnatal placental or umbilical cord histopathological examination, often resulting in delayed intervention. These diagnostic limitations highlight the urgent need for more sensitive early detection methods, though research in this area remains limited.

Received: 25 July 2025
Accepted: 25 September 2025
Published: 4 October 2025

Emerging evidence suggests potential associations between UAT and abnormal clinical parameters. For example, the association of UAT with non-reassuring fetal heart rate (FHR) patterns was reported, particularly recurrent late decelerations or minimal variability, which was likely to reflect chronic fetal hypoxia.[2] Doppler studies show that abnormal velocimetry of umbilical artery may precede UAT diagnosis,[4] while some cases exhibit umbilical cord abnormalities.[5] Limited data also implicate maternal thrombophilia profiles.[6] However, these findings suffer from low positive predictive value: FHR changes are nonspecific to UAT, significant Doppler abnormalities often appear late, and serum biomarkers show inconsistent validation across studies. Importantly, there are few studies systematically assessing the rationality of these parameters in early UAT detection.

Isolated single umbilical artery (iSUA) occurs in 0.5–2% of pregnancies,[7] which typically shows favorable perinatal outcomes despite modestly increased risks of intrauterine growth restriction and preterm birth.[8] However, the similarity in ultrasonographic manifestations between UAT and iSUA complicates clinical management, particularly if color Doppler misses residual flow in the thrombosed artery.[9] Although some discriminators exist as UAT-specific risk factor,[1,10] no studies are performed to systematically compare the clinical parameters between these conditions.

In this study, we compared antepartum findings, including clinical symptoms, coagulation/lipid profiles and umbilical artery Doppler findings, among the pregnant women with UAT, iSUA, and three umbilical vessels, with particular focus on identifying predictors specific to UAT. Furthermore, we examined differential maternal and neonatal outcomes across these three cohorts to clarify the clinical significance of accurate prenatal differentiation.

Materials and Methods

Study Population

The clinical data of pregnant women from Women's Hospital, Zhejiang University School of Medicine were retrospectively collected from January 1, 2020 to December 31, 2024. Pregnant women with UAT were included as the UAT group, while those with iSUA or normal controls defined as three umbilical vessels were as the iSUA and NC groups, respectively. Given that UAT was a rare condition, a census sampling method was employed for the case enrollment. We screened and included all eligible cases of UAT that were pathologically confirmed after delivery in the study period. To control for confounding biases and enhance statistical power, a 1:1:1 matched design was adopted. For each UAT patient, one patient with iSUA and one NC with three umbilical vessels were matched from the contemporaneous database based on the index year of diagnosis. Participants in the iSUA and NC groups were selected using a simple random sampling method from the matched candidate pool.

All participants provided informed consent form. The study was approved by the Institutional Review Board of Women's Hospital, Zhejiang University School of Medicine (No.: IRB-20250114-R) and was conducted in accordance with the Declaration of Helsinki.

Singleton pregnant women with complete medical record and laboratory information were included, and UAT, iSUA or three umbilical vessels were confirmed by ultrasound scans and pathological examinations of the umbilical cord post-delivery. Pregnant women with twins, fetal malformation, chromosome aneuploidy, and genetic alterations were excluded.

Data Collection

The baseline information, laboratory data and relevant perinatal outcomes of participants were collected by reviewing the electronic medical record of our hospital. The baseline information comprised maternal age, body mass index (BMI), gravidity, parity, assisted reproduction, history of spontaneous abortion, use of low molecular weight heparin (LMWH), pregnancy comorbidities and complications, fetal movement response and FHR patterns prior to delivery. Laboratory data comprised the findings associated with coagulation and lipid function, such as activated partial thromboplastin time (APTT), prothrombin time (PT), triglycerides, total cholesterol, and high-density lipoprotein (HDL). Additionally, umbilical artery Doppler ultrasound results before delivery were also recorded. Perinatal outcomes included the gestational age at delivery, rates of cesarean delivery, meconium-stained amniotic fluid (MSAF), fetal weight, Apgar

scores and NICU admission and neonatal mortality. Postpartum pathological findings contained the appearance and weight of placentae, the length and diameter of umbilical cord, abnormal umbilical cord insertion and hypercoiling.[11]

The thrombus sites of umbilical arteries were embedded in paraffin following fixation, and then hematoxylin-eosin (HE) staining was performed on cross-sections to verify the thrombus formation. Two experienced pathologists were responsible for reviewing the stained slides. Only cases with complete image data and confirmed by pathology were included in this study.

