Evaluation of the Placenta and Umbilical Cord
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Abnormal Fetal Umbilical Cord Doppler? What Should I Do Next? A Case Study Demonstrating Corroboration of Umbilical Cord Doppler and Middle Cerebral Doppler

Michelle M. Morrissette, BS, RT(R), RDMS, RDCS, RVT, FASE

Abstract
For the fetus at risk for intrauterine growth restriction (IUGR), umbilical cord Doppler provides the clinician valuable information about fetal circulation. When the cord Doppler is abnormal, spectral analysis of the middle cerebral artery (MCA) gives additional information about perfusion to the fetal brain. This case report describes a 31-week gestational age fetus referred for a biophysical profile and umbilical cord Doppler because of an abnormal nonstress test.

Keywords
umbilical cord Doppler, middle cerebral artery (MCA), biophysical profile (BPP), brain-sparing effect, fetal circulation

Case Report
Clinical Details
A woman in her 30s, gravida 3, para 2, presented for a BPP following a nonreactive stress test. Her past obstetrical history was significant for a stillbirth at 38 weeks. On the basis of the last menstrual period, the fetus had a gestational age of 31 weeks, 2 days, which correlated with a prior gestational age of 19 weeks, 2 days based on a previous sonogram. The nonreactive stress test demonstrated decreased fetal movement. The patient was referred for a BPP with umbilical cord Doppler, which was performed using a Siemens Sequoia (Siemens USA, Washington, DC) using a 4C1-S transducer (bandwidth 4-1 MHz).

The biophysical profile was performed following the American College of Obstetrics and Gynecology guidelines. The BPP assessment included evaluation of fetal
tone, fetal movement, fetal breathing, and amniotic fluid volume.

The fetus scored eight out of a possible eight points. Fetal heart rate was 138 beats per minute, with normal sinus rhythm. Total amniotic fluid index (AFI) was 8 centimeters. Fetal biometry demonstrated a fetus of 29 weeks, 5 days gestational age and in the 23rd percentile for growth.

Umbilical cord Doppler was performed without angle correction and sampled mid-cord. Umbilical cord Doppler samples were also obtained at the fetal and placental ends of the cord. The data obtained from the spectral analysis included standardized measurement of the systolic to diastolic ratio (S/D ratio), pulsatility index (PI), and resistive index (RI). By department protocol, if the umbilical cord Doppler is abnormal, the fetal MCA is sampled and an S/D ratio for the MCA is also calculated.

The spectral analysis of the umbilical cord demonstrated swift upstroke to a systolic peak with loss of diastolic flow (Figure 1). The S/D ratio was calculated at 23, the PI was 1.82, and the RI was 0.96. The umbilical cord was then sampled at the fetal end (Figure 2) and the placental end (Figure 3). Both areas demonstrated the same abnormal Doppler S/D ratio, PI, and RI as mid-cord (see Figure 4 for comparison to normal).

Because of the abnormal results of the cord Doppler, the fetal MCA was then sampled at the junction with the internal carotid artery (Figure 5). The MCA Doppler demonstrated significantly increased velocity through end diastole (see Figure 6 for comparison to normal). The MCA S/D ratio, when compared with the umbilical cord S/D ratio, was markedly reduced at 3.4; the MCA RI was 0.71. This fetus was then referred to the care of a perinatologist.

Discussion

The placenta’s function can be compared with the function of the lungs. The fetus receives oxygen-rich blood and nutrients from the mother via the placenta and...
umbilical vein. The maternal side of the placenta is analogous to a venous lake. On the fetal side of the placenta, villi arise from small branches of the umbilical arteries and vein and project into the placental venous lake. It is at the level of the villi that oxygen (O₂) and carbon dioxide (CO₂) are exchanged by the fetal blood.

