Umbilical Cord Thrombosis: A Rare but Life-threatening Occurrence

Long-xia Tong  
Sichuan University

Ping Xiao  
Sichuan University

Dan Xie  
Sichuan University

Lin Wu (✉ jadeitewl@163.com)  
Sichuan University

Research Article

Keywords: Clinical management, diagnosis, stillbirth, umbilical cord thrombosis

Posted Date: December 17th, 2021

DOI: https://doi.org/10.21203/rs.3.rs-1110644/v1

License: This work is licensed under a Creative Commons Attribution 4.0 International License.
Read Full License
Abstract

**Background:** Thrombosis of umbilical vessels is a rare but life-threatening pregnancy complication. The correct diagnosis and clinical management of umbilical cord thrombosis remain a challenge. This study aimed to evaluate the meaningful clinical manifestations and features of umbilical cord thrombosis and its optimal management options.

**Methods:** This retrospective study analyzed umbilical cord thrombosis cases enrolled from January 1, 2011, to May 31, 2021. Data were collected from medical archives where the diagnoses of all patients were established by histopathology.

**Results:** A total of 66 patients with umbilical cord thrombosis were enrolled, including 20 patients with intrauterine fetal death and 6 with fatal labor induction in the second trimester. The overall incidence of umbilical cord thrombosis was 0.05% (66/123,746), and the incidence increased significantly in the last 2 years, reaching 0.19% in 2021. The chief complaint was decreased fetal movement (25/60) or nonreactive nonstress test (NST) (19/40). In the 20 patients with intrauterine stillbirth, 8 patients had ignored fetal movement and were referred to the hospital because of ultrasound findings of intrauterine stillbirth. Five patients were misdiagnosed with a single umbilical artery on prenatal ultrasound. Twenty patients underwent emergency cesarean section due to decreased fetal movement and unresponsive fetal monitoring; all neonates were alive. The gross examination of the placenta and cord revealed umbilical cord abnormalities in 26 patients (39.4%, 26/66). The pathological examination revealed venous, venous and arterial, and arterial thrombosis in 74.2%, 12.1%, and 13.6% of patients, respectively.

**Conclusions:** The main manifestation of umbilical cord thrombosis was decreased or disappeared fetal movement. The importance of self-counting fetal movement should be emphasized to patients. The abnormalities in the umbilical cord are the main cause of this phenomenon. Focus on counting fetal movements, electronic fetal monitoring, and specific signs during a prenatal ultrasound can help early identification of umbilical cord thrombi. Emergency cesarean section is recommended to reduce the risk of interrupting the umbilical cord blood flow.

1. **Background**

Thrombosis of umbilical cord vessels is a rare occurrence, but it is highly associated with perinatal mortality. The incidence of cord thrombosis is approximately 1/1300 deliveries [1]. The incidence of umbilical cord venous thrombosis is higher, but umbilical cord artery thrombosis is more likely to lead to adverse pregnancy outcomes. However, the correct diagnosis and clinical management remain a challenge. The previous research reports mainly were case reports or small-sample retrospective analyses, and the clinicopathologic features have not been well delineated. Hence, the correct diagnosis and clinical management remain a challenge. In this study, the clinicopathologic data of 66 patients with umbilical cord thrombosis admitted to our hospital were retrospectively analyzed, aiming to evaluate the meaningful clinical manifestations and features, and to evaluate optimal management options.
2. Methods

Data for this study were obtained from placental pathology reports examined by two authors from January 1, 2011, to May 31, 2021, at the West China Second University Hospital, Sichuan University. Written informed consents were obtained from all those patients, and the Institutional Review Board of West China Second University Hospital approved the study. All delivery room staff were trained in fixing umbilical cords and placentas in 10% buffered formalin before submitting them to the pathology laboratory. Medical charts of all patients were available. Neonate weights between 1500 and 2499 g were assigned to the low-birth-weight (LBW) group, and those weighing between 500 and 1499 g to the very low birth weight (VLBW) group [2]. Multiple gestations were excluded from the analysis.