Definition of UAT and iSUA

We made the prenatal diagnosis of UAT based on ultrasonographic findings. The current ultrasound reveals a single visible umbilical artery, but previous ultrasound confirmed bilateral umbilical arteries around the fetal bladder in the transverse pelvic view. Moreover, within the umbilical artery, the ultrasound identified a suspicious intraluminal low-echogenic substance.[12] We diagnosed iSUA during the fetal anatomical scan. The fetal pelvic transverse section only presented a single umbilical artery which encircled the fetal bladder, and meanwhile a single umbilical artery was confirmed using color doppler ultrasound, which showed no fetal malformations or chromosomal abnormalities.[13] All ultrasound examinations were carried out transabdominally by two experienced ultrasound physicians using uniform high-resolution ultrasound equipment.

Statistical Analysis

Statistical analysis was conducted using SPSS 26.0 software (SPSS, Chicago, IL, USA). Student's *t* test or one-way analysis of variance (ANOVA) was used for normally distributed variables, reported as mean ± standard deviation (SD). Mann–Whitney *U*-test was employed for non-normally distributed, describing as median and interquartile [M (Q1, Q3)]. Chi-square test was utilized for categorical variables, showing number (%). Logistic regression models were used to estimate the association between UAT and antepartum findings, in which odds ratios (ORs) and 95% confidence intervals (CIs) were reported. Multivariable model was adjusted for age, BMI, gravidity, and mode of conception. The $p < 0.05$ was considered statistically significant.

Results

Baseline Information of Participants

Between January 1, 2020 and December 31, 2024, a total of 195 participants were equally distributed among UAT (n=65), iSUA (n=65), and NC (n=65) groups. No prominent differences were observed in maternal age, BMI, gravidity, and parity across three groups (all $p > 0.05$). The UAT group exhibited significantly increased proportions of previous spontaneous abortion (18.46% vs 4.62%, $p = 0.028$) and LMWH use during pregnancy (38.46% vs 12.31%, $p = 0.001$) compared with the iSUA group. Notably, none in the NC group required LMWH treatment, resulting in a marked difference compared with the UAT group (0.00% vs 38.46%, $p<0.001$). During pregnancy, the incidence of gestational diabetes mellitus, hypertension, hypothyroidism, and amniotic fluid volume abnormalities were comparable among all groups (all $p > 0.05$; Table 1).

Antepartum Findings of Participants with UAT, iSUA, and Three Umbilical Vessels

Clinical symptoms. Abnormal fetal movement and FHR patterns in the UAT group were more prevalent compared with the iSUA group (16.92% vs 1.54%, $p = 0.006$; 36.92% vs 9.23%, $p < 0.001$) and the NC group (16.92% vs 1.54%, $p = 0.006$; 36.92% vs 6.15%, $p < 0.001$), respectively (Table 2).

Coagulation/ lipid profiles. Coagulation profiles demonstrated that the UAT group had a significantly shorter PT than both the iSUA (12.26±0.45 s vs 12.56 ± 0.67 s, $p = 0.002$) and NC groups (12.26±0.45 s vs 12.55 ± 0.42 s, $p = 0.002$), and a prolonged APTT compared with the NC group (32.52±2.71 s vs 30.89±2.45 s, $p = 0.001$), while blood platelet count and fibrinogen showed no statistical difference (all $p > 0.05$). Lipid analysis indicated lower HDL levels in UAT versus in iSUA (1.89±0.39 mmol/L vs 2.08 ± 0.43 mmol/L, $p = 0.014$) and NC (1.89±0.39 mmol/L vs 2.14 ± 0.50 mmol/L, $p = 0.002$), but not triglyceride and total cholesterol levels (all $p > 0.05$; Table 2).

Table 1 Baseline Characteristics of Women with UAT, iSUA and Three Umbilical Vessels

Characteristics	UAT (n=65)	iSUA (n=65)	NC (n=65)	*p value*		
				UAT vs NC	iSUA vs NC	UAT vs iSUA
Maternal age (years)	30.98±4.31	31.08±4.09	31.51±3.70	0.462	0.544	0.897
BMI (kg/m^2)	26.12±3.86	26.93±3.00	25.97±2.98	0.805	0.101	0.162
Gravidity	1 (1,2)	1 (1,2)	1 (1,2)	0.090	0.442	0.330
Parity	0 (0,0)	0 (0,0)	0 (0,0)	0.371	0.461	0.120
History of spontaneous abortion	12 (18.46%)	3 (4.62%)	5 (7.69%)	0.069	0.715	0.028
Assisted reproduction	5 (7.69%)	6 (9.23%)	5 (7.69%)	1.000	0.753	0.753
Use of LMWH during pregnancy	25 (38.46%)	8 (12.31%)	0 (0.00%)	<0.001	0.006	0.001
Complications or comorbidities						
GDM	7 (10.77%)	6 (9.23%)	10 (15.38%)	0.435	0.286	0.770
HDP	3 (4.62%)	4 (6.15%)	6 (9.23%)	0.490	0.742	1.000
Hypothyroidism	7 (10.77%)	9 (13.85%)	6 (9.23%)	0.770	0.410	0.593
Antiphospholipid syndrome	5 (7.69%)	5 (7.69%)	1 (1.54%)	0.210	0.210	1.000
Polyhydramnios	4 (6.15%)	6 (9.23%)	2 (3.08%)	0.676	0.274	0.742
Oligohydramnios	6 (9.23%)	7 (10.77%)	1 (1.54%)	0.120	0.068	0.770