In the uncompromised fetus, umbilical vein blood is about 80% saturated with oxygen compared with an approximate 98% arterial oxygen saturation in normal adults. Approximately 50% of umbilical vein blood will pass through the fetal liver. The remainder bypasses the liver and enters the inferior vena cava (IVC) via the ductus venosus. Blood from the ductus venosus joins deoxygenated blood returning from the trunk and lower extremities and, along with blood from the liver via the hepatic veins, merges to form streams in the IVC. Within the IVC, the streams of blood will maintain their identity. They are divided into two separate, although unequal, streams by the edge of the interatrial septum (crista dividens). The larger of these two streams is blood mainly from the umbilical vein. This blood is diverted to the left atrium via the patent foramen ovale. The smaller of the two streams of blood enters the right atrium and is joined by blood from the superior vena cava. The superior vena cava is composed of blood returning from the upper parts of the body and from the myocardium. Blood shunted through the foramen ovale to the left atrium is joined by blood returning from the lungs. Blood moves from the left atrium to the left ventricle into the aorta. In the ascending aorta, the majority of the blood goes to the head, upper thorax, and arms. The remainder of the blood joins blood from the ductus arteriosus and supplies the rest of the body and placenta. The majority of the blood in the descending aorta comes from the right ventricle and ductus arteriosus; it will enter the two umbilical arteries and supply the placenta. It is this blood flow from the umbilical arteries that is measured when performing umbilical cord Doppler.

After 30 weeks’ gestational age, the normal umbilical artery flow should have low-resistance characteristics, and the S/D ratio should be 3 or less with perfusion demonstrated throughout systole and diastole (Figure 4). The PI and RI values should be in the 50th percentile for gestational age; accordingly, a 31-week gestational age fetus would be expected to have a PI of 0.997 and RI of 0.600.

The normal fetal MCA will demonstrate a higher resistance waveform than the umbilical cord, although antegrade flow is maintained through the cardiac cycle (Figure 6). The normal MCA S/D ratio will always be greater than the S/D ratio of the umbilical cord for all gestational ages. The PI will have a predicted value for a specific gestational age, and the RI will be in the 50th percentile for gestational age.

Intrauterine growth restriction is compromised fetal growth. According to Callen, “In 1967, Battaglia and Lubchenco defined SGA (small for gestational age) as birthweight being below the 10th percentile for gestational age.” Intrauterine growth restriction is now viewed as a fetus that is failing to achieve its growth potential.

The intrauterine growth–restricted fetus tends to have a poor prognosis, with increased fetal morbidity and mortality.

The IUGR fetus is hypoxic, and in this hypoxic state, the fetal brain circulation vasodilates to allow more oxygenated blood to flow to the head. In doing so, more blood is shunted away from the liver to the head. This shunt, the ductus venosus, will dilate and capture as much as 70% of the umbilical vein blood, therefore increasing the size of the stream of blood passing through the IVC to the left atrium via the foramen ovale. It is this mechanism that affects the size of the fetal liver, altering the abdominal circumference, and making this measurement a sensitive indicator in the diagnosis of IUGR.

Theoretically, the brain-sparing effect is the result of cerebral vasodilatation as a response to the hypoxia. Doppler of the MCA will demonstrate a less resistant waveform than the umbilical artery Doppler with an increase in the diastolic flow. This will be reflected in a decrease in the S/D ratio, PI, and RI, which serve as markers of the brain-sparing effect.

This case demonstrates the merits of performing at a minimum umbilical cord Doppler when performing a BPP. For this fetus, the umbilical cord Doppler demonstrated loss of end-diastolic flow at samples obtained from the middle of the cord, the placental end, and the fetal end. The cord Doppler velocities showed an elevated S/D ratio of 2.3, a PI of 1.82, and an RI of 0.96.
The MCA demonstrated the brain-sparing effect. The MCA Doppler showed a lower resistance waveform than the umbilical artery, with increased flow through end diastole. The S/D ratio of the MCA was considerably less than the S/D ratio of the umbilical cord: 3.4 versus 23. The MCA RI was 0.71 versus the expected value of 0.798 in an uncompromised 31-week gestational age fetus.

Conclusion

This case demonstrated the complementary use of umbilical cord Doppler when performing a BPP examination. The BPP failed to demonstrate any fetal compromise. Addition of the umbilical cord Doppler demonstrated possible fetal distress, notably by loss of end-diastolic flow resulting in an elevated S/D ratio. Addition of MCA Doppler measurements showed increased end-diastolic flow and an S/D ratio less than the umbilical cord S/D ratio, evidence of the brain-sparing effect. These findings were instrumental in referring this patient to a perinatologist. The fetus was eventually delivered by caesarean section due to decreased BPP scores, continued abnormal umbilical cord Doppler, MCA Doppler, and fetal growth in the 10th percentile for age.