Gross features of the placenta and cord were noted in all cases. The umbilical cord abnormalities assessed were marginal/velamentous insertion, long umbilical cord (70 cm or over), short cord (35 cm or less), excessive twisting (more than 0.3 cm/loop, defined by the examining pathologist), reduced diameter (less than 8.0 mm), and presence of true knots. Placentas and cords underwent standard histopathological techniques consisting of sectioning and examining the cut slices. The sections underwent routine processing, embedding, and staining with hematoxylin and eosin.

3. Results

A retrospective examination of the sections revealed 66 patients with umbilical cord thrombosis. The overall incidence of umbilical cord thrombosis was 0.05%, and the incidence increased significantly in the last 2 years, reaching 0.19% in 2021 (Table 1). Gestational age ranged between 22 and 41+1 weeks (mean 35+1 weeks) and a mean maternal age of 30.3 years (range 22–41 years) at parturition (7 patients were over 35 years of age). Their associated clinical features are detailed in Table 2.
Table 1
Incidence of umbilical cord thrombosis during 2011 and 2021

| Year          | Number of umbilical cord thrombosis | Number of deliveries | Incidence of umbilical cord thrombosis (%) |
|---------------|-------------------------------------|----------------------|---------------------------------------------|
| 2011          | 2                                   | 7,600                | 0.03                                        |
| 2012          | 1                                   | 9,644                | 0.01                                        |
| 2013          | 1                                   | 9,191                | 0.01                                        |
| 2014          | 2                                   | 11,264               | 0.02                                        |
| 2015          | 3                                   | 11,492               | 0.03                                        |
| 2016          | 3                                   | 12,411               | 0.02                                        |
| 2017          | 3                                   | 10,594               | 0.03                                        |
| 2018          | 7                                   | 12,363               | 0.06                                        |
| 2019          | 9                                   | 16,059               | 0.06                                        |
| 2020          | 20                                  | 15,913               | 0.13                                        |
| 2021 (5 months) | 14                              | 7,215                | 0.19                                        |
| Total         | 66                                  | 123,746              | 0.05                                        |
### Table 2
Clinical characteristics of cases with umbilical cord thrombosis (*n* = 66)

| Characteristics                                      | N(%) or mean | Range       |
|-----------------------------------------------------|--------------|-------------|
| Maternal age (year)                                 | 30.3         | 22–41       |
| Advanced maternal age                               | 7 (10.6)     |             |
| BMI (kg/m²)                                         | 21.7         | 16.9–33.1   |
| Obesity                                             | 2 (3.0)      |             |
| Gest. age (week)                                    | 35⁺¹         | 22–41⁺¹     |
| <28 (week)                                          | 8 (12.1)     |             |
| <37 (week)                                          | 22 (33.3)    |             |
| ≥37 (week)                                          | 36 (54.5)    |             |
| Gravidity                                           |              | 1–5         |
| 1                                                    | 34 (51.5)    |             |
| 2                                                    | 20 (30.3)    |             |
| >2                                                   | 12 (18.2)    |             |
| Parity                                              |              | 0–2         |
| 0                                                    | 49 (74.2)    |             |
| 1                                                    | 14 (21.2)    |             |
| 2                                                    | 3 (4.5)      |             |
| Maternal comorbidities                              |              |             |
| Gestational diabetes mellitus                       | 11 (16.7)    |             |
| Hypertension                                        | 2 (3.0)      |             |
| Hypothyroidism                                      | 6 (9.1)      |             |
| Stillbirth history                                   | 1 (1.5)      |             |
| Ultrasound shows a single umbilical artery           | 5            |             |
| Neonate                                             |              |             |
| Fetal death                                         | 20           |             |
| 1-min Apgar score of ≤3                              | 3            |             |
| 1-min Apgar score of ≤7                              | 6            |             |
| Characteristics                              | N(%) or mean | Range       |
|---------------------------------------------|--------------|-------------|
| 1-min Apgar score of $\geq 8$               | 31           |             |
| Birth weight (g) ($n = 40$)                 | 2891         | 1280–4100   |
| Very low birth weight                       | 3 (7.5)      |             |
| Low birth weight                            | 8 (20)       |             |
| Fetal death weight (g) ($n = 26$)           | 1692.3       | 173–3220    |
| Umbilical cord abnormalities                | 26 (39.4)    |             |
| Umbilical cord thrombosis ($n = 66$)        | 49           |             |
| Venous thrombosis                           | 8            |             |
| Venous and arterial thrombosis              | 9            |             |