Notes: Data are expressed as n (%), mean ± SD, or M (Q1, Q3).
Abbreviations: UAT, umbilical artery thrombosis; iSUA, isolated single umbilical artery; NC, normal controls with three umbilical vessels; BMI, body mass index; LMWH, low molecular weight heparin; GDM, gestational diabetes mellitus; HDP, Hypertensive Disorders of Pregnancy; SD, standard deviation.

Table 2 Antepartum Findings Between Participants with UAT, iSUA, and Three Umbilical Vessels

Characteristics	UAT (n=65)	iSUA (n=65)	NC (n=65)	*p value*		
				UAT vs NC	iSUA vs NC	UAT vs iSUA
Clinical symptoms						
Abnormal fetal movement	11 (16.92%)	1 (1.54%)	1 (1.54%)	0.006	1.000	0.006
Abnormal FHR patterns	24 (36.92%)	6 (9.23%)	4 (6.15%)	<0.001	0.742	<0.001
Coagulation/lipid profiles						
Blood platelet count (*10^9)	204.60±53.10	197.83±49.80	198.52±48.43	0.493	0.938	0.446
PT (s)	12.26±0.45	12.56±0.67	12.55±0.42	0.002	0.907	0.002
APTT (s)	32.52±2.71	31.72±2.54	30.99±2.19	0.001	0.098	0.069
Fibrinogen (g/L)	4.61±0.60	4.59±0.72	4.52±0.79	0.474	0.592	0.856
Triglyceride (mmol/L)	2.97±1.08	3.20±1.30	3.45±1.80	0.056	0.308	0.368
Total cholesterol (mmol/L)	6.33±1.20	6.62±1.31	6.78±1.58	0.064	0.525	0.223
HDL (mmol/L)	1.89±0.39	2.08±0.43	2.14±0.50	0.002	0.483	0.014
Umbilical artery Doppler						
Gestational age at delivery <37 weeks	n=35*	n=10	n=8			
S/D ratio	2.15±0.47	2.53±0.60	2.57±0.40	0.035	0.866	0.037
PI	0.74±0.21	1.07±0.60	0.93±0.18	0.131	0.337	0.005
RI	0.52±0.13	0.66±0.24	0.59±0.06	0.303	0.324	0.018
Gestational age at delivery ≥37 weeks	n=28	n=55	n=57			
S/D ratio	1.91±0.39	1.92±0.28	2.21±0.25	<0.001	<0.001	0.893
PI	0.63±0.16	0.65±0.15	0.80±0.12	<0.001	<0.001	0.543
RI	0.45±0.08	0.47±0.07	0.54±0.05	<0.001	<0.001	0.322
Postpartum pathological findings						
Weight of placenta (g)	360.00 (307.50, 440.00)	420.00 (360.00,460.00)	460.00 (350.00,510.00)	0.001	0.081	0.006
Umbilical cord length (cm)	51.63±7.42	56.09±9.61	56.95±6.23	<0.001	0.534	0.001
Umbilical cord diameter (mm)	10.00 (8.00, 10.00)	10.00 (9.00, 1.10)	12.00 (10.00, 14.50)	<0.001	<0.001	0.002
Abnormal cord insertion	5 (7.69%)	13 (20.00%)	1 (1.54%)	0.210	0.002	0.042
Hypercoiling	13 (20.00%)	1 (1.54%)	1 (1.54%)	0.002	1.000	0.002

Notes: Data are expressed as n (%), mean ± SD, or M (Q1, Q3). *Two cases in the UAT group showed absent end-diastolic flow in the umbilical artery.
Abbreviations: UAT, umbilical artery thrombosis; iSUA, isolated single umbilical artery; NC, normal controls with three umbilical vessels; PT: Prothrombin time; APTT: Activated partial thromboplastin time; HDL, high-density lipoprotein; S/D, systolic-diastolic duration ratio; RI, resistance index; PI, pulsatility index; FHR, fetal heart rate; SD, standard deviation.

