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REVIEW

Placental and Umbilical Cord Anomalies Detected by Ultrasound as Clinical Risk Factors of Adverse Perinatal Outcome: Case Series Review of Selected Conditions. Part 2: Umbilical Cord Abnormalities

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ABSTRACT

The aim of this second extended review is to describe the pathogenetic mechanisms underlying umbilical cord (UC) anomalies and their relationship with adverse perinatal outcomes. Review of the literature with case presentations to illustrate the relationship between UC pathologies and adverse perinatal outcomes are also reported. Prenatal ultrasound findings and perinatal care in these cases are presented. Our review confirms the ethiopathogenetic role and involvement of UC pathology in a wide variety of obstetric diseases that may jeopardize fetal well-being. Some of these specific pathologies are strongly associated with a high risk of poor perinatal outcomes.

1 | Introduction

The umbilical cord (UC) allows fetal development, adaptation, growth, and overall survival during pregnancy. The UC is of fetal origin and originates from the lower third of the early embryo, in a zone indicated as "the primitive ridge", at the proximal part of the "allantoic core domain". As long as the embryonic disk is fusiform, between the 4th and 6th weeks postconception, the UC develops and fuses with the placental vessels. The primitive UC presents a middle straight section and three or four coils at the fetal and placental ends, respectively.

The proximal fetal end expands in a pouch by the 10th week, holding the intestines up to the 12th week. During this period, the UC is short with a large diameter preventing rotation. The UC progressively grows with vessel elongation within the surrounding Wharton's jelly.

A normal UC is composed of one vein and two arteries that entwine the vein. At term, the average length is 55 cm, presenting three twists and eight coils. Coils are stable, but twists can be unwound. Genetic imprinting determines UC length, diameter, and tensile strength. The UC provides a unique connection between the fetus and the placenta, and even minor anomalies may result in intrauterine fetal demise (IUFD) [1].

UC abnormalities include anomalous insertion, cysts, tomors, hematomas, vasa previa, hypo- or hyper-coiling, knots, entanglements, vascular impairments, and vessel number alterations [2].

The Stillbirth Collaborative Research Network examined the cause of death of 512 stillbirths who underwent a full autopsy. In that casuistry, UC anomalies accounted for 10% of the cases, being more frequent in Caucasians (13%) vessel number to Black women (4%) [3]. In addition, an extensive review evidenced that true knots and multiple nuchal cord entanglements are the main risks for stillbirth [4].

UC anomalies may be detected by adequate ultrasound assessment and fetal heart rate evaluation, as even sporadic cardiac decelerations may be suspicious for a compromised UC, and systematic monitoring of the pregnancy should be planned [5, 6].

Herein, we thoroughly present selected case presentations of UC pathologies diagnosed by prenatal two-dimensional (2D) or three-dimensional (3D) ultrasound with pathology confirmation when available. Etiopathogenesis, clinical outcome, and anatomical and histological features are also discussed. Relevant cases from obstetric tertiary care centers are reported including ultrasound findings and perinatal outcomes to illustrate the review. Clinical data have been retrieved from mothers undergoing routine or targeted obstetric ultrasound at each of our tertiary centers following informed consent. Electronic searches of PubMed/Medline and SCOPUS for topic-related papers were carried out from inception to September 2023. In this Part 2, we will illustrate the following UC anomalies: cysts and pseudocysts, furcate insertion, marginal cord insertion (MCI), velamentous cord insertion with associated vasa previa, cord entanglement in singleton and twin pregnancies, supernumerary vessels, true cord knot with umbilical artery thrombosis, UC tumors (teratoma and angiomyxoma), single umbilical artery (SUA), aneurysmatic dilatation and varices, UC hemorrhagic cyst, and spontaneous rupture of the UC due to agenesis of the Wharton's jelly.

2 | Cord Cyst and Pseudocyst

UC cysts are incidental findings that can occur in up to 3% of pregnancies in the first trimester [7]. UC cysts can be true cysts or pseudocysts. True UC cysts are formed by remnants of embryonic developmental structures (allantois, yolk sac, or omphalomesenteric duct), amniotic inclusion cysts, and cord tumors such as in predominantly cystic UC teratomas. Pseudocysts are driven by focal edema or degeneration of Wharton's jelly, and by abnormal changes in the extracellular matrix components, and can be seen in association with hemangioma/angiomyxoma or hematoma [8, 9]. However, these terms have been used interchangeably in the prenatal literature as the definitive diagnosis requires histologic confirmation. First-trimester UC cysts are usually associated with a good prognosis and disappear by the late first trimester or during the second trimester of pregnancy in most cases [8].

A schematic representation of the anatomical level of the different UC pathologies is shown in Figure 1.

Hannaford et al. conducted a retrospective cohort study with 25 fetuses with UC cysts compared with 85 controls. All cysts disappeared during the ultrasound follow-up performed between

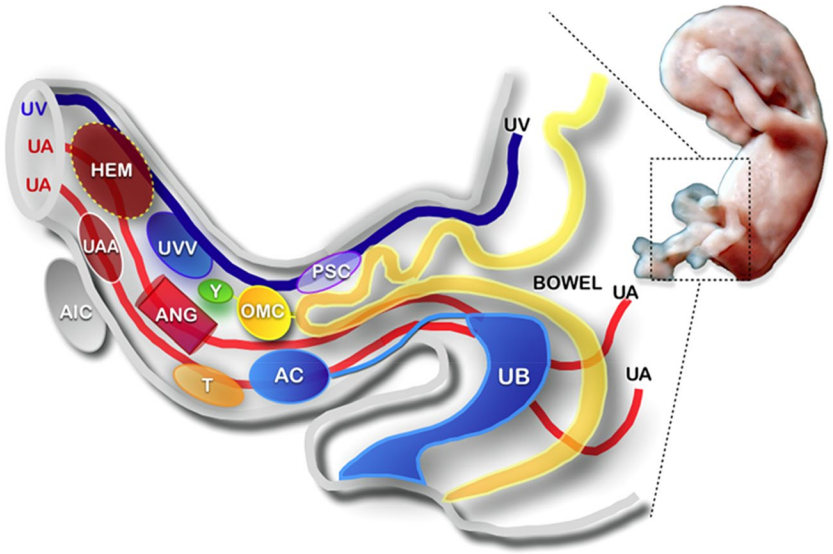

FIGURE 1 | Schematic representation of the umbilical cord displays normal constituents, remnants of embryonic developmental structures (allantoic cysts, yolk sac cysts, and omphalomesenteric duct cysts), and possible cystic masses of embryo and fetus at less than 12 weeks of menstrual age. Abbreviations: AC, allantoic cyst; AIC, amniotic inclusion cyst; Bowel, intestinal loops temporarily herniated into proximal cord; HEM, hematoma; OMC, omphalomesenteric duct cyst; PSC, pseudocyst (mucoid degeneration or edema of Wharton's jelly); U, umbilical vein; UA, umbilical artery; UAA, umbilical artery aneurysm; UB, urinary bladder; UVV, umbilical vein varix; Y, yolk sac cyst; Tumors: ANG, angiomyxoma/hemangioma; T, teratoma.

9 and 20 weeks. Five cases of fetal abnormalities were found in the UC cyst group (11.1%) and eight in the control group (9.4%). They concluded that UC cysts are not associated with adverse perinatal outcomes [10].

In the second and third trimester of pregnancy, however, UC cysts are usually associated with several congenital anomalies as well as chromosomal disorders such as micrognathia, congenital heart diseases, and trisomies 13 and 18 [11–13]. Chen et al. assessed three cases of UC cysts and omphalocele. Two cases with omphalocele were associated with trisomy 18. One fetus had bilateral choroid plexus cysts and fetal growth restriction (FGR), the other one had a cleft lip and palate, SUA, and FGR. Gross and microscopic pathology of the UC confirmed these cysts corresponded to pseudocysts [14].

Sepulveda et al. assessed the prenatal diagnosis, karyotype, and perinatal outcomes of 13 fetuses with UC pseudocyst. The mean prenatal diagnosis was 27 weeks. UC pseudocyst was single in eight, double in one, and multiple in four cases. Ten fetuses had prenatal karyotype which confirmed trisomy 18 in five (50%). All fetuses with trisomy and two with normal karyotype died *in utero* or in the neonatal period [15] (Figures 2–12).

3 | Furcate Insertion of the Cord

Furcate insertion refers to the branching of the umbilical vessels prior to entering the chorionic disc. The vessels are free-floating into the amniotic fluid and lack the protective cover of Wharton's jelly, being at risk of damage by compression, stretching, rupture, and subsequent thrombosis leading to fetal distress, FGR, and/or IUFD [16–18]. The last event may happen in 1.02% of cases, although fetal outcome has been reported tendentially good [18]. Furcate branching is usually located at 1–4 cm from the chorionic disc, but it can be detected up to 18 cm [18] and in association with a bilobed placenta [19]. The etiology of this anomaly is unknown, but it has been suggested to occur as a result of abnormal cord development or focal degeneration of Wharton's jelly [16] (Figures 13–15).

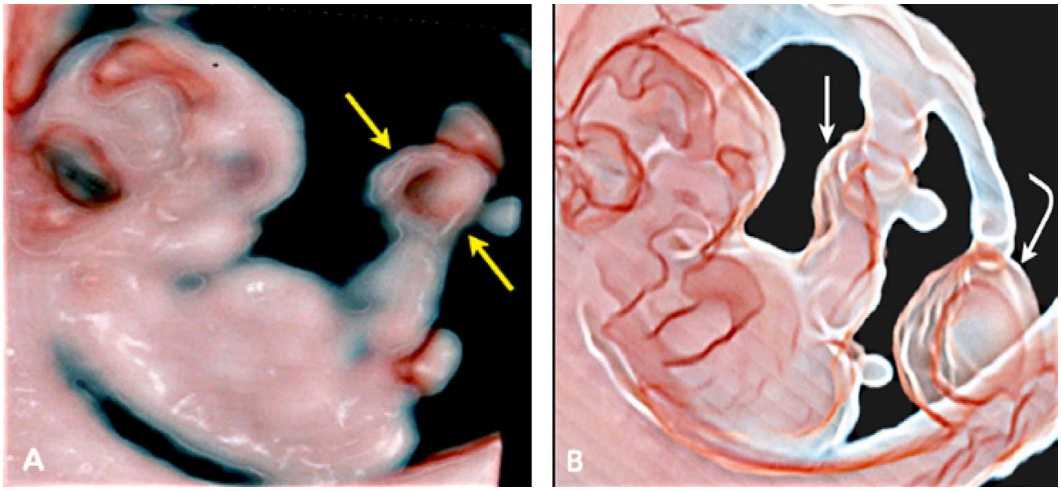

FIGURE 2 | Pregnancy at 8 weeks' gestation. The embryo is displayed by transvaginal three-dimensional scan (3D HDlive) and in a transparency Silhouette mode. The umbilical cord cyst is highlighted by yellow arrows (A). The umbilical cord cyst and the yolk sac are indicated by straight and curved white arrows, respectively (B).

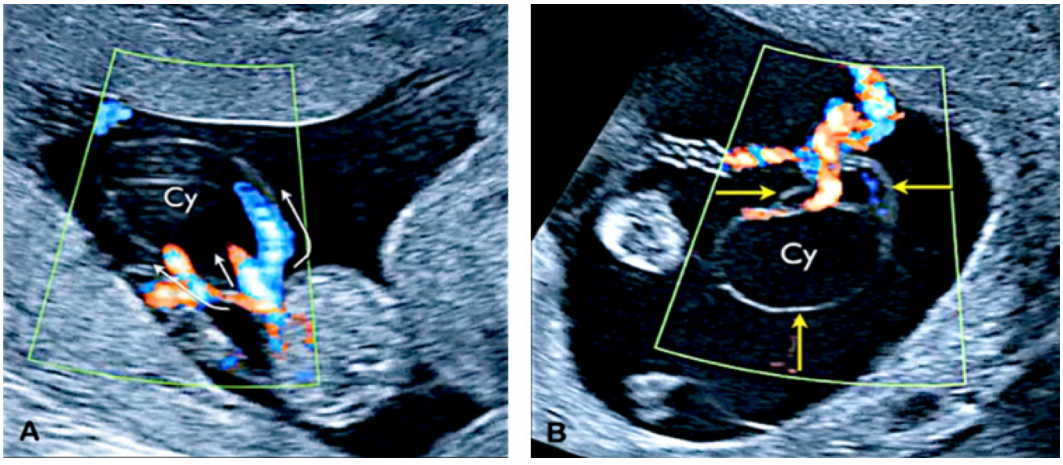

FIGURE 3 | Pregnancy at 13 weeks' gestation. 2D color Doppler ultrasound detects the presence of multiple cord cysts. (A) Axial scan of the fetal abdomen. The umbilical cord vessels are separated (indicated by arrows) by a large cyst (Cy) located near the insertion of the cord on the fetal abdomen. (B) Yellow arrows show the presence of other contiguous cysts (Cy).

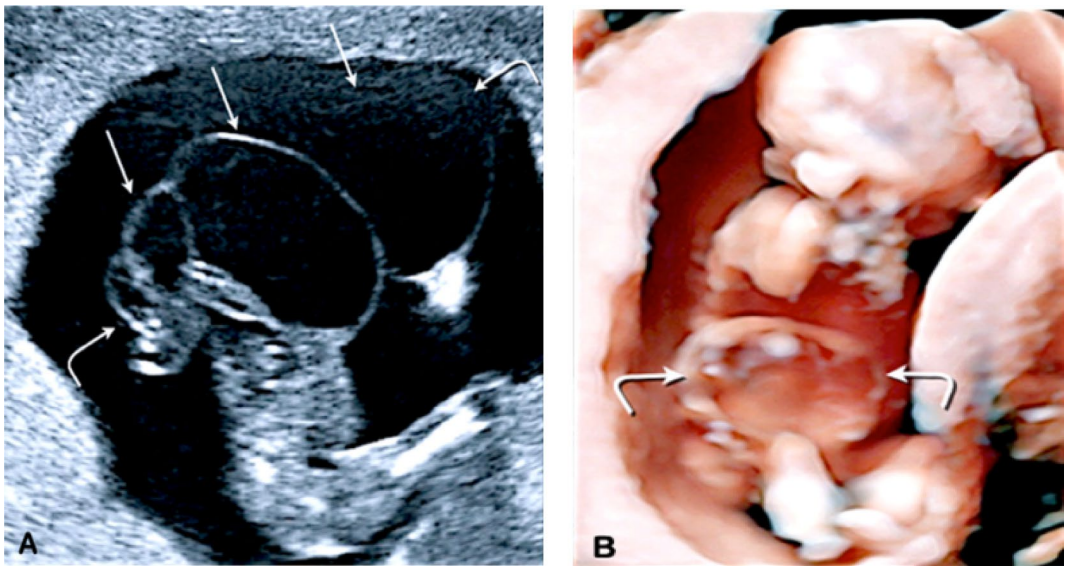

FIGURE 4 | Pregnancy at 13 weeks' gestation. (A) 2D ultrasound displays multiple cysts in the cord (arrows). (B) 3D ultrasound with HDlive highlights the cyst (arrows) close to the insertion of the cord.

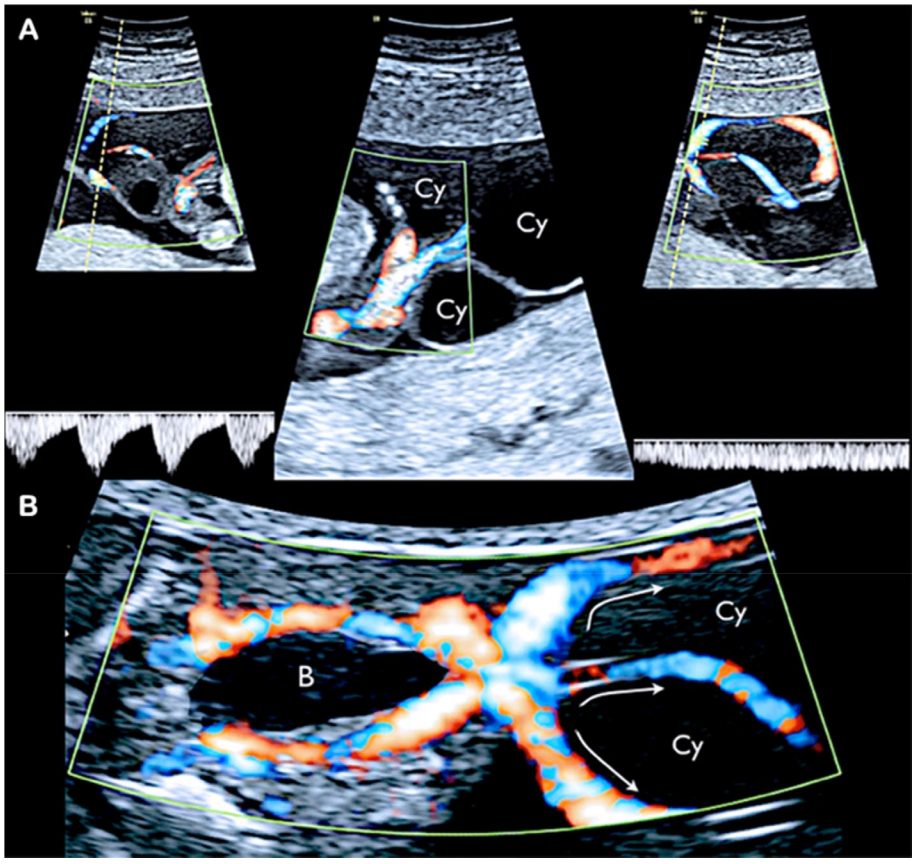

FIGURE 5 | Pregnancy at 15 weeks' gestation. (A) 2D color and pulsed Doppler ultrasound detect normal flow patterns in the vessels of the cord. (B) 2D color Doppler ultrasound displays the umbilical arteries that surround the bladder (B) and the vessels of the cord strongly displaced (curved arrows) by the most proximal cyst (Cy). Abbreviation: Cy, cysts.