Clinical investigations found that 11 (11/66) pregnant women suffered from gestational diabetes mellitus, 6 (9.1%, 6/66) had hypothyroidism, 2 (3.0%, 2/66) had hypertension, 2 (3.0%, 2/66) had obesity (kg/m$^2 \geq 30$), and 1 (1.5%, 1/66) had a history of stillbirth. Among the 66 patients, 20 had an intrauterine stillbirth and 6 had fatal labor induction in the second trimester for the lifeless preterm premature rupture of membrane or abnormal fetal development. The chief complaint was decreased fetal movement accompanied by nonreactive nonstress test (NST), 25 (25/60) patients showed decreased or disappeared fetal movement, and 20 (20/40) patients showed unsatisfactory electronic fetal monitoring (EFM). In the 20 cases of intrauterine stillbirth, 12 patients were admitted to the hospital because the fetal movement had consciously reduced or disappeared, and intrauterine stillbirth was suggested by ultrasound. The other 8 patients ignored fetal movement and were admitted because intrauterine stillbirth was suggested by a routine ultrasound examination. Five patients were misdiagnosed with a single umbilical artery on prenatal ultrasound as one of the umbilical arteries was embolized, showing blocked arterial blood flow; however, one umbilical vein and two umbilical arteries were confirmed after the operation (Table 3) <Split the sentence?? long>. Except for intrauterine stillbirth and induced labor, 20 of the remaining 40 patients underwent emergency cesarean section due to decreased fetal movement and unresponsive fetal monitoring, with 2 neonates having a 1-min Apgar score of $\leq 3$ and 4 having a 1-min Apgar score of $\leq 7$. The other 20 patients with normal NST and fetal movement had a normal vaginal delivery or elective cesarean section, with 1 neonate having a 1-min Apgar score of $\leq 3$ and 2 having a 1-min Apgar score of $\leq 7$. The mean birth weight was 2891 g, which included three VLBW and eight LBW neonates.
Table 3

Patients were misdiagnosed with a single umbilical artery on prenatal ultrasound

| No. | Age (year) | Gest. age (week) | Ultrasound findings                                      | Manage                                             | Neonate       | Cord                      |
|-----|------------|------------------|---------------------------------------------------------|---------------------------------------------------|---------------|---------------------------|
| 1   | 27         | 34+2             | Early conditions unknown; a single umbilical artery at 34 weeks | Delivery for premature rupture of membrane         | 1470, boy     | Reduced diameter, twist   |
| 2   | 31         | 38               | Two umbilical arteries at 25 + 5 weeks; a single umbilical artery at 37 + 1 weeks | Emergency cesarean for not satisfied EFM and fetal movement | 3290, girl   | Excessive short           |
| 3   | 27         | 37+6             | A single umbilical artery at 24 + 5 weeks               | Emergency cesarean for not satisfied EFM and fetal movement | 2590, girl   | Twist                     |
| 4   | 22         | 36+6             | Early conditions unknown; a single umbilical artery at 36 + 6 weeks | Emergency cesarean for not satisfied EFM and fetal movement | 2260, girl   | Reduced diameter, twist   |
| 5   | 28         | 27+3             | Two umbilical arteries at 24 + 5 weeks; a single umbilical artery at 26 + 6 weeks | Vaginally delivered a stillborn                     | 858, girl, fetal death | Reduced diameter  |