Umbilical artery Doppler findings. Umbilical artery Doppler assessment showed distinct patterns when stratified by gestational age. In the preterm subgroup (<37 weeks), the UAT group exhibited lower systolic/diastolic (S/D) ratio, pulsatility index (PI), and resistance index (RI) compared with the iSUA group (p = 0.037, 0.005, and 0.018, respectively), along with lower S/D ratio versus NC (p=0.035). Notably, two cases in the UAT group showed absent end-diastolic flow. In the full-term subgroup (≥37 weeks), both UAT and iSUA groups had lower S/D ratio, PI, and RI than the NC group (all $p < 0.001$), but no prominent intergroup differences (all $p > 0.05$; Table 2).

Postpartum pathological findings. Postpartum pathological examination identified significant differences in umbilical cord characteristics. The UAT group had a shorter umbilical cord length (p<0.001), smaller diameter (p<0.001) and reduced placental weight (median 360 g vs 420 g in iSUA, p=0.006; vs 460 g in NC, p=0.001) compared with other groups. Umbilical cord hypercoiling was more frequent in the UAT group than in the iSUA (p = 0.002) and NC (p = 0.002), although abnormal cord insertion was more common in the iSUA group in comparison to the UAT group (p = 0.042; Table 2).

Association Between Antepartum Findings and UAT

In contrast to the participants with normal fetal movement, we found a significant higher risk of UAT in those with abnormal fetal movement (aOR: 12.92, 95% CI: 1.60–104.13) after adjustment for age, BMI, gravidity, and modes of conception (Table 3). Similarly, abnormal FHR patterns were associated with an 11.90-fold increased UAT risk (95% CI: 3.49–40.62, $p < 0.001$). Among coagulation parameters, each 1-second increment in APTT was associated with 31% higher odd of UAT (OR: 1.31, 95% CI: 1.11–1.53, $p = 0.002$), where each 1-second elevation in PT showed a protective effect (OR: 0.17, 95% CI: 0.07–0.44, $p < 0.001$). For lipid profiles, every 1 mmol/L decrease in HDL was linked to 75% decreased risk for UAT (OR: 0.25, 95% CI: 0.09–0.65, $p = 0.005$). Doppler ultrasound indices revealed significant associations: each 0.1-unit increase in S/D ratio (aOR: 0.85, 95% CI: 0.77–0.95), PI (aOR: 0.61, 95% CI: 0.47–0.79) and RI (aOR: 0.44, 95% CI: 0.27–0.72) was associated with lower risk of UAT. Postpartum pathological measurements showed umbilical cord length (per 1-cm increase: aOR 0.88, 95% CI 0.82–0.94) and diameter (per 1-mm increase: aOR

Table 3 Association Between Antepartum Findings and UAT

Variables	No. of Cases/Total	UAT			
		Age Adjusted	*p* value	Multivariable Adjusted[#]	*p* value
Abnormal fetal movement			0.016		0.016
No	54/118	1 [Reference]		1 [Reference]	
Yes	11/12	13.04 [1.63–104.23]		12.92 [1.60–104.13]	
Abnormal FHR patterns			<0.001		<0.001
No	41/102	1 [Reference]		1 [Reference]	
Yes	24/28	8.93 [2.88–27.64]		11.90 [3.49–40.62]	
PT	–	0.21 [0.08–0.52]	<0.001	0.17 [0.07–0.44]	<0.001
APTT	–	1.30 [1.11–1.53]	0.001	1.31 [1.11–1.55]	0.002
HDL	–	0.24 [0.09–0.63]	0.004	0.25 [0.09–0.65]	0.005
S/D ratio	–	0.86 [0.77–0.95]	0.004	0.85 [0.77–0.95]	0.003
PI	–	0.63 [0.49–0.80]	<0.001	0.61 [0.47–0.79]	<0.001
RI	–	0.46 [0.28–0.74]	0.001	0.44 [0.27–0.72]	0.001
Umbilical cord length	–	0.88 [0.83–0.94]	<0.001	0.88 [0.82–0.94]	<0.001
Umbilical cord diameter	–	0.62 [0.51–0.75]	<0.001	0.60 [0.49–0.74]	<0.001
Hypercoiling			0.009		0.009
No	52/116	1 [Reference]		1 [Reference]	
Yes	13/14	16.00 [2.03–126.33]		15.90 [2.00–126.66]	

Notes: [#] Results were adjusted for age, BMI, gravidity, and modes of conception.
Abbreviations: OR; odds ratio; CI; confidence interval; FHR; fetal heart rate; PT; prothrombin time; APTT; Activated partial thromboplastin time; HDL; high-density lipoprotein; S/D; systolic-diastolic ratio; RI; resistance index; PI; pulsatility index.