4 | Marginal Cord Insertion

MCI is characterized by a normal UC morphology with preserved coverage of umbilical vessels but with a cord insertion into the periphery of the placental disk, typically within and/or less than 2 cm from the margin [20]. MCI is often not considered more than a normal variant, because it does not carry an increased risk of FGR, preterm labor, or peripartum bleeding, and is not associated with vasa previa. A study by Liu et al. assessed the effect of MCI on birth weight and pregnancy duration in singleton pregnancies and concluded that it is not associated with an increased risk of growth impairment or preterm delivery [21]. However,

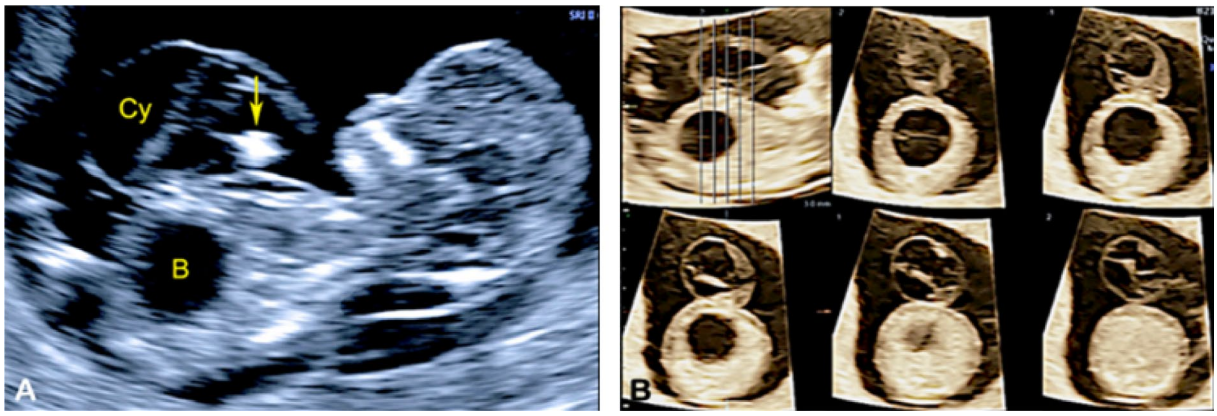

FIGURE 6 | Pregnancy at 13 weeks' gestation. (A) At 2D ultrasound, the fetus shows increased nuchal translucency, megacystis (enlarged bladder denoted by B), umbilical cord cyst (Cy), and hyperechoic area (arrow) due to herniation of the small bowel. (B) 3D ultrasound with tomographic mode and activation of the volume contrast imaging mode allows the visualization of the fetus with serial parallel planes. It is possible to demonstrate the adjacent structures and the extent of the lesion.

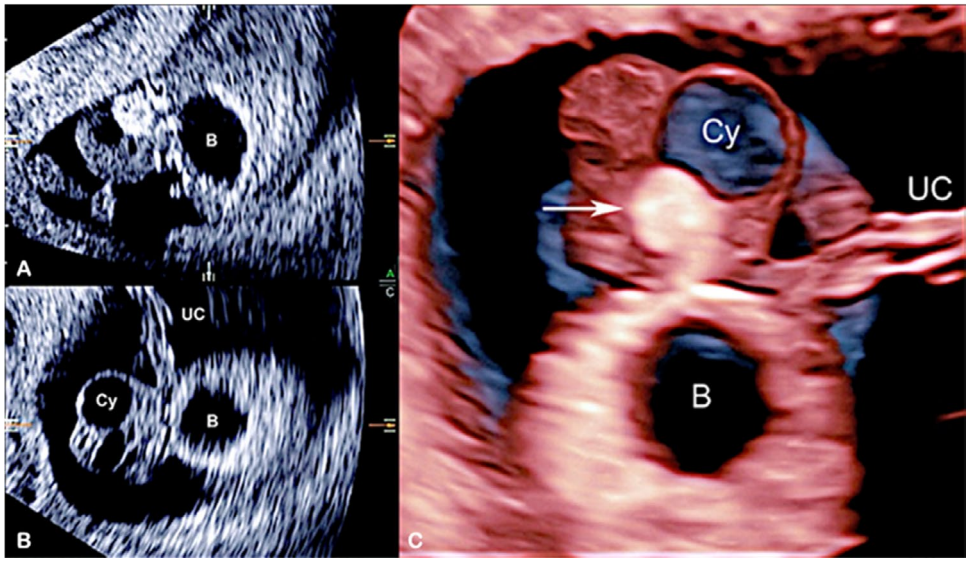

FIGURE 7 | (A-C). Pregnacy at 13 weeks' gestation. 3D ultrasound with a multiplanar display shows megacystic (enlarged bladder denoted by B), umbilical cord cyst (Cy) and bowel herniation. (C) Volume contrast imaging is activated with the result of fewer artifacts and an increased resolution contrast. Bowel herniation (indicated by arrow), megacystis (B) and umbilical cord cyst (Cy) are shown. Abbreviation: UC, umbilical cord. [Correction added on 28 March 2025, after first online publication: Figure 7 has been revised in this version].

MCI less than 0.5 cm from the placental edge may progress to velamentous cord insertion later on in pregnancy [22, 23].

The prevalence of MCI is 7%–9% in singleton pregnancies and 24%–33% in twins [20]. While MCI does not seem related to FGR in singleton pregnancies, it has a higher prevalence in multiple gestations and may lead to unequal sharing of placental tissue that results in growth discordance [20]. Ultrasound data support that with the use of color Doppler ultrasound, placental cord insertion can be visualized in all cases across all gestational ages. Despite the traditional time for visualization of the placental cord insertion has been 16–20 weeks, currently UC insertion can be seen as early as 11–14 weeks with a 100% visualization rate [24, 25] (Figures 16–18).

Recent studies did not show an increased risk for adverse pregnancy outcome in the setting of MCI [26]. No statistically significant correlation has been shown between perinatal outcomes and the measurements of placental cord insertion to placental margin by ultrasound. Notwithstanding, a follow-up in case of MCI involving a low-lying placenta is mandatory [27].

The management of MCI is surrounded by controversy due to possible connection to perinatal complications. A meta-analysis was carried out to study the association with different perinatal outcomes in order to provide reliable and accurate incidences, which allow us to assess the overall risk for pregnancy. The overall prevalence of MCI was 6.15%. Prenatal diagnosis was present in seven studies and postnatal diagnosis in eight studies. When considering pregnancies with prenatal diagnosis of MCI, the risk persisted regarding small for gestational age (SGA) (RR, 1.34; 95% CI, 1.21–1.48), pre-eclampsia (PE) (RR, 1.42; 95% CI, 1.01–1.99), stillbirth (RR,

2.99; 95% CI, 1.03–8.70), preterm delivery (PTD) (RR, 1.41; 95% CI, 1.19–1.68), lower mean gestational age at birth (mean difference, −0.22; 95% CI, −0.33 to −0.11), and lower mean birthweight (mean difference, −122.41; 95% CI, −166.10 to −78.73). Given these results, a prenatal monitoring plan is recommended [28].

In a prospective cohort study carried out to assess MCI and related obstetrical and neonatal outcomes it was documented that low birth weight (LBW) and PTD were significantly associated with MCI associated with increased likelihood of LBW (RR, 4; 95% CI, 1.46–10.99) and PTD (RR, 3.2; 95% CI, 1.53–6.68) as that between MCI and composite adverse obstetrical (RR, 2.33; 95% CI, 1.30–4.19) and neonatal (RR, 2.46; 95% CI, 1.26–4.81) outcomes at multivariate analysis. Serial fetal growth assessment every 4–6 weeks may be warranted in cases of MCI [29].

It would be clinically important for sonographers not to identify MCI by arbitrary cut-offs but by a meaningful threshold derived on the basis of the relationship between prenatal ultrasound measurements and relevant perinatal outcomes. Based on this principle, Wax et al. were able to demonstrate that only a UC insertion-placental edge distance ≤ 1 cm was associated with significantly increased rates of specific adverse pregnancy outcomes (adjusted OR, 3.05; 95% CI, 1.73–5.38; $p < 0.001$) [30]. Also, the study by Allaf et al. showed a high incidence of FGR and oligohydramnios with MCI [29]. The association of FGR with oligohydramnios may suggest a common etiology. Placentae with a displaced cord show a markedly reduced transport efficiency, and hence a lower birth weight might be associated. Placentae with a noncentral cord insertion have a sparser chorionic vascular distribution, as measured by the relative vascular distance [31].

The high frequencies of LBW < 10th percentile for gestational age and oligohydramnios among these pregnancies suggest that an ultrasound follow-up might be warranted for pregnancies with MCI. These follow-up scans should be performed not only to evaluate and estimate fetal growth and amniotic fluid volume but also to reassess MCI to exclude the progression to velamentous cord insertion [30].

5 | Velamentous Cord Insertion and Association With Vasa Previa

Usually, the UC inserts in the central part of the placenta in approximately 90% of the cases. When the insertion of UC occurs at the edge of the placenta it is defined as marginal insertion. When the insertion of UC occurs outside the placenta and the umbilical vessels run without the coverage of the Wharton's jelly, the condition is defined velamentous cord insertion, with an incidence that ranges from 0.5% to 1.69% in singleton pregnancies [32]. The prevalence is higher in nulliparity, twin pregnancies, and in pregnancies obtained by *in vitro* fertilization [33]. Velamentous cord insertion has been associated with adverse perinatal outcomes such as acute distress during labor including variable decelerations, nonreassuring fetal status, and emergency Cesarean deliveries [34].

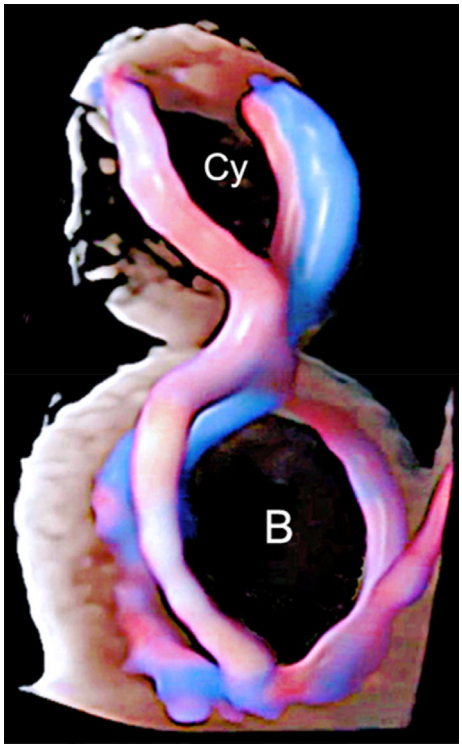

FIGURE 8 | Pregnancy at 13 weeks' gestation. Spatio-temporal image correlation with HD-Flow and "glass-body" rendering mode allows visualization of the vessels around the bladder (B) and umbilical arteries and umbilical vein around the allantoic cyst (Cy).

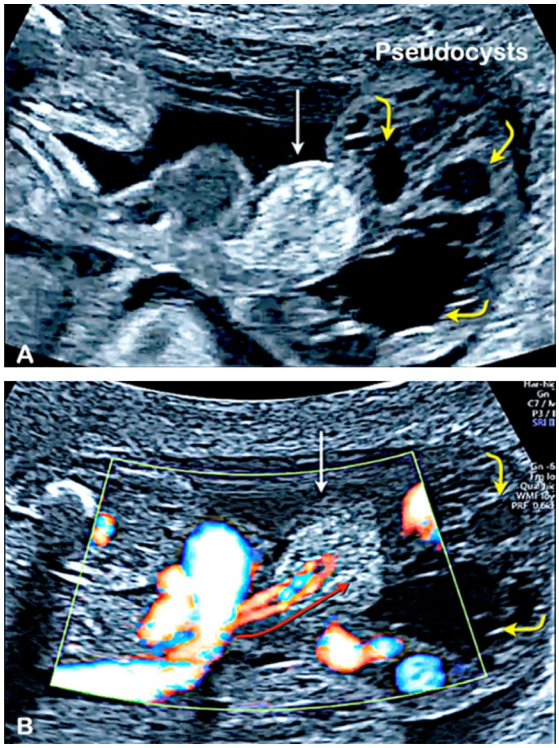

FIGURE 9 | Pregnancy at 22 weeks' gestation. (A) 2D ultrasound allows the identification of a small bowel protrusion (white arrow) into the umbilical cord adjacent to pseudocysts (yellow arrows); (B) 2D color Doppler ultrasound shows intestinal vessels (red arrow).

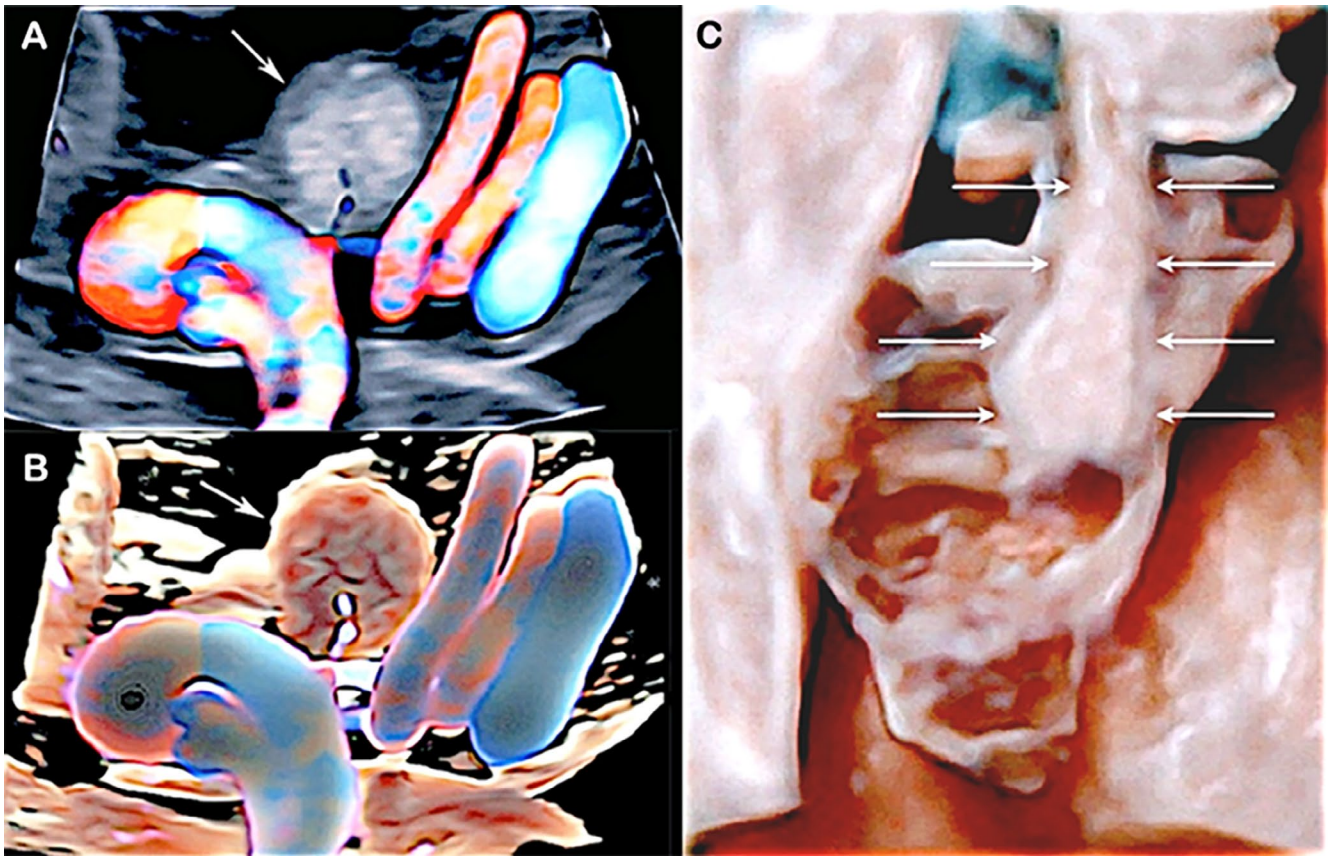

FIGURE 10 | Same case as in Figure 9 at 22 weeks' gestation. (A, B) 3D ultrasound with HD-Flow and spatio-temporal image correlation with color Doppler and "glass body" mode highlights the small omphalocele and umbilical cord vessels; (C) 3D ultrasound with HDlive with Silhouette effect shows the segment of bowel protruding into the cord (white arrows) and the pseudocysts. A small omphalocele may be associated with trisomy 18 and trisomy 21.

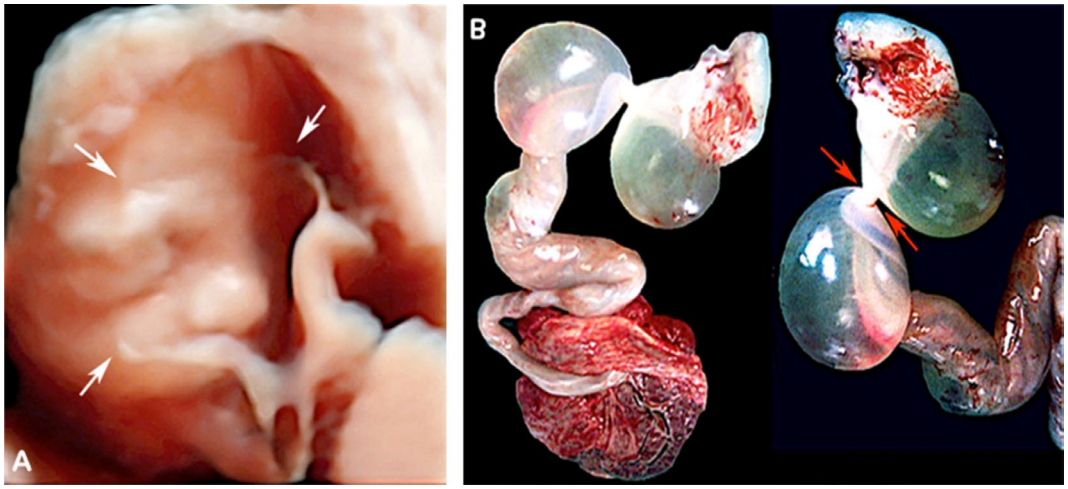

FIGURE 11 | Pregnancy at 24 weeks' gestation. (A) 3D ultrasound with HDlive shows the fetal face through a large cord cyst that stands in front (indicated by arrows). (B) Post-partum anatomical appearance of the large cystic structures in the umbilical cord. The umbilical cord's twist can be clearly seen by the presence of two red arrows.