The gross examination of the placenta and cord revealed that 26 patients (39.4%, 26/66) had umbilical cord abnormalities, including marginal/velamentous insertion, long umbilical cord, short cord, excessive twisting, reduced diameter, and presence of true knots. The pathological examination showed that 49 patients (74.2%, 49/66) had venous thrombosis, 9 (13.6%, 9/66) had arterial thrombosis, and 8 (12.1%, 8/66) had venous and arterial thromboses. Except for 6 patients with fatal labor induction in the second trimester, among the 43 patients with venous thrombosis, 11 had stillbirth and 1 neonate had a 1-min Apgar score of \( \leq 3 \) and 3 neonates had a 1-min Apgar score of \( \leq 7 \); among the 9 patients with arterial thrombosis, 2 had stillbirth and 1 neonate had a 1-min Apgar score of \( \leq 3 \) and 3 neonates had a 1-min Apgar score of \( \leq 7 \); and among the 8 patients with venous and arterial thrombosis, 7 had stillbirth and 1 neonate had a 1-min Apgar score of \( \leq 3 \) (Table 4).
Table 4
Fetal outcomes in 60 patients with umbilical cord thrombosis

|                                | Fetal death | 1-min Apgar score of ≤3, \(N(\%)\) | 1-min Apgar score of ≤7, \(N(\%)\) | 1-min Apgar score of ≥8, \(N(\%)\) |
|--------------------------------|-------------|--------------------------------------|--------------------------------------|--------------------------------------|
| Venous thrombosis (\(n = 43\)) | 11 (25.6)   | 1 (2.37.0)                           | 3 (7.0)                             | 29 (67.4)                           |
| Venous and arterial thrombosis (\(n = 8\)) | 7 (87.5)   | 1 (12.5)                             | –                                   | –                                   |
| Arterial thrombosis (\(n = 9\)) | 2 (22.2)    | 1 (11.1)                             | 3 (33.3)                           | 3 (33.3)                           |

4. Discussion

Thrombosis of umbilical vessels is a rare occurrence, but it is insidiously associated with perinatal morbidity and mortality. According to Heifetz [1], umbilical vascular thrombosis occurs in around 0.08% of deliveries, 0.1% of postpartum autopsies, and 0.4% of high-risk pregnancies. Avagliano [3] reported that up to 10% of 317 spontaneous intrauterine fetal demise cases were caused by thrombosis of umbilical cord vessels. Our hospital is the largest specialized maternity and children's hospital and the treatment center for critical and severe patients in southwest China and has accumulated a lot of case data of patients with umbilical cord thrombosis. The overall incidence of umbilical cord thrombosis was 0.05% (66/123,746), but the incidence increased significantly in the last 2 years, reaching 0.19% in 2021, which entails that such a significant number should be taken seriously.

The pathogenesis of umbilical vascular thrombosis has not yet been fully comprehended. This may be caused by hypercoagulable mechanical injury or abnormal anatomy of the umbilical cord. A pregnant woman's blood is hypercoagulable, and the risk of thrombosis increases from four to five times in pregnancy compared with the nonpregnant cohort [4]. Previous studies showed that when maternal blood glucose levels were unstable, the imbalance in the expression of endothelial vasodilatation factors and shrinkage factors were induced, causing disorder of blood coagulation and the eventual occurrence of blood clots. Zhu [5] demonstrated that 5 out of 10 patients with umbilical cord thrombosis had elevated blood sugar levels, 2 had hypertension, and 2 had hypothyroidism. In our series, 11 out of 66 patients had elevated blood sugar levels, 2 had hypertension, and 6 had hypothyroidism. Elevated blood glucose may lead to the formation of thrombosis; therefore, attention should be prioritized on predisposition and precaution.