Table 4 Maternal and Neonatal Outcomes Between Participants with UAT, iSUA, and Three Umbilical Vessels

Characteristics	UAT (n=65)	iSUA (n=65)	NC (n=65)	*p value*		
				UAT vs NC	iSUA vs NC	UAT vs iSUA
Maternal outcomes						
Gestational age at delivery (weeks)	36.14 (33.29, 37.86)	39.00 (37.93, 39.71)	39.14 (38.07, 40.00)	<0.001	0.235	<0.001
Preterm birth	37 (56.92%)	10 (15.38%)	8 (12.31%)	<0.001	0.612	<0.001
Cesarean delivery	62 (95.38%)	34 (52.31%)	16 (24.62%)	<0.001	0.001	<0.001
Emergency cesarean delivery	40 (61.54%)	18 (27.69%)	12 (18.46%)	<0.001	0.212	<0.001
Neonatal outcomes						
MSAF	14 (21.54%)	10 (15.38%)	9 (13.85%)	0.250	0.804	0.366
Fetal weight (g)	2277.17±705.38	2929.62±624.22	3148.77±595.00	<0.001	0.054	<0.001
<2500 g	40 (61.54%)	16 (24.62%)	7 (10.77%)	<0.001	0.039	<0.001
<1500 g	9 (13.85%)	2 (3.08%)	3 (4.62%)	0.130	1.000	0.059
SGA	21 (32.31%)	8 (12.31%)	4 (6.15%)	<0.001	0.363	0.006
APGAR scores						
<7 at 1 min	8 (12.31%)	2 (3.08%)	0 (0.00%)	0.006	0.496	0.100
<7 at 5 min	2 (3.08%)	0 (0.00%)	0 (0.00%)	0.496	1.000	0.496
NICU admission	30 (46.15%)	6 (9.23%)	3 (4.62%)	<0.001	0.490	<0.001
Neonatal mortality	2 (3.08%)	0 (0.00%)	0 (0.00%)	0.496	1.000	0.496

Notes: Data are expressed as n (%), mean ± SD, or M (Q1, Q3).
Abbreviations: UAT, umbilical artery thrombosis; iSUA, isolated single umbilical artery; NC, normal controls with three umbilical vessels; MSAF, meconium-stained amniotic fluid; SGA, small for gestational age; NICU, neonatal intensive care unit; SD, standard deviation.

0.60, 95% CI 0.49–0.74) were inversely related to UAT risk. Notably, umbilical cord hypercoiling conferred a 15.90-fold higher odd (95% CI: 2.00–126.66, $p = 0.009$).

Comparison of Maternal and Neonatal Outcomes Among Participants with UAT, iSUA, and Three Umbilical Vessels

Maternal outcomes. The UAT group delivered at significantly earlier gestational age (median 36.14 weeks) compared with both iSUA (median 39.00 weeks, $p < 0.001$) and NC groups (median 39.14 weeks, $p < 0.001$). Preterm birth rates were markedly higher in UAT (56.92%) versus iSUA (15.38%, $p<0.001$) and NC (12.31%, $p<0.001$). The cesarean delivery rate was 95.38% in the UAT group, far exceeding 52.31% in the iSUA group ($p < 0.001$) and 24.62% in the NC group ($p < 0.001$), in which 61.54% of UAT cases required emergency cesarean delivery (Table 4).

Neonatal outcomes. Neonates in the UAT group had lower birth weights (2277.17 ± 705.38 g) than those in the iSUA (2929.62 ± 624.22 g, $p < 0.001$) and NC groups (3148.77 ± 595.00 g, $p < 0.001$). The prevalence of SGA substantially higher in UAT (32.31%) compared with iSUA (12.31%, $p=0.006$) and NC (6.15%, $p<0.001$). While 1-minute APGAR scores <7 were more common in UAT (12.31%) versus NC (0.00%, $p=0.006$), 5-minute scores showed no intergroup differences. The NICU admission rate was significantly higher in UAT (46.15%) than in iSUA (9.23%, $p < 0.001$) and NC (4.62%, $p < 0.001$). Two neonatal deaths occurred in the UAT group, despite no statistical differences (Table 4).

Discussion

UAT is rare but can result in serious consequences. Currently, the pathogenesis of UAT is not fully known; it may relate to primary or secondary maternal-fetal thrombosis, vascular mechanical injury and umbilical cord anatomic abnormalities.[2] However, the identification of risk factors for UAT remains challenging due to its rarity and the potential for confusion with iSUA.