When performing routine BPPs, incorporating umbilical cord Doppler will give valuable information about the hemodynamic state of the fetus. When the umbilical cord S/D ratio, PI, or RI is abnormal, addition of MCA Doppler and its values for the S/D ratio, PI, or RI can give added information to the clinician for the management of the pregnancy.

Declaration of Conflicting Interests

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References

Intra-abdominal Umbilical Vein Varix Thrombus: From Diagnosis to Delivery

Michael McFadzen, RDMS, BA1, and Deann Harper, DO1

Abstract
Fetal intra-abdominal umbilical vein varix (FIUVV) is an uncommon finding with poorly understood clinical significance. Numerous fetal complications are associated with this anomaly. This case report demonstrates FIUVV in which thrombus develops leading to early induction of labor for successful delivery. The literature regarding FIUVV is reviewed and discussed with implications for sonographic follow-up during pregnancy and patient management.

Keywords
fetal umbilical vein varix, thrombus, Doppler, sonography

Fetal intra-abdominal umbilical vein varix (FIUVV) is defined as an umbilical vein that is at least 50% wider than the nondilated portion or dilation of 9 mm or greater.1 FIUVV is an uncommon abnormality with poorly understood clinical significance. Only 200 cases have been reported in the past 20 years. A study from Fung et al1 indicated that additional sonographic abnormalities were detected in 31.9% of fetuses with a 13% prenatal loss rate. There is an association of fetal malformations, fetal death, and chromosomal abnormalities; however, more recent studies indicate good fetal outcomes with isolated FIUVV.2 A comprehensive study by Mankuta et al.2 identified 28 cases of FIUVV out of 65,000 births over a 15-year period, with a prevalence of 1 case per 2300 births, and estimated that FIUVV represents 4% of umbilical cord abnormalities.3

FIUVV thrombus or clot is an extremely rare entity and requires close observation and management. Thrombus can block fetal venous circulation and cause sudden fetal death.24 This case follows one FIUVV thrombus through diagnosis, management, and successful delivery.

Case Report
A woman in her early 20s, gravida 1, para 0, presented for her initial sonogram at 19 weeks. The sonogram was normal other than a moderately echogenic bowel (Figure 1). The patient was referred to maternal fetal medicine, which confirmed the echogenic bowel, and an infectious etiology was suggested based on lab titers. The patient had negative herpes simplex type 1 and two IgG titers but an equivocal herpes simplex IgM. Repeat herpes simplex IgM subsequently was positive. Amniocentesis demonstrated normal chromosomes and no intra-amniotic infection. The patient was started on acyclovir, serial growth scans were recommended, and the patient returned to our care. The patient’s 33-week growth scan demonstrated an approximate 1-cm FIUVV adjacent to the fetal bladder (Figures 2 and 3). Twice-weekly Doppler and biophysical profiles scans were initiated to search for

1Aurora Sheboygan Clinic, Sheboygan, WI, USA

Corresponding Author:
Michael McFadzen, RDMS, BA, Department of Obstetrics/Gynecology, Aurora Sheboygan Clinic, 2414 Kohler Memorial Drive, Sheboygan, WI 53081, USA
Email: mcfadzen@msn.com
thrombus or signs of fetal compromise. At 35 weeks, thrombus was detected within the varix (Figures 4 and 5).

On the basis of the diagnosis of varix thrombus at 35 weeks and the potential for fetal complications from FIUVV thrombus, the patient underwent induction of labor. Continuous fetal monitoring was employed. The fetus developed repetitive variable heart decelerations, so a primary low transverse cesarean section was performed. A stable 2380-gram female with Apgar scores of 8 and 10 was delivered. There were no apparent signs of intrauterine growth restriction or infection.

**Discussion**

Diagnosis of FIUVV is defined by an umbilical vein that is at least 50% wider than the nondilated portion or dilation of 9 mm or greater. Due to increasing awareness and improved imaging technology, the frequency of diagnosis has increased in the past several years. However, the diagnosis of FIUVV thrombus remains very rare and is made by evidence clot within the varix. Only a few cases have been documented worldwide. Diagnosis is suggested with the sonographic finding of an anechoic structure adjacent to the fetal urinary bladder. Color Doppler is performed to determine vascularity and search for thrombus, which is characterized by local flow disturbances or, in the case of complete thrombosis, an absence of flow.