In a retrospective cohort study of 2327 pregnancies complicated by velamentous cord insertion, there was an increased risk of IUFD, PTD < 37 weeks, manual placenta removal, and postpartum hemorrhage [35]. De Los Reyes et al. performed a systematic review and meta-analysis about the association of velamentous cord insertion with adverse perinatal outcomes in singleton pregnancies. Six studies were included in the analysis, being 16 295 pregnancies with velamentous insertion and 1.366.485 controls. Velamentous insertion was associated with PTD, Cesarean delivery, small for gestational age and IUFD [36].

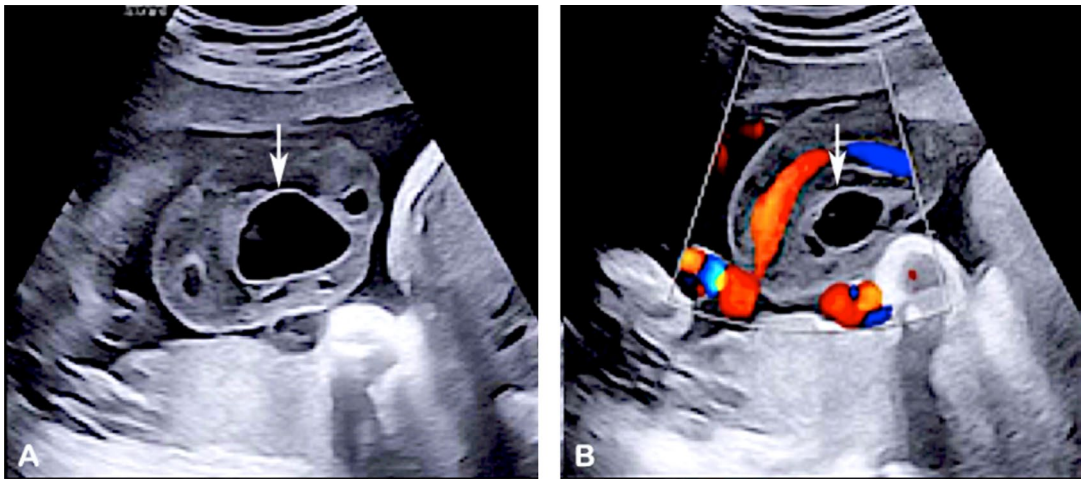

FIGURE 12 | Transabdominal ultrasound in the axial plane shows an umbilical cord cyst (white arrow) in both B-mode (A) and color Doppler ultrasound (B) in a fetus at 31 weeks' gestation. Note the edematous umbilical cord.

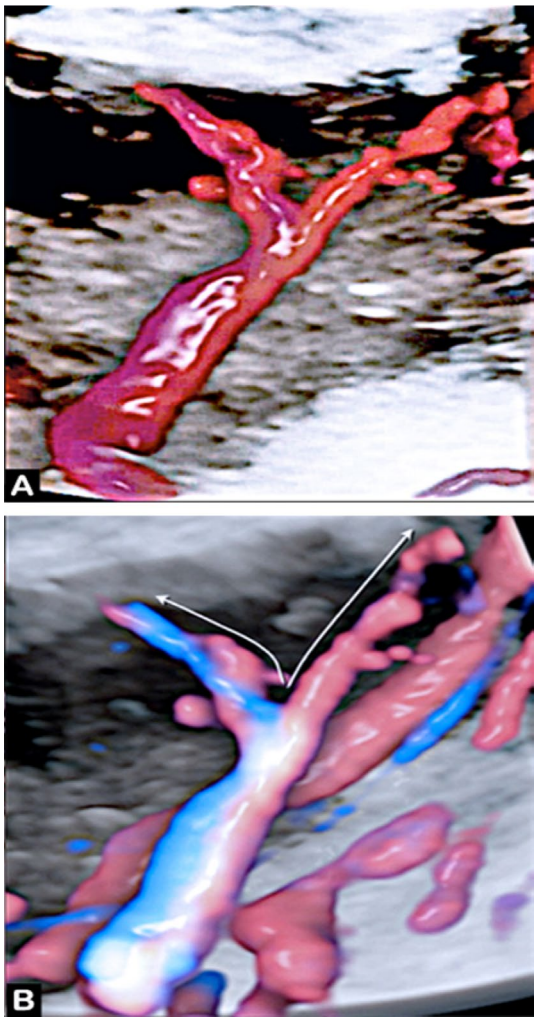

FIGURE 13 | Pregnancy at 12 weeks' gestation. Umbilical furcate cord insertion. Transvaginal sonography. 3D ultrasound with "glass body" rendering mode and HDlive Flow shows (A) the umbilical furcate cord insertion on the placenta with monochrome and (B) without monochrome technique (arrows).

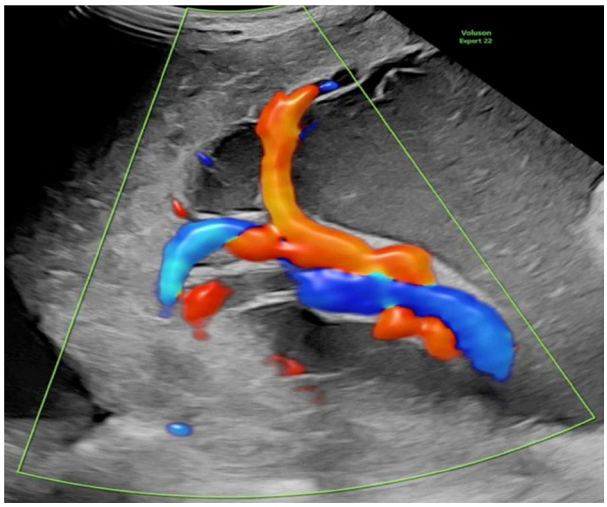

FIGURE 14 | Transabdominal color Doppler ultrasound at 33 weeks' gestation shows the insertion site of the umbilical cord. Note furcate insertion due to the branching of an umbilical artery before reaching the chorionic plate.
Source: Courtesy of Raquel Garcia-Rodriguez, MD.

Lee et al. assessed the clinical significance of velamentous cord insertion in 941 twin pregnancies. In this series, fetuses with a diagnosis of velamentous insertion showed a higher prevalence of vasa previa and placenta accreta spectrum in twins than in controls; however, velamentous insertion was not associated with other adverse perinatal outcomes such as FGR, twin-to-twin transfusion syndrome, and birthweight discordance in monochorionic-diamniotic twin pregnancies [37].

In a recent systematic review and meta-analysis by Siargkas et al., a total of nine cohort and two case-control studies, of which four had prenatal and seven had postnatal velamentous insertion diagnosis were included. Compared with control groups, velamentous insertion showed a higher risk for small for gestational age neonates, preeclampsia, pregnancy-induced hypertension, stillbirth, abruptio placenta, retained placenta,

fetal bleeding, PTD, emergency Cesarean section, 1- and 5-min Apgar score <7, and neonatal intensive care unit admission [38, 39] (Figures 19–22).

6 | Vasa Previa

Vasa previa is defined as an abnormal vascular condition in which the fetal blood vessels lie closely on the internal cervical os, crossing the membranes without placental tissue or Wharton's jelly protection. Vasa previa may be related to a velamentous cord, or to a multilobated or succentuariate placenta, where the fetal vessels traverse the membranes connecting the placental tissue [40].

Since the fetal vessels run freely within the membranes, close to the cervical internal os, spontaneous or iatrogenic rupture of membranes may easily injure them, potentially causing hypovolemic or hemorrhagic shock and IUFD [41].

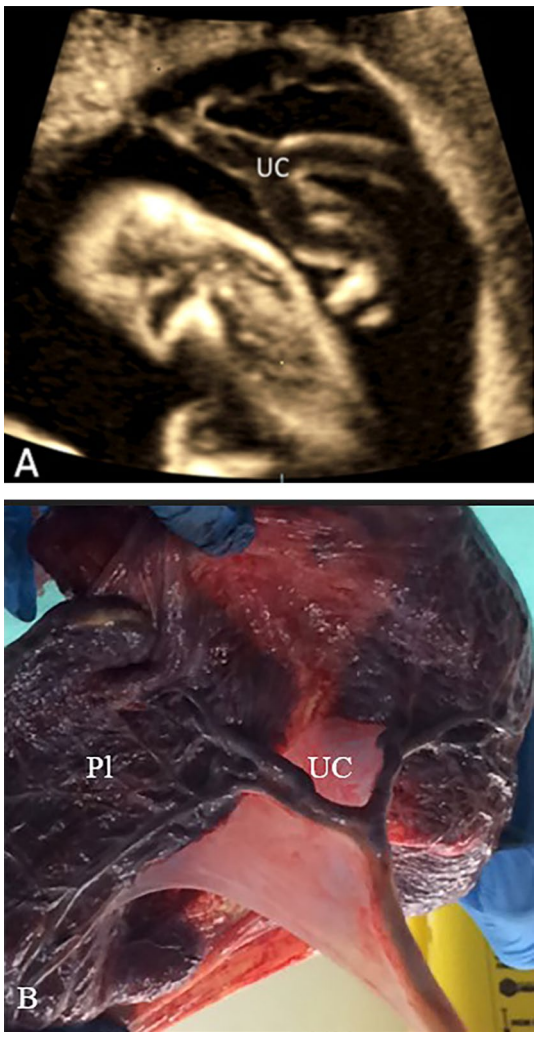

FIGURE 15 | (A) Transabdominal ultrasound performed at 28 weeks' gestation showed a furcate insertion of the umbilical cord (UC). (B) Macroscopic specimen of the UC and placenta (Pl) obtained at the time of delivery.

Vasa previa can be diagnosed antenatally, increasing the chance of live births. On the other hand, lack of prenatal detection raises the risk of fetal/neonatal morbidity and mortality [42].

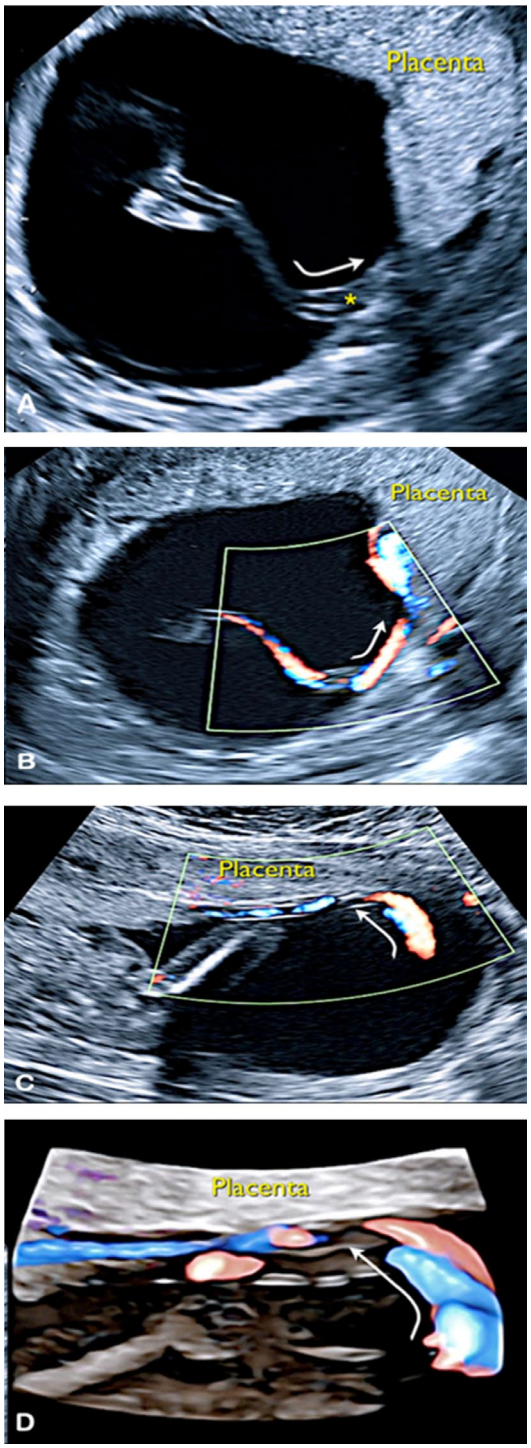

FIGURE 16 | (A, B) Marginal cord insertion (MCI) at 12 and 15 weeks' gestation. 2D ultrasound and color Doppler show the umbilical cord insertion-placental edge distance of a few millimeters at 12 weeks' gestation. (C, D) Color Doppler and 3D ultrasound with "glass body" rendering display the umbilical cord insertion-placental edge distance of more than 1 cm. MCI is characterized by a normal umbilical cord morphology with preserved coverage of umbilical vessels but with a cord insertion into the periphery of the placental disk, typically less than 2 cm from the edge. Asterisk, cord insertion site; arrows, umbilical cord.

Vasa previa can be accurately identified in daily ultrasound practice contributing to reduce up to 10% the stillbirth rate [43]. According to Zhang et al., 9.5% of cases diagnosed with vasa previa during the second-trimester scan presented marginal insertion of the umbilical cord during the first-trimester screening [43].

A systematic review and meta-analysis have confirmed the importance of prenatal screening strategies to implement vasa previa diagnosis and pregnancy management [44] (Figures 23–25).

A clinic-diagnostic algorithm for appropriate diagnosis of UC abnormalities and antenatal management is summarized in Appendix A.

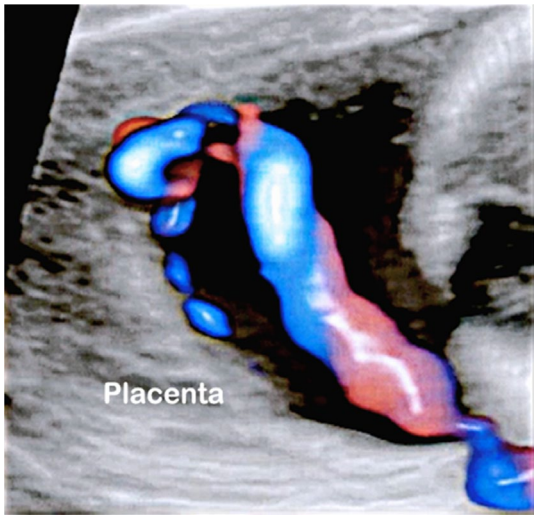

FIGURE 17 | Pregnancy at 17 weeks' gestation. Placenta with marginal cord insertion at 3D ultrasound with "glass-body" rendering mode.

7 | Cord Entanglement: Singleton Pregnancies

UC entanglement includes several sonographic and postnatal presentations such as a true knot of the UC, cases with ≥ 3 loops of nuchal cords, any combination of a true knot and nuchal cord, or any entanglement (nuchal or true knot) in the presence of a SUA in singleton gestations [45]. Sepulveda reported good perinatal outcomes in 10 singleton pregnancies complicated with triple nuchal cord detected by ultrasound during late pregnancy [46]. However, this prenatal finding was also associated with a high rate of Cesarean deliveries. In preterm pregnancies, multiple loops reduced spontaneously in the majority of cases, so expectant management was advocated. In term pregnancies, the decision regarding the optimal timing and mode of delivery should be discussed with the parents taking into account the individual clinical *scenarios* (Figures 26–29).

8 | Cord Entanglement: Monoamniotic Twins

UC entanglement can be also seen in monochorionic–monoamniotic twins [47]. Linde et al. assessed the risk factors and adverse perinatal outcomes for long UC, entanglement, and UC knots in singleton pregnancies. Increasing parity, maternal height, body mass index, and diabetes mellitus were associated with an increased risk of a long UC. Large placenta, birth weight, and fetal male gender were associated with long UC, which was associated with a high risk of IUFD and early neonatal death. At term, UC knot was associated with a risk of perinatal death [48].

Nkwabong et al. reported a case–control study including 114 neonates with nuchal UC entanglement at delivery compared with 228 controls. The risk factors for nuchal entanglement were UC length ≥ 70 cm, pregnancy > 42 weeks, marginal insertion, and male fetus [49]. In a systematic review, Pergialiotis et al. assessed

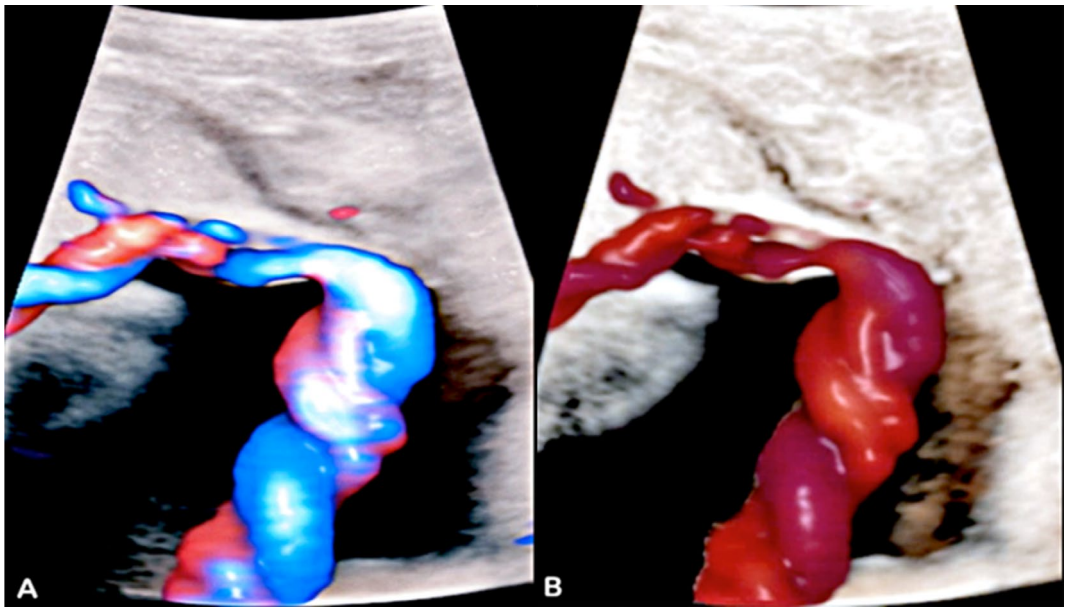

FIGURE 18 | (A) Pregnancy at 27 weeks' gestation. Marginal placental cord insertion using color Doppler ultrasound. (B) Spatio-temporal image correlation with HD-Flow in "glass body" rendering mode allows us to accurately display the distance between the insertion of the umbilical cord and the placental edge.