Previous studies [6, 7] showed that cord anomalies might induce flow stasis and thrombosis of the umbilical cord, such as marginal/velamentous insertion, long umbilical cord, short cord, excessive twisting, reduced diameter, and presence of true knots. Sato [8] reported that 82% of patients with umbilical arterial thrombosis were associated with an abnormal umbilical cord. In this study, the gross examination of the placenta and cord revealed that 26 patients (39.4%, 26/66) had umbilical cord
abnormalities. Matsumoto [9] reported that umbilical vein varix was associated with thrombosis in the varix.

The patient does not have typical clinical signs and symptoms; therefore, it is difficult to detect prenatally. The main manifestation was decreased or disappeared fetal movement. In this study, 20 patients had severe adverse pregnancy outcomes of intrauterine stillbirth due to neglected fetal movement, or fetal movement significantly reduced or even disappeared before the patient came to the hospital. The umbilical cord comprises one umbilical vein and two umbilical arteries protected by Wharton jelly. In recent decades, prenatal care has significantly improved, and the evolution of ultrasound imaging has been key in this advancement. When one of the umbilical arteries is embolized, arterial blood flow is blocked; a single umbilical artery of the cord is easily misdiagnosed by an ultrasound examination. Obstetricians should be vigilant if ultrasound imaging shows suspected umbilical vascular thrombosis or shows one umbilical artery when previously two were seen. In this study, five patients were misdiagnosed with a single umbilical artery on prenatal ultrasound. The importance of self-counting fetal movement should be emphasized to patients, and the prenatal diagnosis of umbilical artery thrombosis remains a clinical challenge.

Fetal death has been found to occur rapidly after an abnormal fetal NST result. Many studies believed that a cesarean section should be performed without delay [10, 11, 12]. In this study, 20 patients underwent emergency cesarean section due to decreased fetal movement and unresponsive fetal monitoring; all neonates were alive, with 2 neonates having a 1-min Apgar score of ≤3 and 6 neonates having a 1-min Apgar score of ≤7. The fetus should be closely monitored and interventions implemented as early as possible to improve the prenatal detection rate of umbilical vessel thrombosis and avoid adverse pregnancy outcomes. The fetus should be closely monitored and interventions implemented as early as possible to avoid adverse pregnancy outcomes. However, sudden fetal death could still occur without any foretelling signal. For the patients with umbilical artery thrombosis suspected by ultrasound, determining how often the examination should be performed to find the best term for the termination of pregnancy before the onset of fetal distress or death is controversial. Especially in the case of early preterm, ultrasonographic scans are required weekly from diagnosis to 28 weeks, fetal cardiac monitoring along with the scans are required twice a week thereafter, and elective delivery by cesarean section is required following antenatal corticosteroid therapy for fetal lung maturation.

Umbilical vein thrombosis is more common than umbilical artery thrombosis, but umbilical artery thrombosis is associated with increased fetal and perinatal morbidity and mortality. Heifetz [1] reported that venous, venous and arterial, and arterial thromboses occurred in 70%, 20%, and 10% of patients, respectively. This study showed that venous, venous and arterial, and arterial thromboses occurred in 74.2%, 12.1%, and 13.6% of patients, respectively, and the probability of intrauterine fetal death was 25.6%, 87.5%, and 22.2%, respectively. This study showed that umbilical venous and arterial thromboses were more likely to lead to adverse pregnancy outcomes.
Nevertheless, this study had several limitations. First, this is a retrospective analysis; a large sample and comparative studies should be analyzed to get a more comprehensive understanding of umbilical vessel thrombi. Second, the long-term follow-up of neonates is inadequate. Thus, we could not evaluate survival rates and long-term implications of babies born with umbilical cord thrombosis. However, the data in this study permitted a general assessment of the clinical characteristics and perinatal outcomes of umbilical cord thrombosis.