The diameter of the typical intra-abdominal umbilical vein increases approximately linearly from 3 mm at 15 weeks to 8 mm at term. Detection of FIUVV should prompt a thorough examination of the fetus to look for any additional sonographic anomalies, including a fetal survey and echocardiography. Close observation and
regular surveillance, including Doppler examinations and biophysical profiles, are indicated when FIUVV is seen. Fetal hemolytic disease should be ruled out, and karyotyping should be considered if other anomalies are present.

There are considerable differences reported in fetal outcome in the published FIUVV studies.\(^1,5,6\) Recent studies show improved detection rates, likely due to equipment advancements and practitioner awareness.\(^2\) Outcomes have been shown to be better when diagnosis of FIUVV occurs late in pregnancy.\(^1,7\) The authors surmise that improved outcomes are due to the presence of an isolated FIUVV, not complicated by other fetal abnormalities. Still, evaluation is necessary to rule out associated malformations and complications such as thrombus.

Clinical management of isolated FIUVV should follow standard established protocols, with good fetal outcomes expected.\(^2\) Sonographic assessment, including careful Doppler evaluation, should be performed biweekly to search for thrombus and hydrops and to monitor varix size.\(^2\) Delivery is recommended if thrombus is identified. This case reinforces the importance of careful and complete fetal evaluation on surveillance sonography.

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Umbilical vein varix (UVV) is defined as a focal enlargement of the umbilical vein and represents approximately 4% of fetal umbilical cord malformations. This rare anomaly, which was first described in autopsies of stillborn infants, can occur either intra- or extra-abdominally. Varicose dilation of the umbilical vein may be identified by sonographic examination, appearing as an anechoic cystic mass between the abdominal wall and the inferior part of the liver. Its vascular nature should be confirmed by Doppler ultrasonography to differentiate it from other intra-abdominal cystic lesions, such as urachal or choledochal cyst, distended gallbladder, and others.

There is no single universally accepted criterion for the in utero diagnosis of UVV. Some suggest an umbilical vein diameter of >9 mm or an index portion of the umbilical vein that is at least 50% wider than the nondilated portion. Others have defined it as a measurement that is more than two standard deviations above the mean for gestational age. Sepulveda et al defined UVV as a focal dilatation of the intra-abdominal portion of the umbilical vein, with a transverse diameter at least 1.5 times greater than the diameter of the intrahepatic umbilical vein. Using this criterion (which avoids the umbilical vein diameter relationship to gestational age), the authors identified cases of UVV as early as 22 weeks’ gestation, with a median gestational age of 27 weeks.

The reported neonatal outcome of fetuses with UVV varies widely due to its rarity, hence the small sample sizes of the case series in the literature. Earlier studies reported high fetal mortality, but more recent reports have demonstrated no association between UVV and intrauterine fetal death. However, more recent studies have demonstrated no association between UVV and intrauterine fetal death. The most common related sonographic abnormalities to UVV were malformation of the cardiovascular system, fetal hydrops, fetal anemia-related complications, umbilical vessel abnormalities, and intrauterine growth restriction. Trisomy 21, 18, and 9 and triploidy have also been described in association with UVV.

### Abstract

Umbilical vein varix (UVV) is defined as a focal enlargement of the umbilical vein and represents approximately 4% of fetal umbilical cord malformations. The reported neonatal outcome of fetuses with UVV varies widely due to its rarity, hence the small sample sizes of the case series in the literature. Earlier studies reported high fetal mortality, but more recent reports have demonstrated no association between UVV and intrauterine fetal death. A recent study has described a possible association between UVV diagnosed prenatally and child developmental delay. The present study of fetuses with UVV was done to evaluate and compare the levels of triple test serum biomarkers used for Down syndrome screening (human chorionic gonadotropin, α-fetoprotein, and unconjugated estriol) between a group of fetuses with uneventful obstetric outcome versus a subgroup of children with developmental delay.