Hypercoagulability is one of key elements that are responsible for thrombosis,[14,15] in which PT is primarily used to evaluate the extrinsic pathway of the coagulation cascade. Shortened PT may indicate a hypercoagulable state and increase the thrombotic risk.[16] APTT is commonly used to monitor the patients receiving heparin therapy.[17] Our findings showed shortened PT and prolonged APTT as significant determinants for the occurrence of UAT, indicating that UAT

may be associated impaired coagulation, and prolonged APTT may be associated with frequently used LMWH during pregnancy.

Lipid metabolism disorders have been increasingly recognized as significant contributors to thrombosis.[18] Although hyperlipidemia and low HDL concentrations have been thought as the risk factors for arterial thrombosis, their roles in UAT are less clear. Our study found that HDL levels and PT were both significantly lower in the UAT group than iSUA and NC groups, indicating a hypercoagulable state and lipid metabolism disorder in pregnant women with UAT. This aligns with Virchow's hypothesis, namely hypercoagulability and vascular injury synergize to promote thrombosis.[19] Notably, iSUA showed no coagulation and lipid metabolism disorders, which contributed to distinguishing from UAT and validating thrombophilia as a UAT-specific risk factor.

Ultrasonography is a preferred method for prenatal detection of umbilical cord abnormalities. Regarding the umbilical artery Doppler indices, our findings showed that at delivery, both the UAT and iSUA groups exhibited significantly lower S/D ratio, PI, and RI values compared to the NC group, suggesting that there was an increased need for blood flow between the fetus and the mother when only a single umbilical artery was functional, consistent with previous findings.[20,21] However, compared with the NC group, the decreased proportions of these indices were greater in the UAT group, unveiling the compensatory changes in blood flow velocity of the remaining vessels, placental and fetal hemodynamic adaptations. If umbilical cord thrombosis occurs and the contralateral umbilical vessels are unable to compensate, this may result in elevated S/D ratios, PI, and RI. In severe cases, end-diastolic flow may be absent in the umbilical artery, leading to severe fetal hypoxia and potentially causing a series of adverse outcomes. In our study, two patients with absent diastolic flow in the umbilical arteries underwent emergency cesarean section, and the neonatal outcomes were favorable. However, assessing the risk for the fetus solely based on umbilical artery Doppler flow parameters is unreliable. Two neonates died after birth in the UAT group, without any abnormalities in umbilical artery Doppler ultrasound blood flow but decreased fetal movement and disappearance of baseline variability in FHR. Future research should extend beyond umbilical artery Doppler flow parameters to incorporate a comprehensive evaluation of other fetal indices, including but not limited to the middle cerebral artery PI, ductus venosus waveform, and fetal intrauterine condition.[21] This holistic approach will improve the accuracy of fetal risk prediction and enhance the management of high-risk pregnancies.

Anatomical abnormalities of the umbilical cord are also one of the factors in the formation of UAT. Congenital umbilical cord dysplasia may lead to increased vascular resistance and turbulent blood flow, creating a prothrombotic environment.[22] Our findings highlight several pathological findings that may contribute to the formation of umbilical cord thrombosis. Shorter and narrower umbilical cord, as well as hypercoiling are all potential risk factors that warrant further investigation. In our study, umbilical cord hypercoiling was identified to be a prominent determinant for UAT. It can result in excessive twists and turns of the cord, impede blood flow, thus leading to stasis and subsequent thrombus formation.[23] Clinically, early identification of these risk factors through prenatal ultrasound imaging is crucial for timely intervention. In cases where hypercoiling or other anatomical abnormalities are detected, close monitoring of fetal well-being and umbilical cord blood flow is recommended to prevent adverse outcomes.

In our study, the iSUA group demonstrated a favorable pregnancy outcome, similar to that of the normal umbilical cord group. However, the pregnant women with UAT showed an increased risk of adverse perinatal outcomes. These may reveal that adverse perinatal outcomes are more likely to occur in the pregnant women with UAT, but not the women with iSUA, although they both manifest a single umbilical artery through ultrasound examinations. Overall, UAT poses a greater risk than iSUA, emphasizing the importance of timely detection and intervention in pregnant women with UAT.

When umbilical cord thrombosis is highly suspected based on Doppler ultrasound, most patients choose to terminate the pregnancy by cesarean section.[14] However, this can lead to iatrogenic preterm birth and increased NICU admission rates. When umbilical cord thrombosis is detected, neither precipitate decisions for emergency cesarean section nor blind expectant management should be adopted. In our opinion, the timing of pregnancy termination should be considered based on multiple factors, such as the mother's perception of fetal movements, FHR patterns results, ultrasound reports, and the fetal condition itself. In our study, abnormal fetal movement and FHR patterns were identified as independent risk factors for UAT, highlighting the importance of fetal distress signals as critical clinical markers to potentially reflect hypoxic injury from thrombotic vascular obstruction. Although chronic thrombosis develops slowly, its impacts on the

maternal-fetal interface are adverse.[24] Thus, it is indispensable to fully communicate with the patient and closely monitor the fetal condition when expectant management is chosen. The focus of managing chronic thrombosis lies in how to safely prolong the gestational age. There have been suggestions that LMWH is used to prolong pregnancy in patients with UAT, but this remains controversial.[25,26] At present, the duration of expectant management is still uncertain. Studies with larger samples are needed to assess its effectiveness.