5. Conclusions

Umbilical cord thrombosis is rare, but can lead to severe adverse pregnancy outcomes. Its incidence has increased significantly in recent years; therefore, obstetricians should pay more attention to it. Abnormal umbilical cord, hypercoagulability, and abnormal blood glucose are high-risk factors for umbilical cord thrombosis. The main clinical manifestations of the patients were decreased fetal movement and abnormal fetal monitoring. A few patients showed two umbilical arteries in the previous ultrasound, but the second ultrasound suggested a single umbilical artery; such patients should be highly alerted for the possibility of an umbilical cord thrombosis. In the case of neonatal survival, active termination of pregnancy is an effective therapeutic measure to reduce perinatal death. The main manifestation is umbilical vein thrombosis, but venous and arterial thromboses are more likely to lead to adverse fetal pregnancy outcomes.

Abbreviations

LBW: low-birth-weight; VLBW: very low birth weight; NST: nonreactive nonstress test; EFM: electronic fetal monitoring

Declarations

Acknowledgments:
Authors want to thank all the pregnant women for their involvement to this study.

Authors’ contributions:
Long-xia Tong: Data curation, formal analysis, and writing of original draft; Ping Xiao: Data curation; Dan Xie and Lin Wu: reviewing, editing, and supervision. Dan Xie and Lin Wu contributed equally to this study.

Funding
Not applicable.

Availability of data and materials
The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

The use of patients’ data was approved by the Institutional Ethics Committee of the West China Second Hospital, and all patients provided written informed consents. All methods were performed in accordance with the relevant guidelines and regulations.

Consent for publication

Consent to publish clinical details of the mothers and babies included in the current study was obtained from the mothers.

Competing interests

The authors declare that they have no competing interests

References

1. Heifetz SA, Thrombosis of the umbilical cord: analysis of 52 cases and literature review. Pediatr Pathol. 1988; 8(1): 37–54.
2. Starnberg, J; Norman, M; Westrup, B; Berglund, SK. Lower cognitive test scores at age 7 in children born with marginally low birth weight. Pediatr Res. 2018 06; 83(6):
3. Avagliano, L; Marconi, AM; Candiani, M; Bulfamante, G. Thrombosis of the umbilical vessels revisited. An observational study of 317 consecutive autopsies at a single institution. Hum Pathol. 2010 Jul; 41(7): 971–9.
4. Konkle BA. Diagnosis and management of thrombosis in pregnancy. Birth Defects Res C Embryo Today. 2015 Sep; 105(3): 185–9.
5. Zhu, Y; Beejadhursing, R; Liu, Y. 10 cases of umbilical cord thrombosis in the third trimester. Arch Gynecol Obstet. 2021 07; 304(1): 59–64.
6. Chan, JS; Baergen, RN. Gross umbilical cord complications are associated with placental lesions of circulatory stasis and fetal hypoxia. Pediatr Dev Pathol. 2012V15N6: 487–94.
7. Peng, HQ; Levitin-Smith, M; Rochelson, B; Kahn, E. Umbilical cord stricture and overcoiling are common causes of fetal demise. Pediatr Dev Pathol. 2006; 9(1): 14–9.
8. Sato, Y; Benirschke, K. Umbilical arterial thrombosis with vascular wall necrosis: clinicopathologic findings of 11 cases. Placenta. 2006; 27(6-7): 715–8.
9. Matsumoto, Y; Yanai, A; Kamei, S; Fujita, K. A Case Report of Umbilical Vein Varix with Thrombosis: Prenatal Ultrasonographic Diagnosis and Management. Case Rep Obstet Gynecol. 2019; 2019: 7154560.
10. Lutfallah, F; Oufkir, N; Markou, GA; Poncelet, C. A Case of Umbilical Artery Thrombosis in the Third Trimester of Pregnancy. Am J Case Rep. 2018V19N: 72–75.

11. Dussaux, C; Picone, O; Chambon, G; Cordier, AG. Umbilical vein thrombosis: to deliver or not to deliver at the time of diagnosis? Clin Case Rep. 2014 Dec; 2(6): 271–3.

12. Kanenishi, K; Nitta, E; Mashima, M; Hata, T. HDlive imaging of intra-amniotic umbilical vein varix with thrombosis. Placenta. 2013V34N11: 1110–2.