### Keywords

umbilical vein varix, developmental delay, sonography, triple test serum biomarkers
The maternal triple serum markers conducted in the second trimester for Down syndrome (DS) screening are human chorionic gonadotropin or its free β-subunit (βhCG), α-fetoprotein (AFP), and unconjugated estriol (uE3). Elevated levels of maternal serum hCG (MShCG) and low levels of AFP and uE3 have been found to be associated alone or in combination with an increased risk for fetal DS. However, unexplained elevations of maternal serum AFP (MSAFP) and/or hCG exist in approximately 1% of the obstetric population and are associated with an increased risk of adverse pregnancy outcome, including miscarriages, low birth weight, preterm labor, abruptio placenta, preeclampsia, intrauterine fetal death, and a wide spectrum of fetal and placental malformations.

While reviewing the literature, we found only one anecdotal case report describing a combination of extra-abdominal UVV, elevated MSAFP of a 2.9 multiple of the normal median (MoM), and mesenchymal dysplasia of the placenta verified on postpartum histopathological examination. Obstetrical and postnatal courses were uneventful. Recently, our group described a possible association between UVV diagnosed prenatally and child developmental delay. In the present study, we have attempted to evaluate and compare the levels of triple test biomarkers between a group of fetuses with uneventful obstetric outcome versus a subgroup of children with developmental delay. All fetuses were diagnosed with UVV prenatally. To our knowledge, this profile of the developmental delay has not been previously reported.

**Methods**

The study design, patient population, methods, and baseline characteristics have been previously reported, and the study was approved by the institutional Clinical Research Committee prior to initiation. The study included fetuses with UVV that were referred to our Ultrasound Unit between 2005 and 2011. All underwent a detailed anomaly scan in the community. For the purpose of this study, only singleton pregnancies that were diagnosed with fetal intra-abdominal UVV were included. Prenatal workup of this referral group was composed of fetal echocardiography, a targeted ultrasonographic examination for possible associated malformations, and genetic counseling. Follow-up included a biweekly fetal well-being assessment using ultrasonography with Doppler flow studies, paying particular attention to fetal growth and vascular flow patterns within the variceal component for evidence of turbulence or thrombi. During the first years of our study, planned delivery was conducted at 36 to 37 weeks’ gestation after lung maturity was proven by amniocentesis. Later, induction of labor or planned delivery was conducted only upon obstetric indication and not because of the presence of the varix.

After delivery, all newborns were assessed by a pediatrician specialist to rule out any additional anomalies or dysmorphic features. For the current study, we retrieved data from the patients’ medical records on the second-trimester triple test results. Data regarding patient demographics, pregnancy, and obstetrical outcome as well as infant and child follow-up were obtained from the medical records in the obstetric, pediatric, and child developmental clinics and by telephone interview to the parents.

Developmental delay was assessed by a telephone interview using a questionnaire based on the Ages and Stages Questionnaire. If the child’s score was below the cutoff in one or more domain(s), the families were offered a formal cognitive assessment by our pediatrician and developmental psychologist team.

**Screening Tests**

The second-trimester screening test was derived from the combination of triple serum markers and maternal age, and results were calculated using commercial software. The maternal serum markers evaluated in this study were maternal serum hCG or its free β-subunit (FβhCG), AFP, and uE3. The serum samples were tested in a routine analytical run together with regular maternal serum samples, all in the same prenatal Down syndrome screening program. Testing was carried out in a manner that was blinded to group classification; that is, samples from our study cases and those of other pregnant women were assessed in the same laboratory. The measured marker levels were expressed as multiples of the gestation-specific normal medians (MoM). Median values for each serum analyte were calculated against completed menstrual weeks and adjusted for maternal weight. We compared results with reference MoM values that were calculated from our own local population as established in Zer Medical Laboratories (certified and authorized by the Ministry of Health, Israel).

**Statistical Analysis**

Standardized kurtosis showed that the data were derived from a normal distribution and were expressed as a mean and standard deviation. Frequencies were expressed as percentages. Statistical analysis was performed using the Fisher exact test for intergroup comparison of developmental delay. Student t test was used to compare the second-trimester markers between different groups. AFP and hCG concentrations were logarithm transformed to follow normal distributions; uE3 showed normal Gaussian distribution.
A one-sample *t* test was applied to compare the results among the study and control groups to normal population values. A *P* value < .05 was considered significant. Calculations were performed in the statistical laboratory at Tel Aviv University using SPSS software (version 13; SPSS, Inc, an IBM Company, Chicago, Illinois).