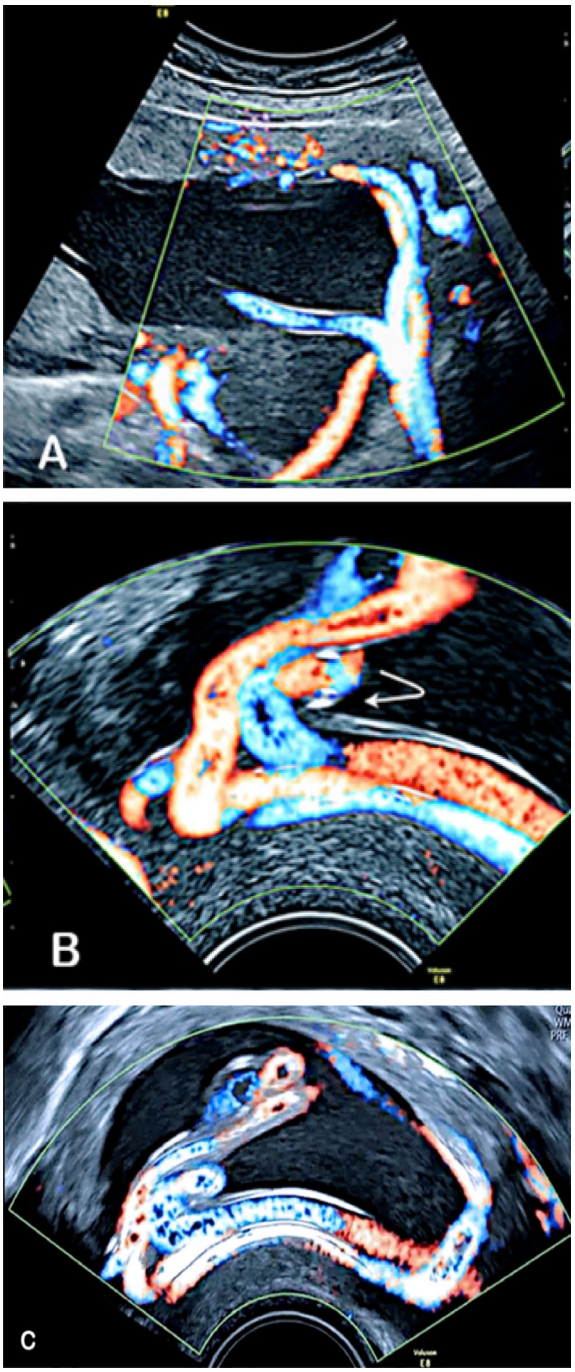

FIGURE 19 | Velamentous cord insertion at 21 weeks' gestation. (A) Transabdominal and (B, C) transvaginal color Doppler ultrasound allow to display umbilical cord inserted at the periphery of the placenta (variable distance from the placenta). The umbilical vessels diverge from each other and travel between the chorion and the amnion toward the placenta (mangrove tree sign). Velamentous cord insertion is associated with vasa previa if it is located in the lower uterine segment. Umbilical cord insertion is indicated by the curved arrow.

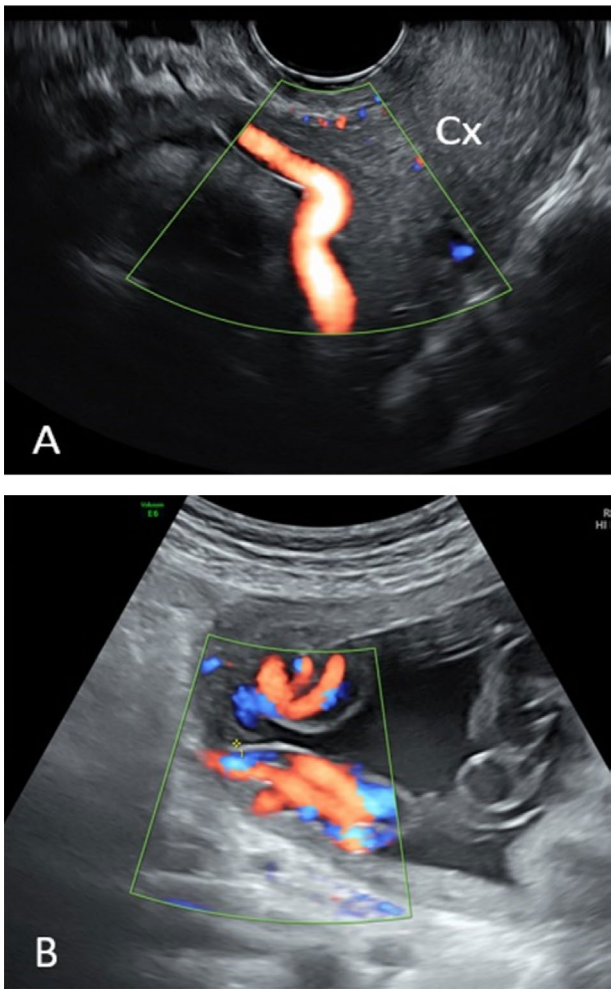

FIGURE 20 | (A) Transvaginal scan identifying a vasa previa by color Doppler ultrasound. The vessels are crossing the internal cervical os. (B) Transabdominal ultrasound showing the velamentous cord insertion by color Doppler ultrasound at 21 weeks' gestation. Abbreviation: Cx, Cervix.

the impact of UC entanglement on adverse perinatal outcomes. Twenty articles were included in the analysis with 267 233 pregnant women (50 103 with UC entanglement and 217 130 controls): entanglement was associated with 5-min Apgar score < 7, fetal distress, and pH < 7.1 [50].

Dias et al. assessed the perinatal outcomes in 18 monochorionic-monoamniotic twin pregnancies with UC entanglement. All pregnancies with entanglement diagnosed by B-mode and color Doppler had obstetric complications including two cases of IUFD at 19 weeks' gestation. The overall perinatal loss rate was 11.1% after 16 weeks and 5.9% after 20 weeks' gestation [51]. The first-trimester ultrasound diagnosis of UC entanglement, using color Doppler ultrasound, is feasible in monochorionic-monoamniotic twin pregnancies.

Entanglement was suspected and diagnosed by demonstrating differing fetal heart rate patterns in the same direction on UA Doppler waveform spectral analysis of a common mass of cord vessels in two monochrionic-monoamniotic twin pregnancies [52]. Importantly, an extended review over 10 years to analyze the impact of cord entanglement in monoamniotic twins over perinatal outcome has demonstrated that prenatal ultrasound detection of cord entanglement did not improve the outcome but also did not improve morbidity and mortality rate when compared with controls. In this review, the

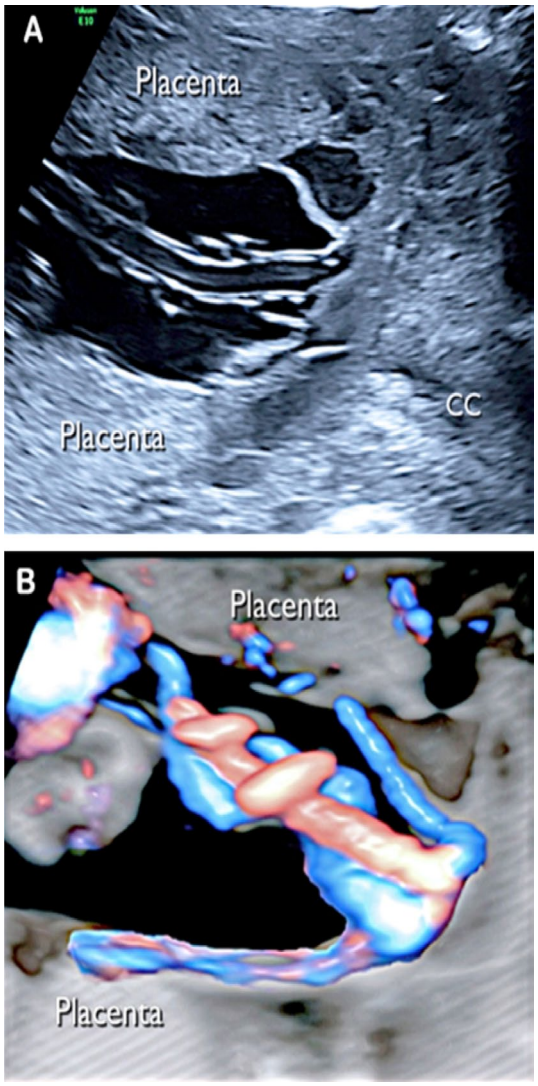

FIGURE 21 | Pregnancy at 20 weeks' gestation. (A) 2D ultrasound and (B) 3D ultrasound using "glass-body" rendering mode with HDlive Flow displays vasa previa type 2 as a result of a bilobed low-lying placenta (*placenta bipartita*) with velamentous cord insertion. Abbreviation: CC, cervical canal.

minimum prevalence of cord entanglement in monoamniotic twins has been assumed to be 55.4% [53]. Mortality rate in monoamniotic twins has been reported in the range between 30% and 70% and other research teams questioned that maybe a more appropriate group of control could be fetuses from monochorionic-diamniotic twin pregnancies rather than from dichorionic twin pregnancies or normal singletons [54–57] (Figures 30–32).

9 | Supernumerary Vessels

Two arteries and one vein normally reside within the UC. More vessels are uncommon and are defined as "supernumerary vessels" or the term "multi-vessel cord" can be used.

The most common persistent vessel is the right umbilical vein, which normally regresses by the 6th to 7th week of gestation when the left umbilical vein anastomoses with the hepatic sinusoids ensue [16, 58].

Persistence of the right umbilical vein has been found associated with cardiovascular and gastrointestinal congenital anomalies such as *situs inversus*, atrial-septal defects, duodenal atresia, bowel malrotation, and imperforate anus [58]. In addition, fetal hydrops, cleft lip, and cleft palate might also be present [59].

An additional artery may be the result of a division of one umbilical artery during its early development, through a failure of the fusion of the primitive umbilical arteries with the descending aorta, or a lack of coalescence of the arterial plexus in the formation of the allantoic artery [16]. Since three arteries and one vein are quite peculiar, associated congenital anomalies are yet to be defined. This vascular combination was described in a stillbirth, with no other malformations [59].

Literature data on a five-vessel cord (i.e., four arteries and one vein or three arteries and two veins) is described in only few reports and has been detected in twin pregnancies as in conjoined twins [60, 61]. Occurrence in singleton pregnancies has also been described [58, 61–63] (Figures 33 and 34).

10 | True Cord Knot With Umbilical Artery Thrombosis

UC knots are a relatively rare diagnosis in prenatal care, with severe potential implications for fetal well-being. These knots can be classified as either true knots, where the UC loops around itself, or false knots, which are mere bulges caused by redundant cord length or vessels. While false knots are usually harmless, true knots can lead to severe complications, including compromised blood flow, fetal distress, and even IUFD. Prenatal suspicion of a true UC knot arises when a gray-scale ultrasound shows an UC cross-section encircled by a circular loop [64]. Advances in 3D and Doppler ultrasound facilitate the confirmation of this diagnosis and help differentiate true knots from false knots, which typically present with a four-leaf clover appearance [65].

A constricted true knot can be identified by pulsed Doppler velocimetry of the umbilical artery, revealing cord compression [66].

True knots represent a risk factor for the development of an uncommon but serious fetal complication, associated with placental hypoperfusion and increased rates of perinatal morbidity, consisting of umbilical vessel thrombosis. This occurs when blood flow through the cord is significantly restricted, leading to the formation of blood clots within the umbilical vessels. Prenatal sonographic demonstration of a SUA following an earlier diagnosis of two umbilical arteries should raise suspicion for the possibility of umbilical artery thrombosis [67]. On color Doppler, the "orange grabbed sign" is a distinctive feature of umbilical artery thrombosis. This appearance occurs when the occluded artery and the normal artery are encircled by the uterine vein, resembling "an orange being grasped by a hand" [68]. Umbilical artery thrombosis can lead

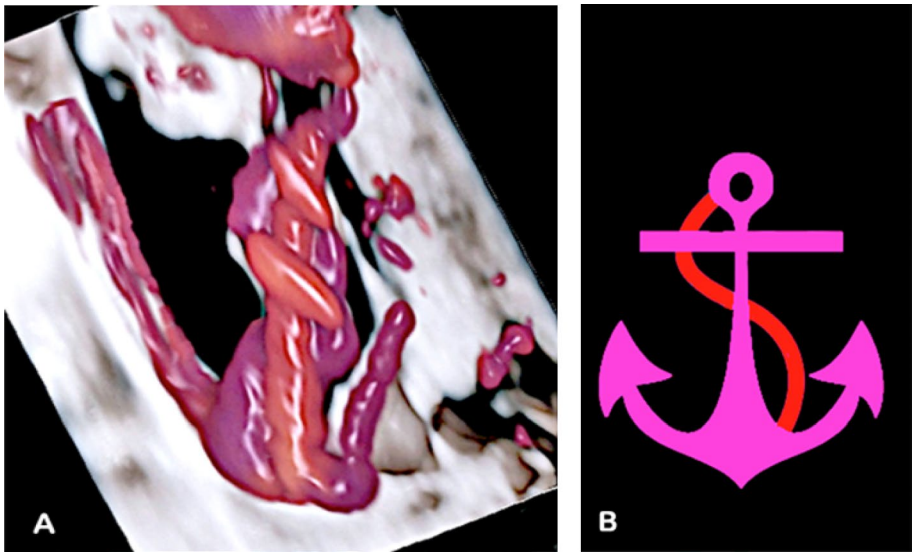

FIGURE 22 | Same case as in the previous image. *Placenta bipartita* with vasa previa. (A) *Placenta bipartita* located in the lower uterine segment with symmetrical velamentous cord insertion may assume a characteristic "anchor shape" (B).

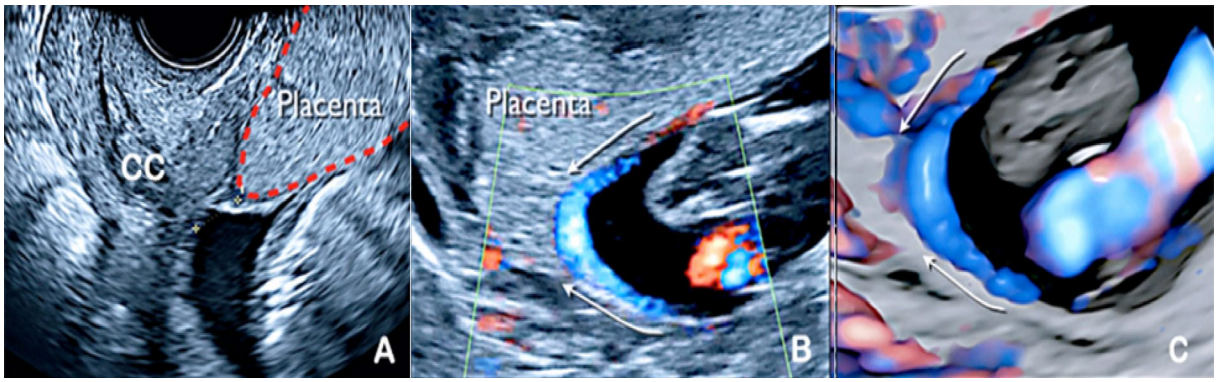

FIGURE 23 | Pregnancy at 20 weeks' gestation. (A) 2D transvaginal sonography indicates a low-lying placenta where placental edge (red dotted line) distance from internal cervical os is ≤2 cm; (B, C) Transvaginal color Doppler ultrasound and 3D ultrasound with "glass-body" rendering mode in the lower uterine segment indicates (white arrows) free vessels along the internal cervical os, as vasa previa. Abbreviation: CC, cervical canal.

to feto-maternal transfusion, FGR, IUFD, meconium-stained amniotic fluid, acute fetal distress during labor, neonatal organ infarction, and cerebral palsy [69]. Umbilical artery thrombosis is a rare condition with no established consensus on treatment. Given its potential risks, management may involve planned Cesarean delivery preceded by antenatal corticosteroid therapy to promote fetal lung maturation [70] (Figures 35–39).

11 | Cord Teratoma

UC teratoma has been rarely reported in the literature. Teratomas derive from the three germ cells (ectoderm, mesoderm, and endoderm) and they are characterized histologically by mature and/or immature tissues. The presence of neuroblasts classifies the tumor as an immature type. The location along the UC may vary and it can be detected in any place along the UC. Adverse effects may be fetal hydrops and cardiac failure due to its rapid growth. They can also produce compression of the umbilical vessels and subsequent fetal death. Omphalocele has been the most frequent associated anomaly, though other malformations have been detected including hydrocephalus, bladder exstrophy, and atrioventricular canal defect [71–73] (Figure 40).

12 | Angiomyxoma of the Cord

This UC condition refers to a vascular tumor of benign origin that develops from a proliferation of capillary vessels intermixed with fibromixoid stroma located within the tumor [74, 75]. It may be associated with the degeneration of Wharton's jelly and pseudocyst. This uncommon vascular neoplasm has been traditionally classified as "hemangioma" and this term has been used interchangeably with angiomyxoma. However, this lesion should be correctly referred to as angiomyxoma due to the myxomatous stromal component [76–79]. The term hemangioma should be used for congenital hemangioma only [74] and immunohistochemically positive for GLUT-1 [80]. Angiomyxoma has also been seen as associated with amnionic epithelial inclusion cysts, a condition that has been pathologically demonstrated in a fetus

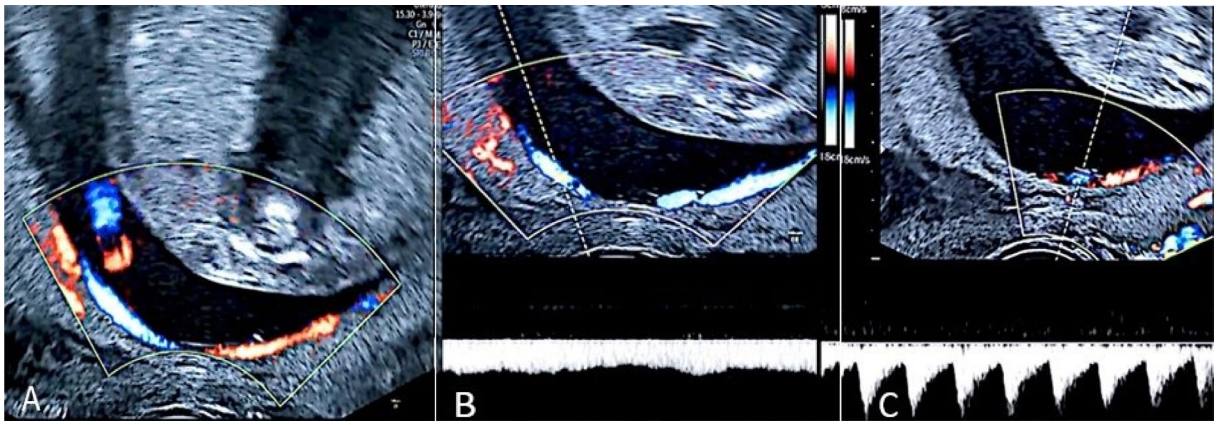

FIGURE 24 | (A) Second trimester 2D transvaginal ultrasound color and pulse wave spectral Doppler ultrasound can recognize venous (B) and arterial vessels (C) along the lower uterine segment as vasa previa.