The findings in our study are supported by several key strengths. One of the strengths is the multimodal diagnostic approach employed in our study, which allows for a more comprehensive and accurate diagnosis of umbilical cord abnormalities, thereby enhancing the reliability of our findings. Unlike previous studies solely relied on the ultrasound, our study integrated the data of multiple factors, such as clinical history, maternal blood markers and umbilical artery Doppler ultrasound blood flow. Additionally, our study provides a comparative analysis of outcomes among the pregnant women with UAT, iSUA, and normal cords with three umbilical vessels. This comparison enables us to identify UAT-specific risk more effectively, providing valuable insights into the unique clinical implications of UAT. Importantly, the relatively large sample size of our study enhances the statistical power and generalizability of our findings. Despite these strengths, our study has several limitations. First, the retrospective design may introduce potential biases and limit the causal inferences that can be drawn from the data. Second, while our study includes a range of diagnostic modalities, there is room for improvement in the ultrasound Doppler parameters. In the future, the studies should focus on addressing these limitations and prospectively incorporating a more comprehensive set of ultrasound Doppler indicators, such as the middle cerebral artery peak systolic velocity, middle cerebral artery pulsatility index and the cerebroplacental ratio, to enhance the diagnostic accuracy and understanding of pregnant women with UAT.

Conclusion

This study comprehensively delineates the antepartum findings and perinatal consequences of UAT, demonstrating that abnormal fetal movement and FHR patterns, prolonged APTT and umbilical cord hypercoiling as independent risk factors for UAT. These findings establish a multimodal diagnostic framework integrating clinical, hematological, and sonographic markers, substantially enhancing the potential for early prenatal detection and effectively distinguishing UTA from iSUA. Notably, UAT confers significantly higher risk of preterm birth, SGA, cesarean delivery and NICU admission rates than iSUA and normal cords with three umbilical vessels. This work provides a foundation for improving risk stratification and timely management of this silent obstetric disease.

Ethical Approval

The study was approved by the Institutional Review Board of Women's Hospital, Zhejiang University School of Medicine (No.: IRB-20250114-R) and was conducted in accordance with the Declaration of Helsinki.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Funding

There is no funding to report.

Disclosure

The authors declare no conflict of interest.

References

1. Wu X, Wei C, Chen R, et al. Fetal umbilical artery thrombosis: prenatal diagnosis, treatment and follow-up. *Orphanet J Rare Dis*. 2022;17(1):414. doi:10.1186/s13023-022-02563-8