**Results**

Overall, 36 fetuses were identified with UVV in our patient population. Of these, 31 (86%) were included in our study, excluding five (14%) twin pregnancies. UVVs were identified at a range of 20 weeks’ to 36 weeks’ gestation (mean ± SD, 30.5 ± 4.5 weeks) (Figure 1). The average UVV diameter was 11.9 mm (range, 8–17 mm). Mean maternal age of the UVV group was 31.9 ± 4.3 years (range, 23–44 years). Gestational age at delivery was 37.2 ± 2.1 weeks (range, 32–41 weeks’ gestation). Newborn birth weight was 2812.7 ± 526.7 g (range, 1710–3810 g). Apgar scores at 1 and 5 minutes were 8.8 ± 12 and 9.8 ± 0.6, with a range of 2 to 10 and 7 to 10, respectively. Child age at follow-up evaluation was 2.5 ± 1.8 years (range, 0.2–6.8 years).

In six (16.7%) cases of UVV, other anomalies were detected on ultrasonographic examination. Mild to moderate hydronephrosis was the most common finding, accounting for three (50%) of these abnormalities. One case of UVV was diagnosed with DiGeorge syndrome, one with an atrial septal defect/ventricular septal defect, and one with a single umbilical artery. There were no cases of intrauterine fetal or neonatal death.

Median hCG, AFP, and uE3 levels are shown in Table 1. The median hCG, AFP, and uE3 levels of women in the entire UVV study group were not significantly different from the control reference group. In addition, these markers were not significantly different between the two subgroups of developmental delay versus normal development cases as well as compared with the overall and control laboratory data.

**Discussion**

With the improvements in image quality and Doppler capabilities in ultrasonography over the past years, the frequency and awareness of the diagnosis of UVV have increased substantially. In the current study, the MoM levels of triple test biomarkers in fetuses diagnosed with...
UVV were not significantly different among a group of children with uneventful pregnancy outcome compared with a subgroup of children with developmental delay as well as in comparison to a normal reference group.

Some studies have suggested that placental pathology may be associated with increased levels of hCG or elevated AFP. Hypoxia increases hCG overproduction in trophoblastic cells cultured in vitro.25 Placental pathology at delivery, such as infarction, ischemic changes, villitis, and intervillous thrombosis, has been associated with increased hCG concentrations.26 All of these placental pathologies may cause inadequate trophoblastic remodeling of the maternal uterine vasculature with an absence of physiologic changes in the spiral arteries, leading to placental hypoxia and hCG overproduction.

Other studies have suggested that placental pathology may permit a more rapid diffusion of AFP from the fetoplacental compartment to the maternal compartment, resulting in elevated AFP levels in maternal serum.27,28 This hypothesis is further supported by Mulch et al,21 who presented a case report where UVV was associated with an elevated maternal serum AFP on prenatal testing and mesenchymal dysplasia on pathological evaluation of the placenta. In the patient’s case report, they found long-standing mural thrombi in the varix on postpartum histopathological examination that were not detected on prenatal ultrasound. Vascular flow, however, was never fully compromised by the thrombi, as verified by Doppler flow studies and normal fetal growth. Their study emphasized the fact that a meticulous examination of the placenta and placental structures should undergo careful examination, both gross and microscopic, following delivery.

**Developmental delay** is a term that generally refers to children who do not show the expected developmental properties according to their age. The US Census Bureau has reported a 4.5% rate of developmental disability among children up to five years of age.29 The precise mechanism by which UVV may be associated with postnatal developmental delay abnormalities in apparently normal fetuses is yet unknown. Recently, our group proposed various possible hypotheses.22

Some of the proposed mechanisms that may cause in utero fetal death may also be relevant for postnatal developmental delay. UVV predisposes to thrombosis, due to significant abnormal flow patterns within the varix such as flow separation, turbulent blood flow, and shearing stress.7,30 One hypothesis suggests an early episode in which fragmentation and dispersal of the microthrombi occurs with paradoxical embolization through a patent foramen ovale. This can even be supported by the paradoxical embolism phenomenon, in which systemic passage of thrombi through an interatrial conduit (right-to-left shunt) is thought to be the mechanism of stroke in patients with patent foramen ovale (PFO). Small blood clots and microaggregates of venous origin may cross the PFO, thereby escaping lysis in the lungs and leading to clinically significant sequelae in the brain. The shunting of these particles could occur after a Valsalva maneuver or in relation to a chronic condition causing increased pulmonary artery pressure.31 An association between thrombosis of the UVV and disseminated intravascular coagulation also has been recently reported, suggesting that postnatal developmental delay abnormalities may be a result of consumption of coagulation factors on the thrombogenic surface of the UVV segment, with the subsequent occurrence of micro-infarctions in various areas throughout the brain.32,33