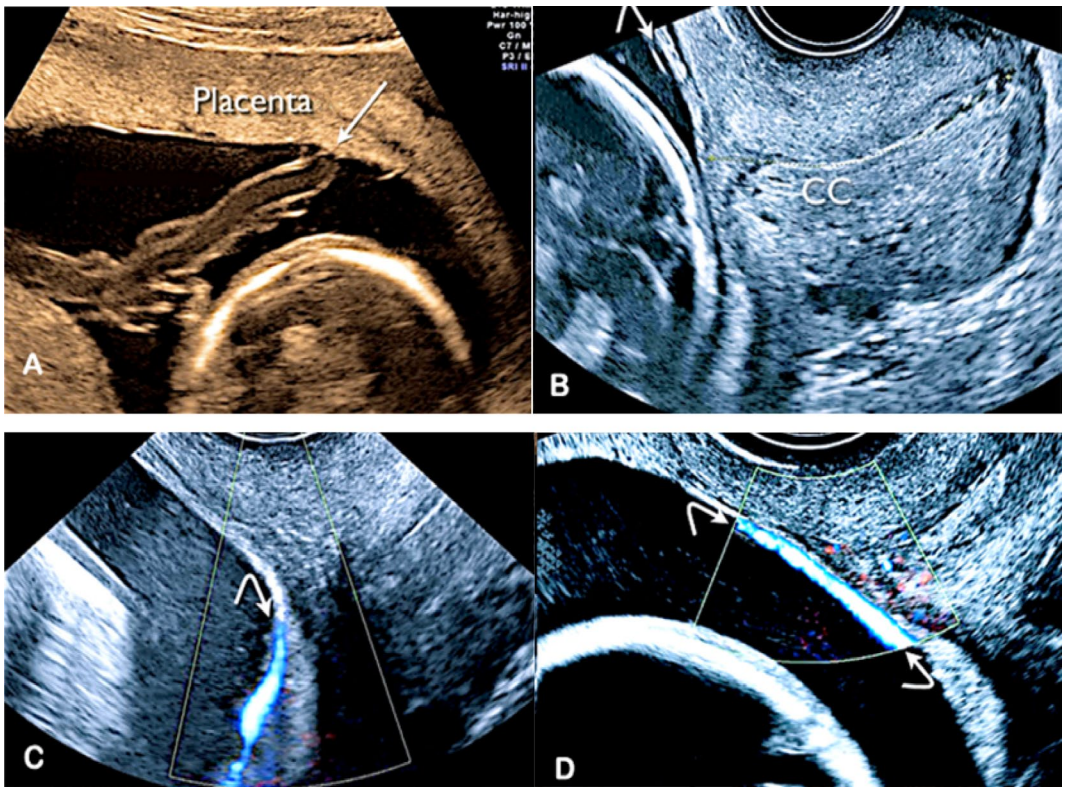

FIGURE 25 | Pregnancy at 23 weeks' gestation. 2D transabdominal and transvaginal sonography. (A) 2D transabdominal ultrasound shows a marginal placental cord insertion (indicated by a straight arrow). (B) 2D transvaginal and color Doppler ultrasound (C, D) allow to display a fetal vessel covering the internal cervical os (indicated by curved arrows). Abbreviation: CC, cervical canal.

of 26 weeks' gestation following IUFD [81] and with only eight cases reported in the medical literature [82]. This pathologic condition of the UC may cause a series of obstetric complications that might severely jeopardize fetal well-being. These include hemorrhage and/or thrombotic events ranging from placental insufficiency with FGR to IUFD or congestive heart failure leading to fetal hydrops. In addition, mechanical compression of the umbilical vessels can lead to a hypoplastic umbilical artery and even IUFD [83–88].

Akiba et al. have described the ultrasound characteristic of hemangioma using 3D ultrasound with HDlive application [89]. In our case, a 3D ultrasound performed using "glass body" rendering clearly rendered how the umbilical vessels are compressed by the angiomyxomatous tissue with the UC distally located to angiomyxoma (Figure 41).

13 | Single umbilical artery

SUA may derive from primary agenesis, subsequent thrombotic atrophy, or lack of regression of the single allantoic artery of the body stalk. The regressed artery may be identified histologically as a muscular remnant, whether the degeneration occurred in the early stages of gestation or later [90, 91]. Arterial regression usually affects the left one, however, no explanation for

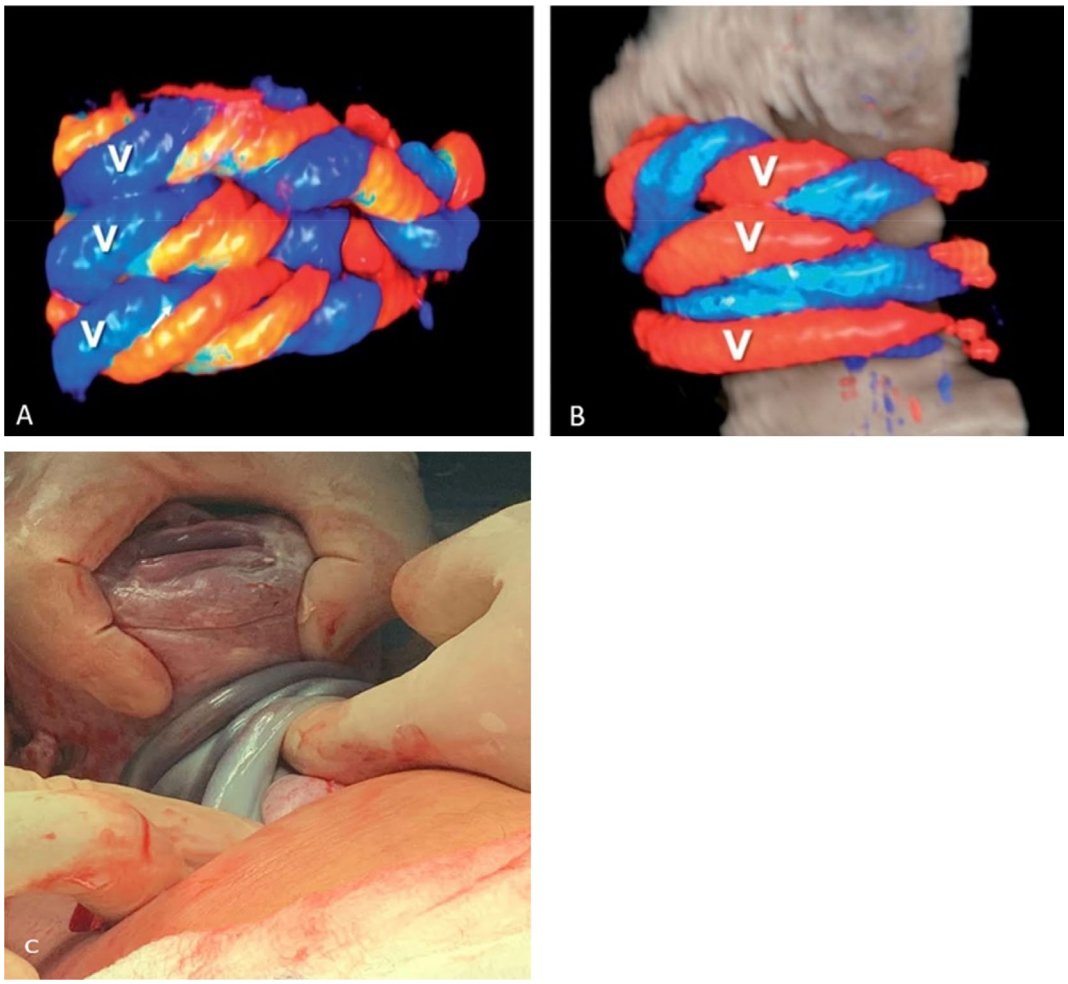

FIGURE 26 | (A) 3D color Doppler ultrasound shows a triple nuchal cord at 37 weeks' gestation [46]. (B) 3D ultrasound using "glass body" rendering mode shows the relation of the vessels with the fetal neck [46]. (C) At Cesarean section, an unreductable triple nuchal cord was confirmed. UV, umbilical vein. *Source*: Courtesy of Juan L. Alcalde, MD.

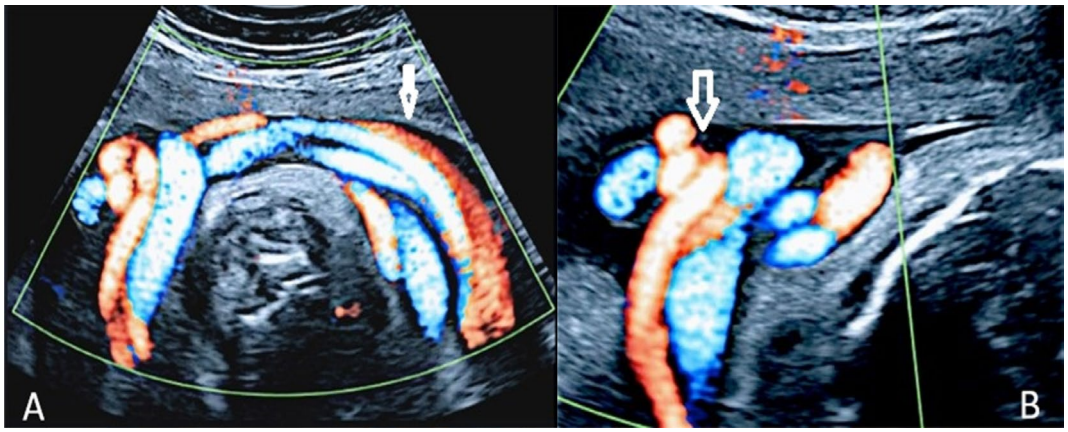

FIGURE 27 | (A, B) Transabdominal 2D ultrasound documenting an association of cord entanglement (closed arrow) and true cord knot (open arrow).

this higher frequency has been found [92]. The absence of the right umbilical artery seems more associated with gastrointestinal and genitourinary anomalies, confirming SUA as a soft marker for potential malformations, prompting more accurate investigations [93]. SUA can be an isolated finding in 84.6% of pregnancies, but in the other 15.4% congenital anomalies and/or chromosomal alterations may be found [94]. Genetic aneuploidies are more frequent in the agenesis type of SUA and a non-reassuring fetal status may be more associated with the thrombotic atrophy of the artery [91] (Figures 42 and 43).

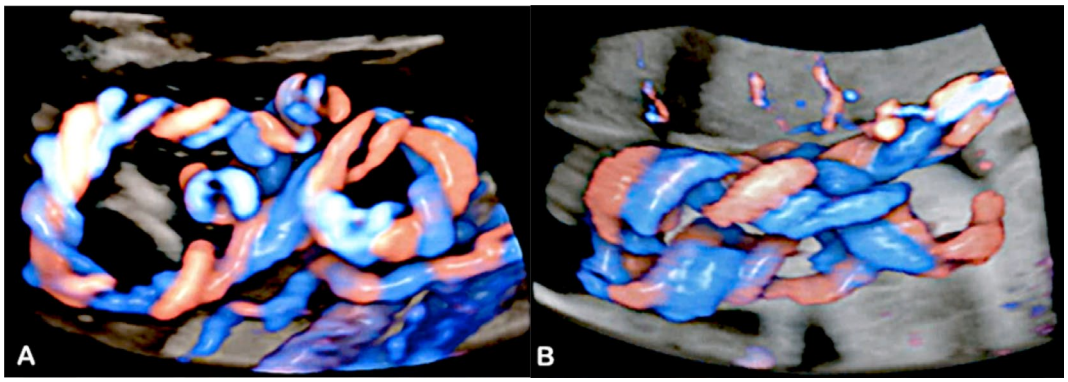

FIGURE 28 | Singleton pregnancy. Entanglement of the cord at 19 and 29 weeks' gestation. An excessively long umbilical cord may be associated with increased coiling and an increased risk of entanglement and knotting. (A) 3D ultrasound with "glass-body" rendering mode shows a free tangle of cord loops in the second trimester, and (B) a braided cord in the third trimester.

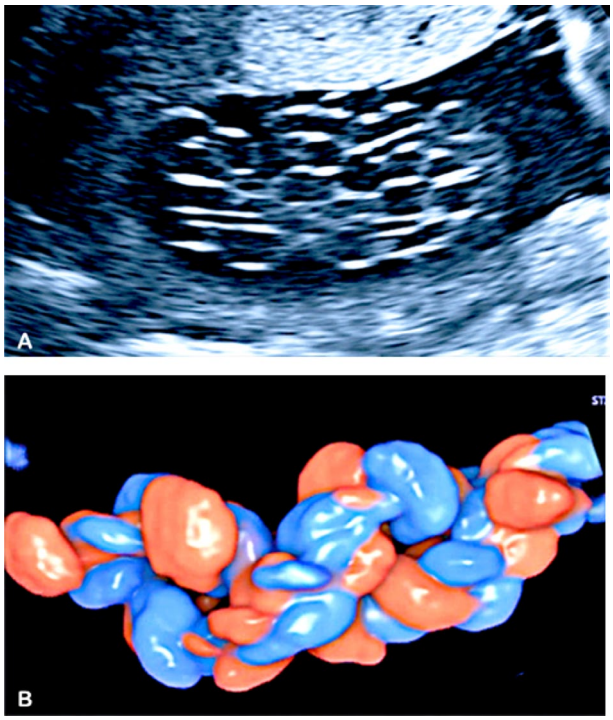

FIGURE 29 | Entanglement of the umbilical cord at 20 weeks' gestation. (A) 2D ultrasound: the umbilical cord has a "honeycomb-like" pattern. (B) 3D ultrasound with "glass-body" rendering mode: the umbilical cord vessels appear stacked upon each other because the cord is hypercoiled.

14 | Umbilical Vein Varix and Umbilical Artery Aneurysm

The UC can occasionally exhibit vascular abnormalities such as varices and aneurysmatic dilatation associated with various etiologies, including congenital vascular malformations, or pathological conditions affecting the vessel walls as an intrinsic congenital weakness or thinning of the vessel wall. The prenatal diagnosis can be made by identifying a focal dilation of the UC with blood flow visible on color Doppler ultrasound. Umbilical vein varix (UVV) is defined as an enlargement of the umbilical vein. UVV or variceal dilatation of the umbilical vein is one of the umbilical anomalies that occur in either the intra- or extra-abdominal portion of the UC.

We will describe only extra-abdominal types, also called intra-amniotic UVV. Their frequency is reported to be between 1.95% (in a random selection of placentae) and 3.8% (in stillborn infants). The vein is more commonly affected than the arteries, and the site of variceal or aneurysmal dilatation is most often near the UC insertion [95].

2D, color Doppler, and 3D ultrasound allow to detect one or more dilatations at the level of the UC, characterized by dilatation with intermittent or continuous bidirectional turbulent flow in the ectatic area [96–98].

UVV can be associated with fetal anomalies and a high incidence of perinatal complications. In case of associated abnormalities, fetal genetic testing should be offered.

Adverse fetal complications have been reported including compression of the UC vessels and kinking of the UC, intra-amniotic UVV rupture, thrombosis inside the aneurysmal dilation, intracord hemorrhage, and hematoma. Ultrasound examinations could reveal variceal dilatation taking on an aneurysmal appearance with acute massive thrombosis inside the varix. Additional risks to massive thrombosis include consumptive coagulopathy, thrombus dislodgement, intra-abdominal thrombi extension, umbilical venous embolism, and vessel occlusion [99, 100].

Intra-abdominal UVV may be associated with FGR, SUA, cerebral palsy, fetal-maternal hemorrhage, fetal anemia, hydrops, and IUFD.

Severe fetal anemia in massive intra-amniotic UVV with increased dilatation of the umbilical vein with thrombus, sometimes associated with hematoma, can be detected by color and spectral Doppler ultrasound. Doppler assessment can show an elevated middle cerebral artery peak systolic velocity > 1.5 multiples of the median suggesting fetal anemia [101, 102]. Moreover, fetal anemia may also be caused by intermittent turbulent flow-provoking hemolytic anemia (schistocystic hemolysis). Both

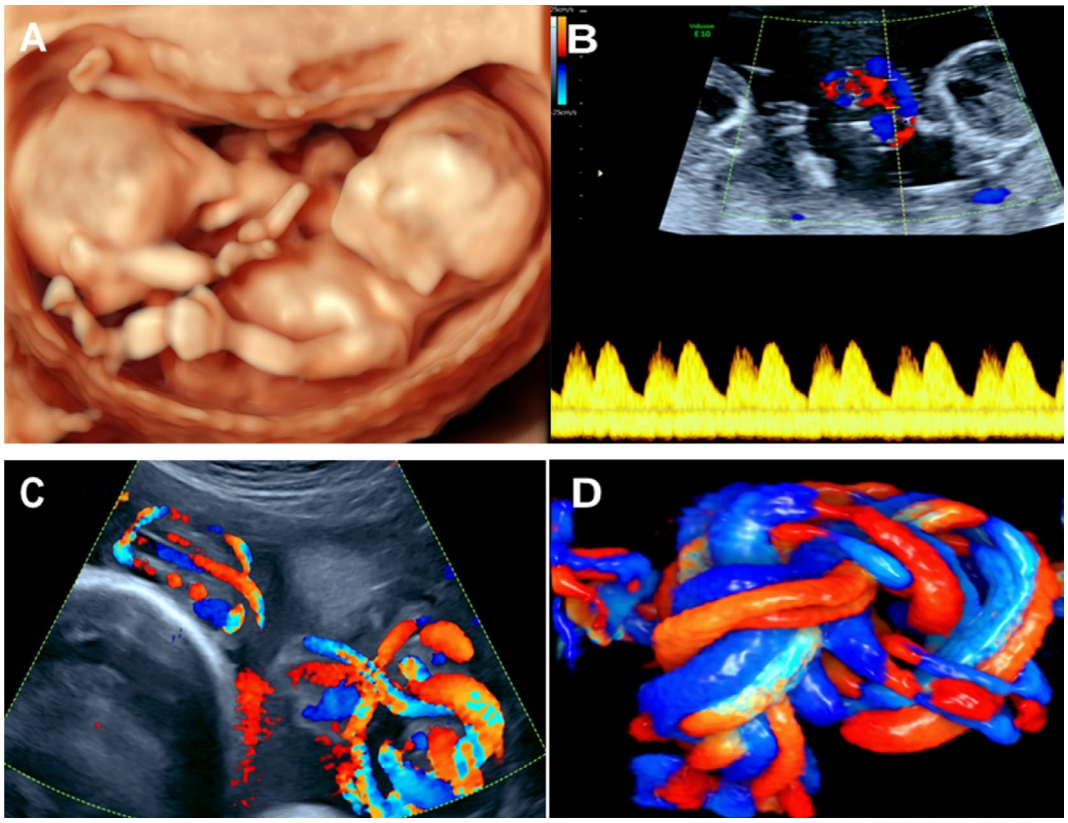

FIGURE 30 | Monochorionic-monoamniotic twins with umbilical cord entanglement. (A) A 3D surface rendering scan shows monoamniotic twins. No separating membrane was identified. Both heads are clearly seen. (B) Spectral Doppler ultrasound waveform analysis shows synchronous fetal heart rate patterns. Later second trimester scan shows entanglement of the cords with conventional color Doppler (C) and 3D angioscan (D).