2. Romani E, Marinelli L, Ponziani I, et al. Umbilical artery thrombosis: a case report of prenatal diagnosis and systematic review of the literature. *Eur J Obstet Gynecol Reprod Biol*. 2024;296:6–12. doi:10.1016/j.ejogrb.2024.02.016
3. Zhan J, Wang D, Luo C, et al. Umbilical vascular thromboembolism: high-risk factors, diagnosis, management, and pregnancy outcomes: a scoping review. *Ther Clin Risk Manag*. 2024;20:597–610. doi:10.2147/TCRM.S478593
4. Hong SJ, Hong LW, He XQ, et al. Ultrasound blood flow characteristics changes in fetal umbilical artery thrombosis: a retrospective analysis. *World J Clin Cases*. 2024;12(2):240–248. doi:10.12998/wjcc.v12.i2.240
5. Zhu Y, Beejadhursing R, Liu Y. 10 cases of umbilical cord thrombosis in the third trimester. *Arch Gynecol Obstet*. 2021;304(1):59–64. doi:10.1007/s00404-020-05910-x
6. Li X, Chen W, Liu T, et al. Umbilical artery thrombosis and maternal positive autoimmune antibodies: two case reports and a literature review. *Front Med Lausanne*. 2023;10:1187492. doi:10.3389/fmed.2023.1187492
7. Hua M, Odibo AO, Macones GA, et al. Single umbilical artery and its associated findings. *Obstet Gynecol*. 2010;115(5):930–934. doi:10.1097/AOG.0b013e3181da50ed
8. Siargkas A, Giouleka S, Tsakiridis I, et al. Prenatal diagnosis of isolated single umbilical artery: incidence, risk factors and impact on pregnancy outcomes. *Medicina*. 2023;59(6):1080. doi:10.3390/medicina59061080
9. Tanaka K, Tanigaki S, Matsushima M, et al. Prenatal diagnosis of umbilical artery thrombosis. *Fetal Diagn Ther*. 2014;35(2):148–150. doi:10.1159/000355601
10. Pan S, Xu A, Lu X, et al. Umbilical artery thrombosis risk factors and perinatal outcomes. *BMC Pregnancy Childbirth*. 2024;24(1):137. doi:10.1186/s12884-024-06335-z
11. Kalluru PKR, Kalluru HR, Allagadda TR, et al. Abnormal umbilical cord coiling and association with pregnancy factors. *J Turk Ger Gynecol Assoc*. 2024;25(1):44–52. doi:10.4274/jtgga.galenos.2023.2023-3-3
12. Ebbing C, Rasmussen S, Kessler J, et al. Association of placental and umbilical cord characteristics with cerebral palsy: national cohort study. *Ultrasound Obstet Gynecol*. 2023;61(2):224–230. doi:10.1002/uog.26047
13. Li TG, Guan CL, Wang J, et al. Comparative study of umbilical cord cross-sectional area in foetuses with isolated single umbilical artery and normal umbilical artery. *J Obstet Gynaecol*. 2022;42(5):935–940. doi:10.1080/01443615.2021.1962818
14. Lutfallah F, Oufkir N, Markou GA, et al. A case of umbilical artery thrombosis in the third trimester of pregnancy. *Am J Case Rep*. 2018;19:72–75. doi:10.12659/AJCR.906859
15. Li H, Qufeng W, Wei W, et al. Umbilical artery thrombosis: two case reports. *Medicine*. 2019; 98:e18170.
16. Dorgalaleh A, Favaloro EJ, Bahraini M, et al. Standardization of prothrombin time/international normalized ratio (PT/INR). *Int J Lab Hematol*. 2021;43(1):21–28. doi:10.1111/ijlh.13349
17. Toulon P, Smahi M, De Pooter N. APTT therapeutic range for monitoring unfractionated heparin therapy. Significant impact of the anti-Xa reagent used for correlation. *J Thromb Haemost*. 2021;19(8):2002–2006. doi:10.1111/jth.15264
18. Spasic I, Ubavic M, Sumarac Z, et al. Influence of lipid metabolism disorders on venous thrombosis risk. *J Med Biochem*. 2021;40(3):245–251. doi:10.5937/jomb0-27106
19. Malone PC, Agutter PS. The aetiology of deep venous thrombosis. *QJM*. 2006;99(9):581–593. doi:10.1093/qjmed/hcl070
20. Baron J, Weintraub AY, Sciaky Y, Mastrolia SA, Speigel E, Hershkovitz R. Umbilical artery blood flows among pregnancies with single umbilical artery: a prospective case-control study. *J Matern Fetal Neonatal Med*. 2015;28(15):1803–1805. doi:10.3109/14767058.2014.968845
21. Tu P, Zhang X, Zhong C, et al. Hemodynamic changes and perinatal outcome associated with umbilical artery thrombosis: a retrospective study. *Orphanet J Rare Dis*. 2024;19(1):100. doi:10.1186/s13023-024-03107-y
22. Devlieger H, Moerman P, Lauweryns J, et al. Thrombosis of the right umbilical artery, presumably related to the shortness of the umbilical cord: an unusual cause of fetal distress. *Eur J Obstet Gynecol Reprod Biol*. 1983;16(2):123–127. doi:10.1016/0028-2243(83)90109-0
23. Sharma R, Radhakrishnan G, Manchanda S, et al. Umbilical coiling index assessment during routine fetal anatomic survey: a screening tool for fetuses at risk. *J Obstet Gynaecol India*. 2018;68(5):369–375. doi:10.1007/s13224-017-1046-8
24. Klaritsch P, Haeusler M, Karpf E, et al. Spontaneous intrauterine umbilical artery thrombosis leading to severe fetal growth restriction. *Placenta*. 2008;29(4):374–377. doi:10.1016/j.placenta.2008.01.004
25. Wang T, Yao Y, Xu T, et al. Application of low molecular weight heparins in umbilical artery thrombosis: a case series and review of the literature. *Medicine*. 2023; 102:e33501.
26. Zhao P, Lu Y, Liu S, et al. Evaluating the efficacy of low-molecular-weight heparin in managing umbilical artery thrombosis during pregnancy: does it offer therapeutic benefits? *Front Med Lausanne*. 2025;12:1540685. doi:10.3389/fmed.2025.1540685