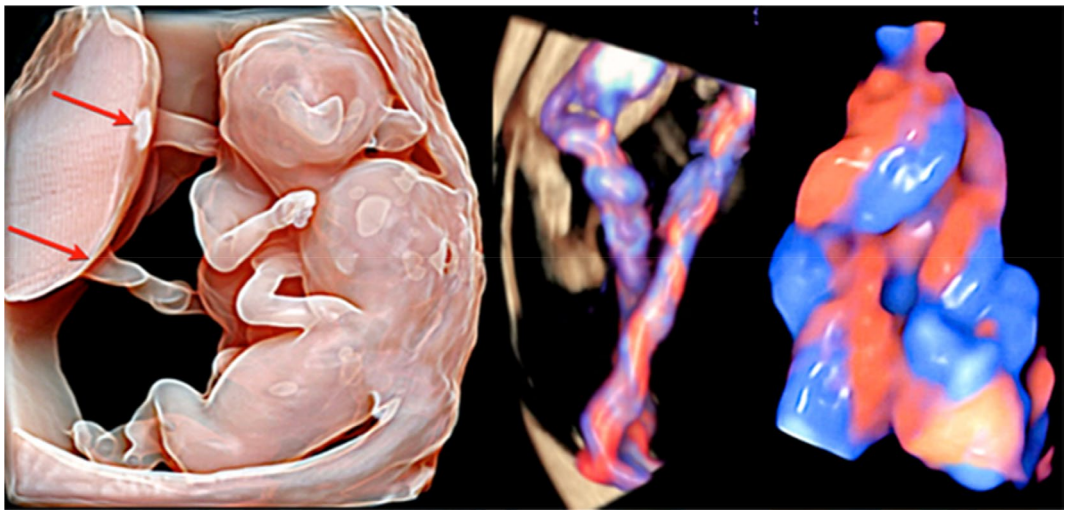

FIGURE 31 | Monochorionic-monoamniotic twin pregnancy at 11 weeks gestation. (A) 3D ultrasound HDlive with Silhouette effect and (B) using 4D spatio-temporal image correlation. The cord cross, entanglement, and knotting can be detected already before the end of the first trimester. The placental insertion of the umbilical cords is shown (red arrows).

thrombosis and fetal hemolytic anemia, if diagnosed in the second trimester, can cause IUFD. Intrauterine transfusion can improve fetal circulatory failure and anemia allowing the gestation period to be prolonged [102]. It is suggested a close fetal monitoring and ultrasound follow-up. The timing of delivery remains a challenging decision in the preterm period; however, the presence of any suspicious signs that could cause IUFDs should prompt a Cesarean delivery [98, 102].

The prenatal detection rate of this rare developmental anomaly is reported to be 79%. Fetal heartbeat abnormalities and fetal deaths were reported as 50% and 14%, respectively. Eighty-six percent of patients had intra-UC thrombosis and only one case had hemolytic anemia [102] (Figures 44 and 45).

Umbilical artery aneurysm (UAA) is a very rare and occasionally lethal condition, potentially associated with a SUA (66%), chromosomal aneuploidies (trisomy 18) (22%), FGR, fetal anemia, cardiac failure, fetal structural anomalies, and IUFD [2, 45, 103].

Nevertheless, in spite of the rarity of this condition, to date, only 18 prenatal diagnoses of an UAA have been reported in the literature. This is a significant finding because of its high association with fetal life-threatening complications such as rupture, thrombosis, and compression of the umbilical vein [104, 105]. Prenatal sonographic diagnosis of this condition is characterized by a focal enlargement of the UC due to aneurysmal dilatation of the umbilical artery of varying size. The vessels of the UC appear to splay around the mass seen on color Doppler examination [106].

Color and spectral Doppler imaging confirms pulsatile, turbulent arterial blood flow [107, 108] and any echogenic or hyperechogenic structure within the aneurysm likely indicates a mural thrombus. Interestingly, in most cases, the location of the UAA is next to the placental insertion site in 12 out of 18 cases (66%) [105].

The congenital weakness or thinning of the vascular wall could be the most probable etiological factor. It is likely that Wharton's jelly plays a crucial role in preventing aneurysmal dilatation of the umbilical vessels when a significant weakness of the arterial wall develops. UAAs are located either close to the fetus or close to placental insertion, where the umbilical vessels branch into the chorionic plate and probably lose the protection of Wharton's jelly [109, 110].

UAAs often coexist with the Wharton's jelly degenerative pseudocyst that is often found adjacent to the aneurysm itself [111]. This seems to confirm the aforementioned protective effect of Wharton's jelly on the umbilical vessels [112]. With an increase in the size of the aneurysm, a deterioration of the fetal condition may be manifested with a reverse umbilical artery flow and an increase in middle cerebral artery peak systolic velocities [106]. The risk of occurrence of a high-output cardiac failure is closely correlated with an increase in the size of the aneurysmal sac, which leads to a reduction in the volume of circulating fetal blood and a consequent increase

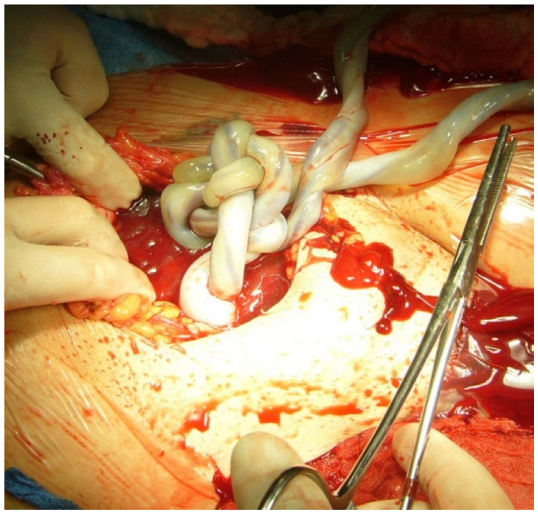

FIGURE 32 | Cord entanglement in a monochorionic-monoamniotic twin pregnancy at the time of Cesarean section.
Source: Courtesy of Rodrigo Saez, MD.

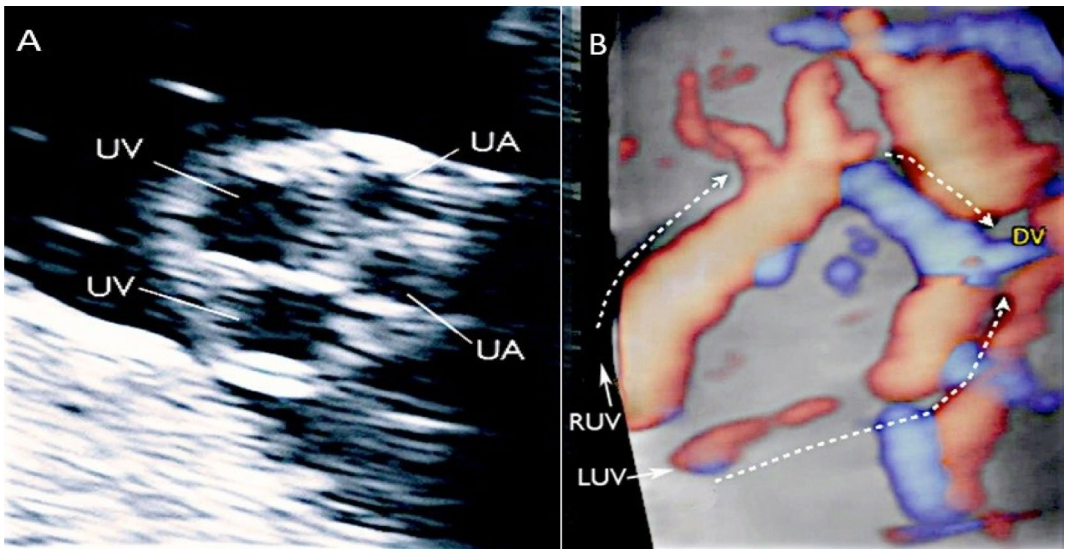

FIGURE 33 | 2D ultrasound and color Doppler in "glass-body" mode and HDlive Flow. (A) The axial section of the umbilical cord shows four umbilical vessels (two veins and two arteries). (B) The transverse section of the fetal abdomen detects the left and the right umbilical vein with the presence of the ductus venosus. Abbreviations: DV, ductus venosus; LUV, left umbilical vein; RUV, right umbilical vein; UA, umbilical artery; UV, umbilical vein.

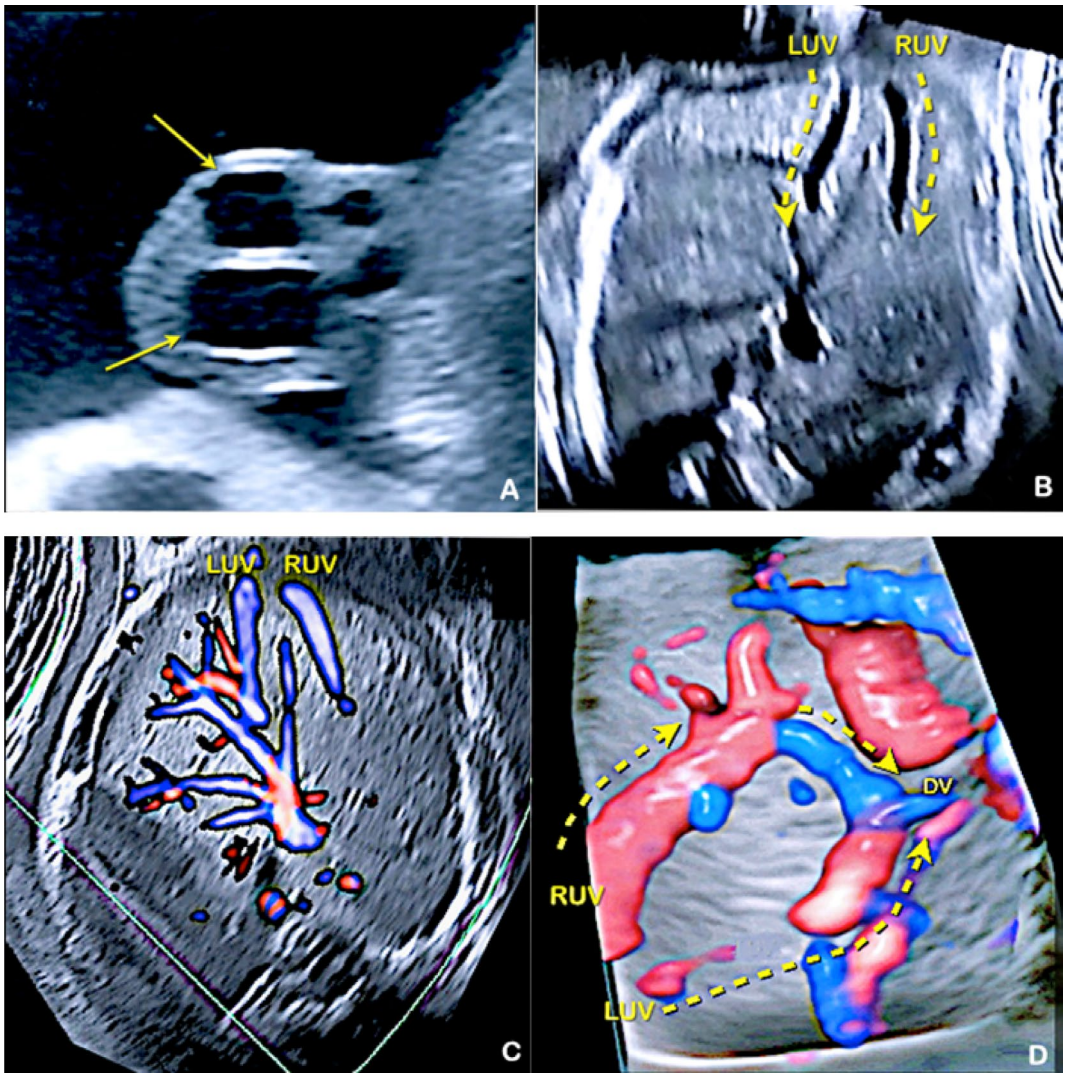

FIGURE 34 | Pregnancy at 28 weeks' gestation. (A) 2D ultrasound in the axial section of the umbilical cord shows four umbilical vessels: two veins (indicated by yellow arrows) and two arteries. (B) The axial cross-section of the abdomen displays both the left (LUV) and the right umbilical (RUV) veins entering the fetal abdomen (dashed arrows). (C, D) 2D color Doppler ultrasound and spatio-temporal image correlation HD-Flow with "glass-body" rendering mode point out the course of the LUV, RUV, and ductus venosus (dashed arrows). Abbreviations: DV, ductus venosus; UA, umbilical artery; UV, umbilical vein; LUV, left umbilical vein; RUV, right umbilical vein.

in resistance at the level of the umbilical artery, increasing systemic pressure [103]. Assessment of the middle cerebral artery peak systolic velocity can accurately diagnose fetal anemia. In the UAA, fetal anemia and thrombocytopenia result from thrombus formation, an expanding aneurysm can compress the umbilical vein leading to mural thrombosis, or an abnormal, thin wall of the vessel is also prone to rupture, which may result in a perivascular hematoma [112]. In addition to fetal anemia, disseminated intravascular coagulation may develop *in utero*, induced by the consumption of coagulation factors due to umbilical vein thrombosis or immediately after birth [103].

Umbilical vessel aneurysms can be associated with trisomy 18 or 13. If fetal malformations or FGR are detected, prenatal karyotyping is mandatory to guide clinical management in these cases. A normal karyotype, and in the absence of sonographically detectable morphologic anomalies, close fetal surveillance, and early delivery have been suggested to impact the likeliness of survival. Antenatal management strategies include serial ultrasound assessment, testing to identify FGR, and delivery by planned Cesarean delivery between 32 and 34 weeks when fetal lung maturity is achieved in order to avoid IUFD in more than 60% of cases, mainly due to aneurysmal thrombosis, hematoma, possible vascular compression (umbilical vein) and/or aneurysmal rupture [105, 110, 113]. With regard to making a decision for delivery by Cesarean section, the increase in the size of the UAA (> 5 cm) and the evaluation of fetal anemia by middle cerebral artery peak systolic velocity have particular importance [103].

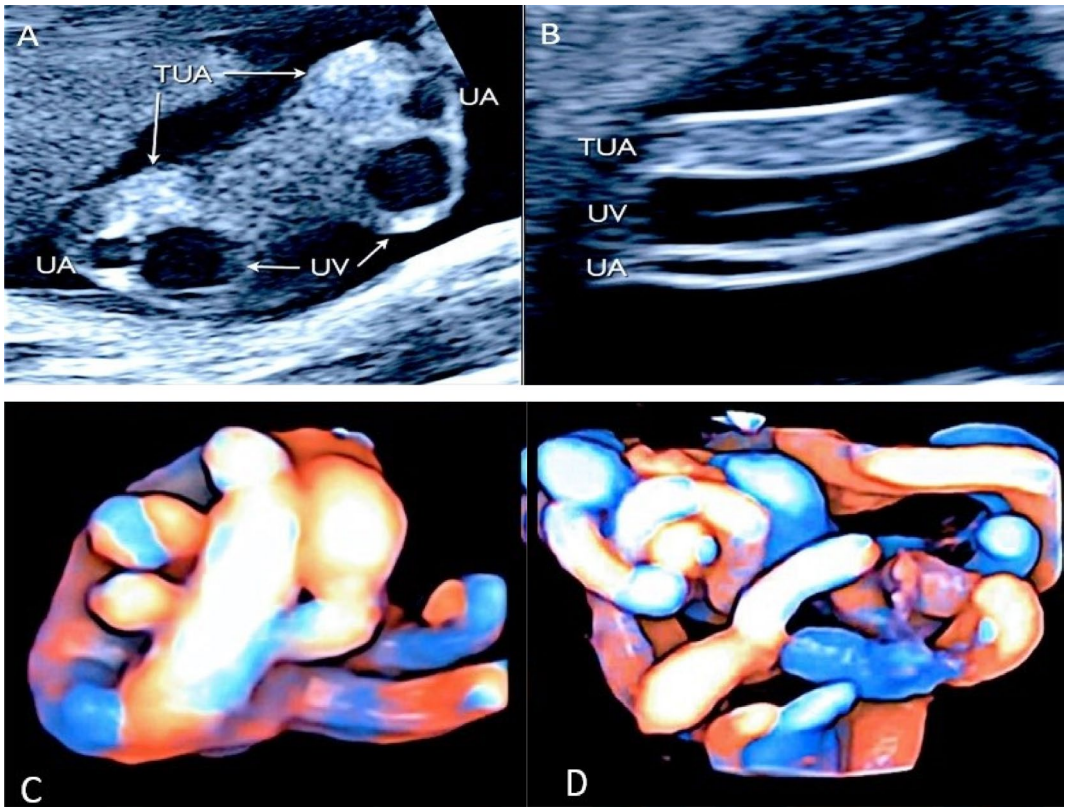

FIGURE 35 | (A) 2D ultrasound showing hyperechogenicity at the level of one umbilical artery (UA) affected by thrombotic phenomenon (TUA, white arrows) in axial and in (B) sagittal plane. 3D rendering using 4D angio spatio-temporal image correlation Doppler ultrasound (C, D). Abbreviation: UV, umbilical vein.

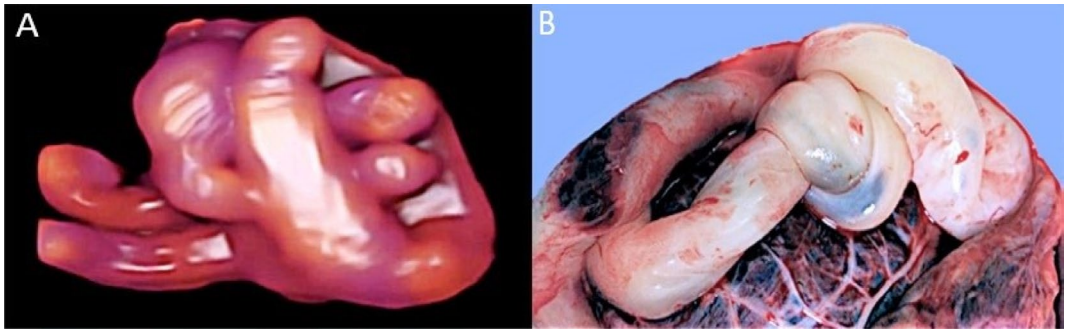

FIGURE 36 | (A) 3D ultrasound was performed with 4D angio spatio-temporal image correlation and "glass body" rendering mode in a case of true cord knot and thrombosis of the umbilical artery with gross pathology confirmation (B).

A clinic-diagnostic algorithm for appropriate diagnosis and antenatal management is summarized in Appendix B.

15 | Hemorrhagic Cord Cyst

Hemorrhagic UC cysts or hematomas of the UC are typically pseudocysts that have developed a blood component, often due to rupture of small blood vessels within the cyst or the UC itself. On prenatal ultrasounds, UC hemorrhagic cysts look like solid-appearing masses attached to or within the UC, lacking the internal color spots of blood vessels. These pseudotumors can form spontaneously but are more commonly a result of procedures like amniocentesis, cordocentesis, or fetal transfusion. Spontaneous hemorrhagic cysts have been associated with a short UC and UC cysts [114]. The size and shape of hemorrhagic cysts vary depending on when they develop: acute hemorrhagic cysts appear isoechoic or heterogeneous, while chronic ones are hypoechoic or anechoic. This condition can lead to altered umbilical artery flow velocimetry due to compression, as well as changes in fetal heart rates. Although often found incidentally, pregnancies with hemorrhagic UC cysts require special monitoring, including twice-weekly blood flow velocity assessments and non-stress tests [115] (Figures 46 and 47).

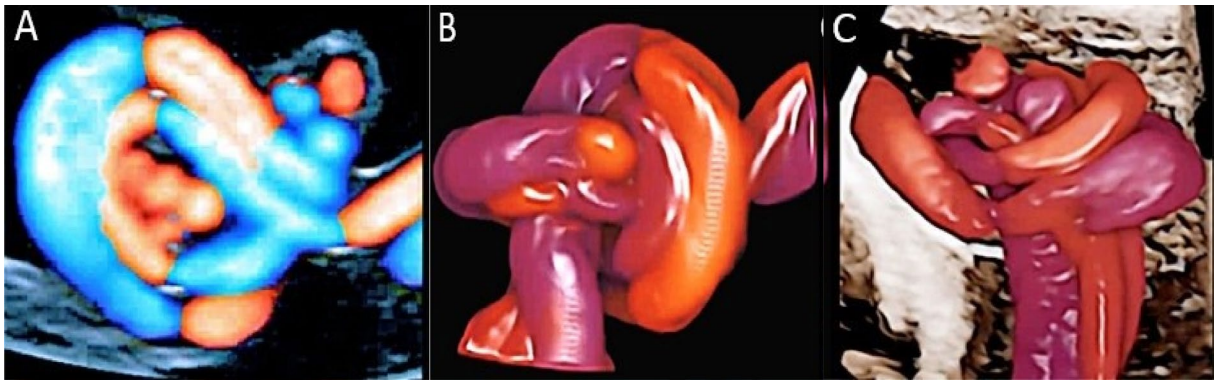

FIGURE 37 | (A) 3D ultrasound was performed with color Doppler ultrasound, (B) 4D angio spatio-temporal image correlation, and (C) with "glass body" rendering mode in a case of true cord knot.

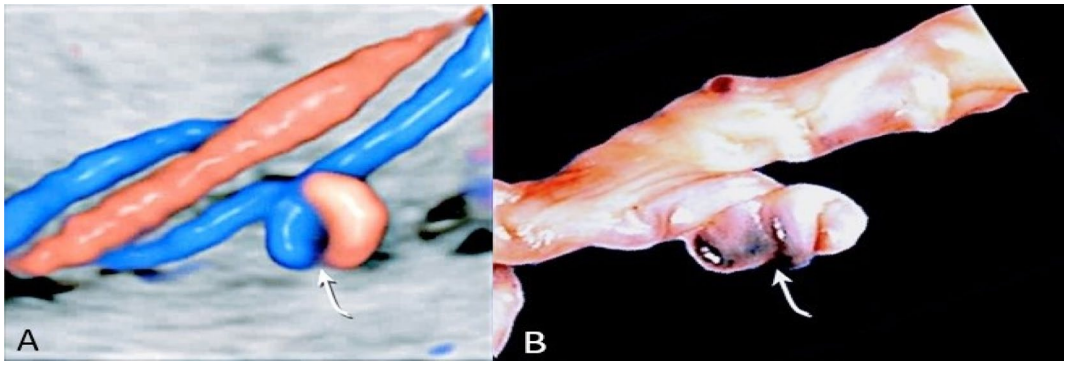

FIGURE 38 | (A) Color Doppler ultrasound performed by transabdominal approach in a 20 weeks' gestation: a false knot of the umbilical cord is seen (arrow) with (B) gross pathology confirmation following delivery (arrow).

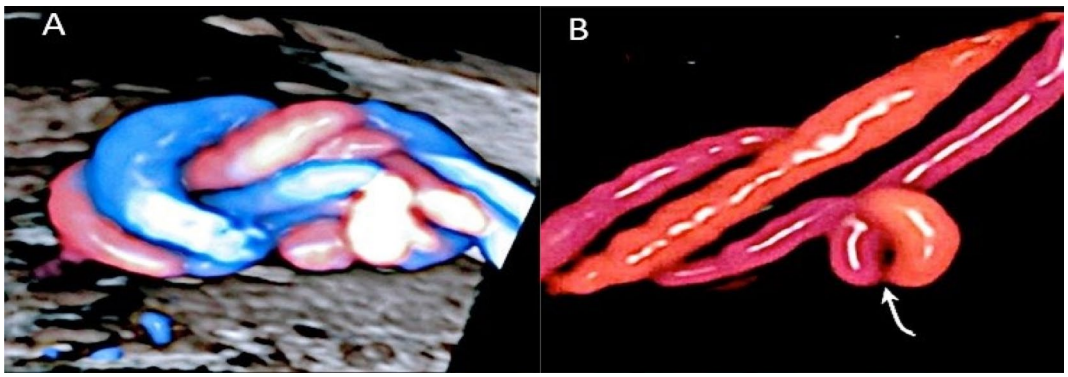

FIGURE 39 | In this case, (A) using color Doppler ultrasound and (B) 4D angio spatio-temporal image correlation, a coexisting true knot with a false knot of the umbilical cord is clearly rendered (curved arrow).

16 | Spontaneous Cord Rupture due to Congenital Absence of Wharton's Jelly

Wharton's jelly is a specialized connective tissue made up of myofibroblasts and extracellular matrix, primarily protecting the umbilical blood vessels. It neutralizes external pressure on blood flow between the placenta and fetus, ensuring adequate blood flow during pregnancy or delivery. The complete or partial absence of Wharton's jelly is a very rare abnormality, with only a few cases reported in the literature, which could lead to impaired feto-placental circulation and consequent fetal loss [116–118]. Theories on the pathogenesis of absent Wharton's jelly include potential degeneration, early incomplete fusion of amniotic and mesenchymal umbilical tissue, or hypoplasia of the amnion leading to secondary loss of Wharton's jelly [119]. This condition could in rare cases lead to ulceration of the umbilical vessels resulting in intra-amniotic fetal hemorrhage, fetal exsanguination, and stillbirth presenting suddenly and without warning. Clinical presentation includes

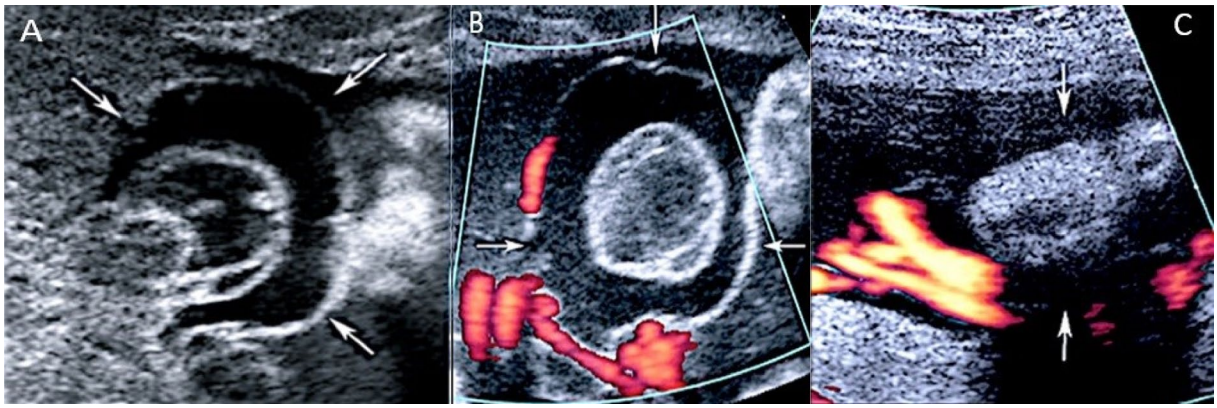

FIGURE 40 | UC teratoma. (A) 2D ultrasound, (B) color and (C) power Doppler ultrasound detected a rounded mass with mixed content positioned near the insertion of the cord at the placental side. Echoic and hypo-anechoic areas with pseudocystic parts adjacent to the mass were seen (white arrows).

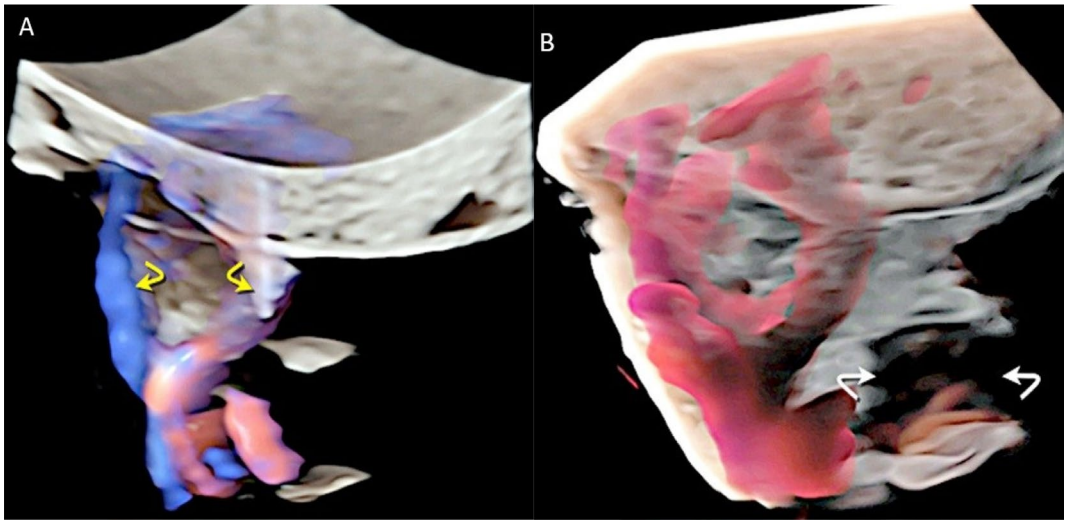

FIGURE 41 | 3D ultrasound using "glass-body" rendering mode. The umbilical vessels are compressed by the angiomyxomatous tissue (A, yellow curved arrows). The umbilical cord is distally located to angiomyxoma (B, white curved arrows).

sudden changes in fetal heart rate patterns or vaginal bleeding if the rupture occurs near the placental insertion site. In cases where rupture is suspected, immediate medical intervention is crucial though outcomes are often poor due to the sudden and severe nature of the event [120] (Figure 48A,B).

A clinic-diagnostic algorithm for appropriate diagnosis and antenatal management is summarized in Appendix C.

17 | Conclusion

From the analysis of our clinical series and that of the medical literature, it is evident that congenital anomalies, perturbation, and defective UC anomalies have a great impact on fetal well-being. In such cases, the fetus may be jeopardized with subsequent *in utero* as well as *ex utero* obstetric complications and be associated with poor perinatal outcomes.

Clinical firm conclusions can be made: (a) ultrasound detection of the UC should be recommended at the time of the first trimester screening scan; (b) the use of 3D ultrasound enables the visualization and analysis of UC vessels from the 8th week of gestation onwards; (c) when UC pathology is suspected, an extended, dedicated ultrasound is recommended; (d) prenatal counseling and genetic workup based on non-invasive prenatal testing or array-comparative genomic hybridization, as well as genome sequencing may be required; (e) the use of Doppler ultrasound is advocated as it allows detection of circulatory abnormalities and enables a more accurate definition and interpretation in case of FGR; (f) smaller vessels can be made visible only by the demonstration of blood flow, by using color Doppler, power Doppler or high-definition flow; (g) UC vessels have a spatial course and the 3D reconstruction can demonstrate the course and branching of the vessels; (h) 3D applications enhance the levels of transparency and the spatial and depth effect of the vessel's course; and (i) gross pathology and microscopic examination of the UC should be recommended in all cases of fetuses with obstetric complications during pregnancy or during labor and in the early neonatal period, with particular attention in cases of early poor and adverse perinatal outcome [121, 122].

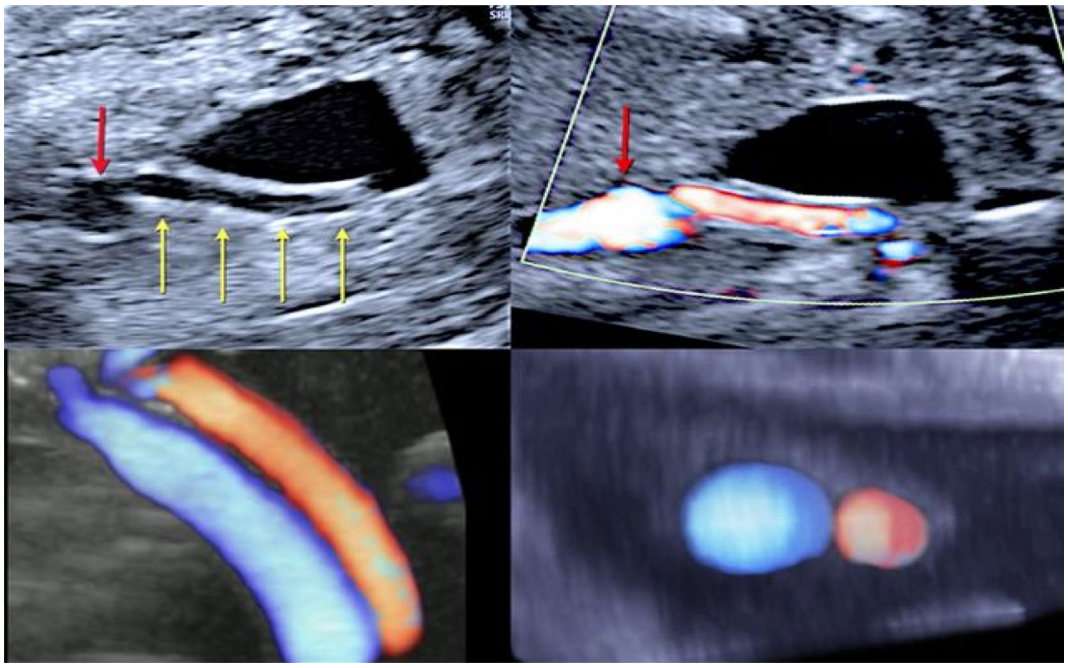

FIGURE 42 | 2D ultrasound, 2D color Doppler, and "glass body" rendering mode. Single umbilical artery (SUA): right umbilical artery is indicated by yellow arrows; a concomitant intra-abdominal vein varix is indicated by the red arrow. Longitudinal and axial scans of an uncoiled umbilical cord confirm the presence of an SUA.

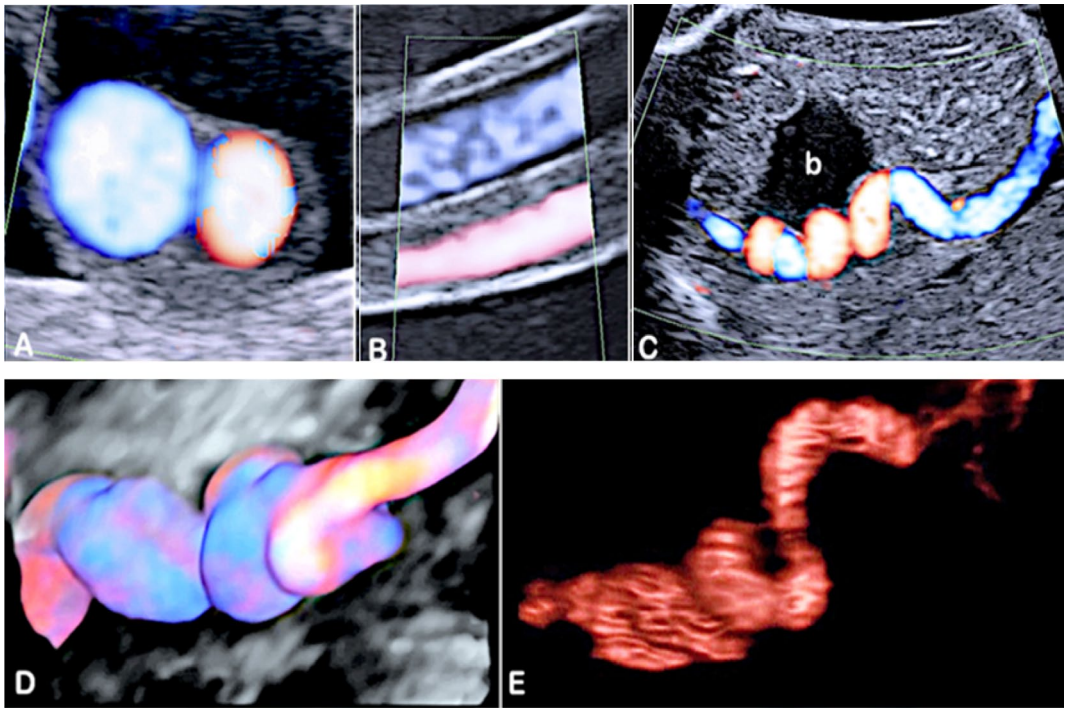

FIGURE 43 | (A, B) Pregnancy at 21 weeks' gestation. 2D color Doppler ultrasound. Axial and longitudinal sections of the UC show a single umbilical artery. (C) Axial scan of the fetal pelvis highlights a particular paravesical coiled course of the single umbilical artery. (D, E) 3D ultrasound with "glass-body" rendering mode and 4D angio spatio-temporal image correlation volume display with B-flow specify the course of the umbilical artery. Abbreviation: (b) bladder.

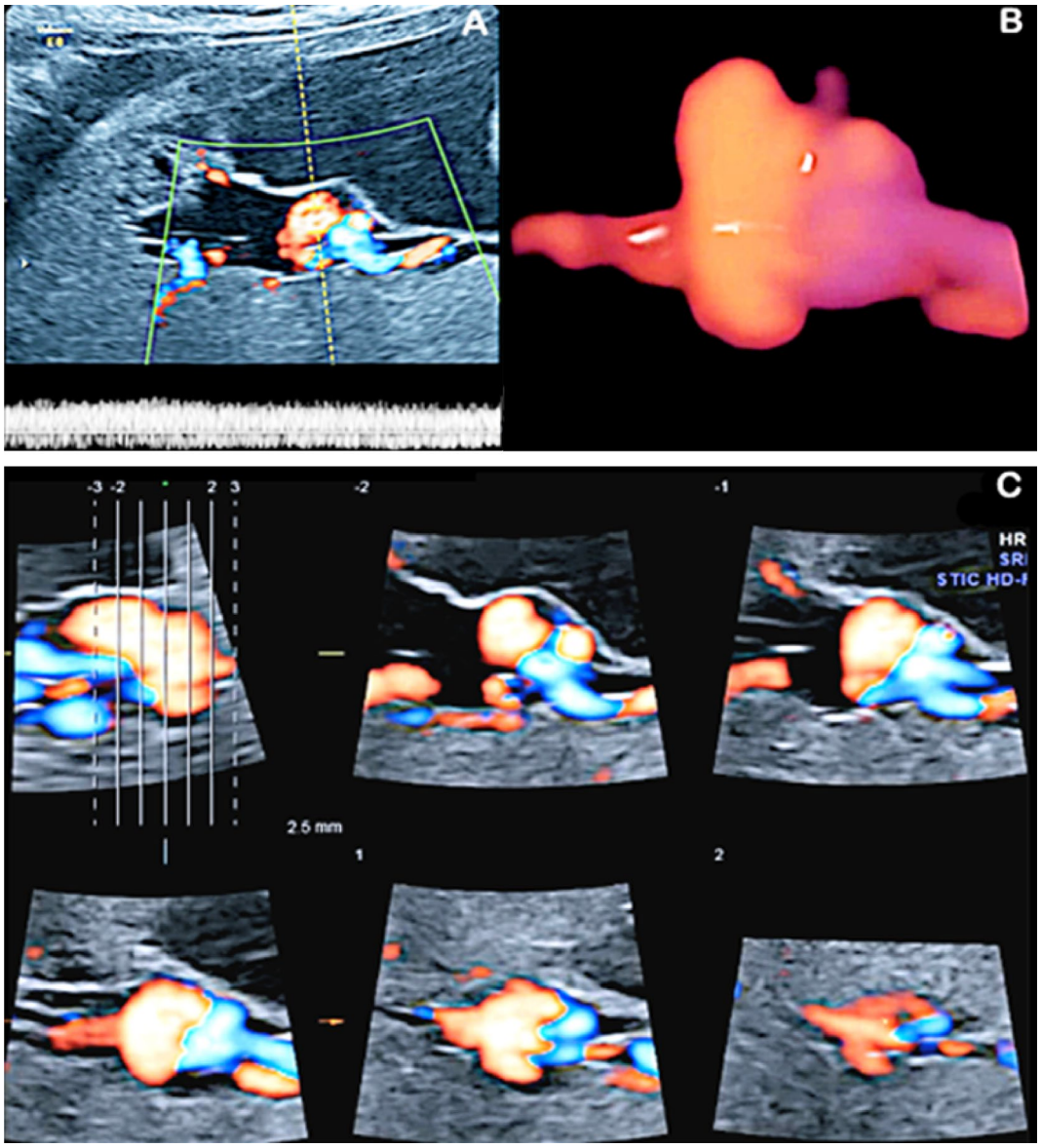

FIGURE 44 | Pregnancy at 25 weeks' gestation. Dichorionic-diamiotic placentation with a fused placenta. Aneurysmal dilatation of the umbilical vein near the insertion site of the cord on the placenta. (A) Color and spectral Doppler ultrasound imaging show vascular flow, a venous waveform, and a turbulent flow. These findings are indicative of umbilical cord varix. (B) The large varix may also be visualized by 4D angio spatio-temporal image correlation with color Doppler HD-Flow and by (C) tomographic ultrasound imaging mode presenting different planes of the varix.

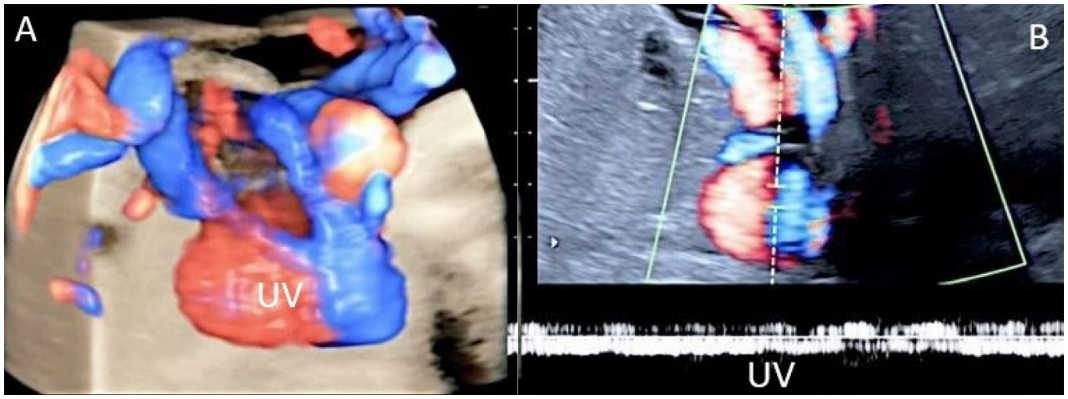

FIGURE 45 | (A) 3D ultrasound in "glass-body" rendering mode showing a localized aneurysmatic dilatation of the umbilical vein (UV) near the insertion of the cord on the fetal abdomen. (B) 2D ultrasound color and spectral Doppler show a bidirectional turbulent flow within the varix.

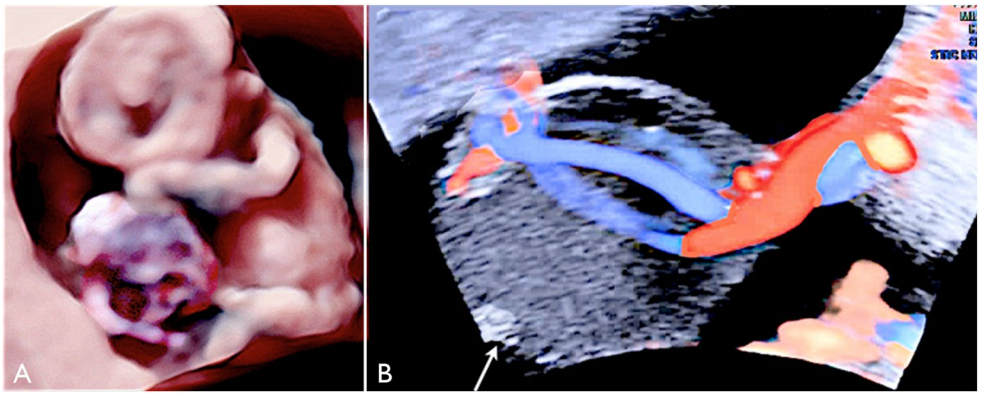

FIGURE 46 | (A) Fetus at 13 weeks' gestation. 3D ultrasound performed with HDlive allows the detection of a cord's hemorrhagic cyst. (B) Doppler ultrasound with "glass-body" rendering confirms the presence of a hemorrhagic cyst of the umbilical cord. Note a blood clot within the cyst (white arrow).

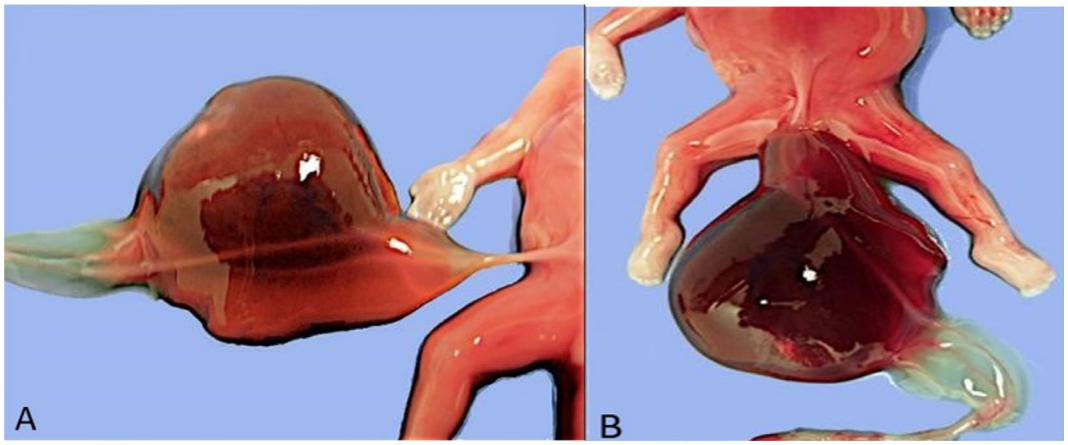

FIGURE 47 | (A, B) Pathologic correlation at the 13 weeks' gestation following spontaneous abortion.

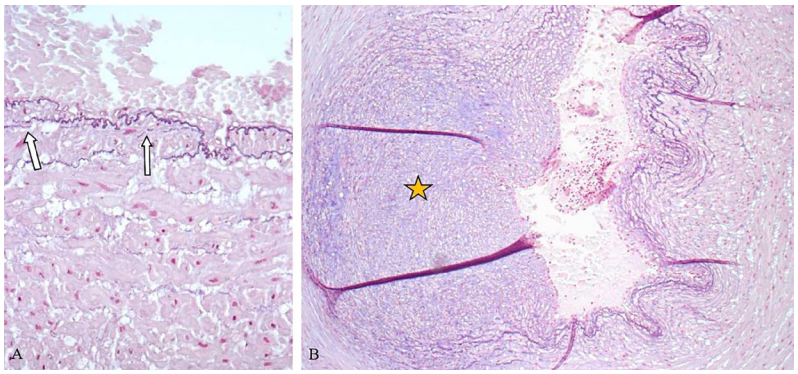

FIGURE 48 | (A) Histological examination showed a rupture in the wall of the umbilical vein, with discontinuity in the layers of the subintimal and internal elastic (white arrows), and (B) peripheral dissection of one umbilical artery associated with subintimal myxoid degeneration and widespread disruption of the elastic fibers (yellow star).

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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Appendix A

See Figure A1.

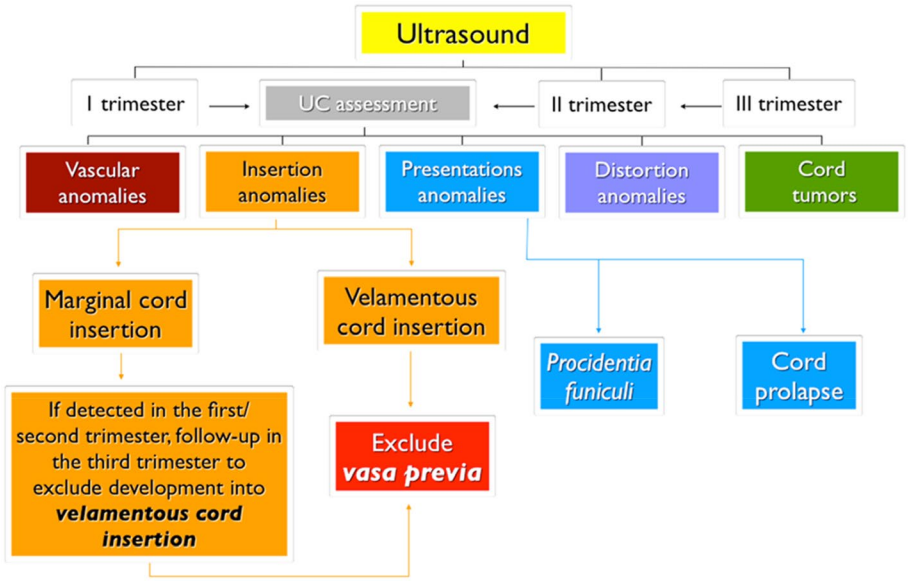

FIGURE A1 | This diagram shows a suggested algorithmic stepwise simplified approach for the ultrasound assessment and management of umbilical cord abnormalities, combined with a detailed study of the fetal anatomy. Abbreviation: UC, umbilical cord. Adapted from Moshiri et al. [2].

Appendix B

See Figure B1.

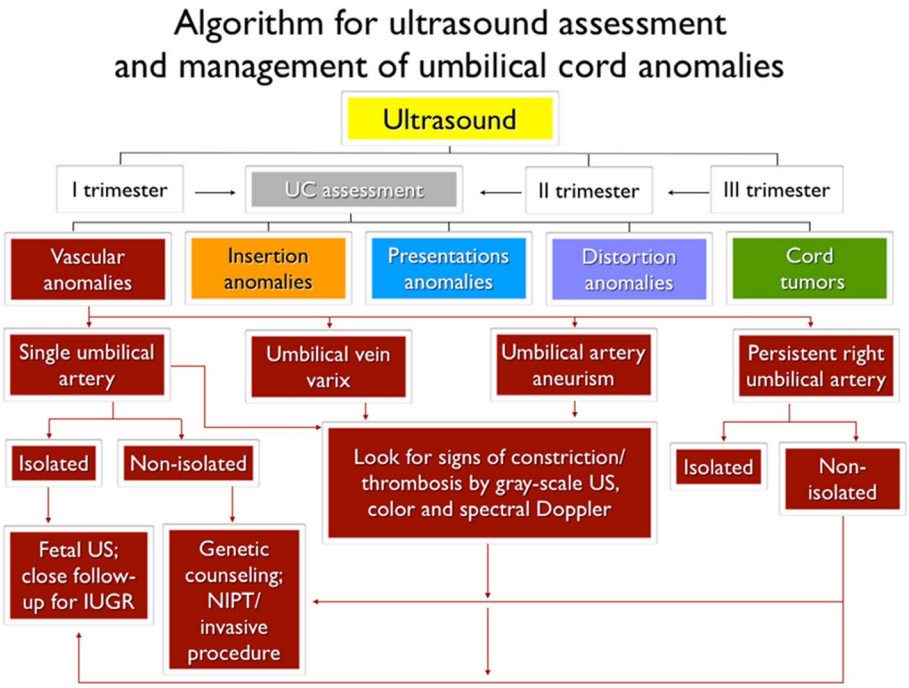

FIGURE B1 | This diagram shows a suggested algorithmic stepwise simplified approach for the ultrasound assessment and management of umbilical cord abnormalities, combined with a detailed study of the fetal anatomy. Abbreviation: IUGR, intrauterine growth restriction; NIPT, non-invasive prenatal testing; UC, umbilical cord; US, ultrasound. Adapted from Moshiri et al. [2].

Appendix C

See Figure C1.

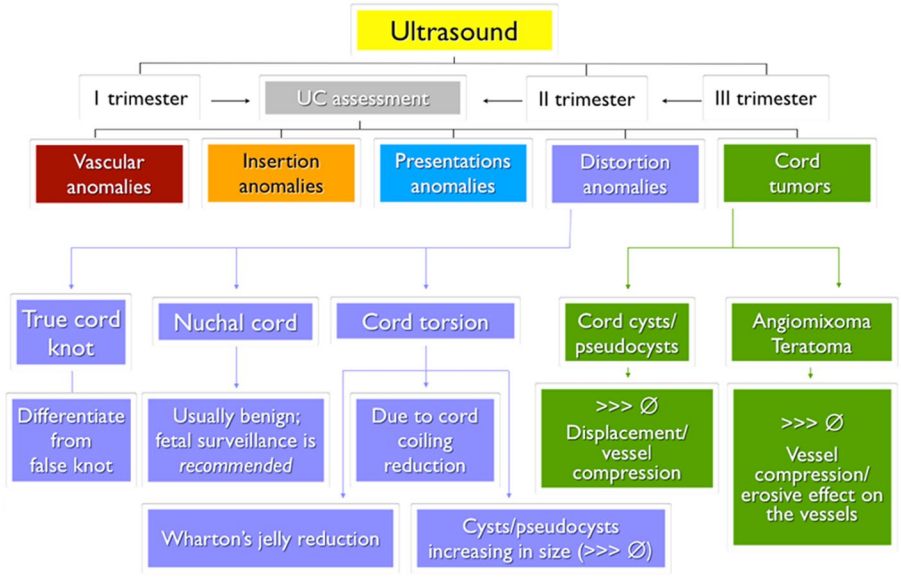

FIGURE C1 | This diagram shows a suggested algorithmic stepwise simplified approach for the ultrasound assessment and management of umbilical cord abnormalities, combined with a detailed study of the fetal anatomy. Abbreviation: UC, umbilical cord. Adapted from: Moshiri et al. [2].