Another hypothesis by which UVV may be associated with postnatal developmental delay abnormalities may mimic one or several of the mechanisms by which a varicocele (an abnormal dilation of the spermatic veins within the scrotum) can cause abnormalities of the testis and semen parameters by increased scrotal temperature, reflux of toxic metabolites, decreased volume of blood flow, and anoxia.34

Despite the above hypotheses relating pre- and postnatal compromise to the fetal varix formation and its
sequelae, early imprints of the effects of the varix were not found in the mid-gestation triple test profile in our entire study population or in the subgroup of the developmentally delayed children. This may be explained by the supposition that some of the adverse mechanisms previously mentioned develop later in gestation after this test is conducted or that there is simply no relation between the two events.

In conclusion, this is the first study to evaluate and compare the levels of triple test biomarkers between fetuses diagnosed with UVV prenatally and later found to have developmental delay in postnatal life and a subgroup of children with UVV and uneventful obstetric outcome. Overall, the entire study cohort, as well as the two subgroups, had triple test results similar to those found in general population. Additional studies should be conducted to verify our results.

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1. The normal fetal Middle Cerebral Artery (MCA) will demonstrate ___________ resistance wave form from the Umbilical Cord.
   A. A higher
   B. A lower
   C. The same
   D. A Slower

2. In the Intra-Uterine Growth Restrictive) IUGR fetus, The Ductus Venosus will dilate and capture as much as ___________ of the umbilical Vein blood.
   A. 50%
   B. 60%
   C. 70%
   D. 90%

3. Regarding the triple test markers: The maternal serum markers evaluated in this study were:
   A. UVV, Maternal Serum hCG, AFP
   B. AFP, Maternal Serum hCG, UVV
   C. Maternal Serum hCG, UE3, UVV
   D. Maternal Serum hCG, AFP, UE3

4. When the spectral analysis of the umbilical cord is abnormal, the following fetal vasculature should be sampled:
   A. Middle cerebral artery and or the posterior cerebral artery
   B. Posterior cerebral artery and or ductus venosus
   C. Middle cerebral artery and or ductus venosus
   D. Ductus venosus and or carotid artery

5. Oxygen (O2) and carbon dioxide (Co2) are exchanged by the fetal blood on the fetal side of the placenta via the:
   A. Venous lake
   B. Villi
   C. Lungs
   D. Umbilical artery

6. The use of umbilical cord Doppler was thought to be a useful addition to what type of fetal exam?
   A. 2nd trimester screening exam
   B. 1st trimester screening exam
   C. All fetal ultrasound exams
   D. Bio-Physical Profile

7. In the uncompromised fetus, umbilical vein blood has an oxygen saturation of:
   A. 50%
   B. 60%
   C. 80%
   D. 85%

8. A focal enlargement of the umbilical vein which represents approximately 4% of fetal umbilical cord malformations best describes what?
   A. A triple test marker
   B. Umbilical artery varix
   C. Fetal hydrops
   D. Umbilical vein varix

9. A recent study has described a possible association with Umbilical Vein Varix (UVV) diagnosis prenatally and what?
   A. Child development delay
   B. High fetal mortality
   C. Placental pathology
   D. hCG overproduction

10. The diameter of the typical intra-abdominal umbilical vein increases in a linear fashion approximately from:
    A. 2mm at 15 weeks to 5mm at term
    B. 3mm at 15 weeks to 8mm at term
    C. 8mm at 15 weeks to 15mm at term
    D. 1.5cm at 15 weeks to 2.0 cm at term

11. The definition of a fetal intra-abdominal umbilical vein varix is one that is
    A. 20% over the non-dilated portion
    B. 40% over the non-dilated portion
    C. 50% over the non-dilated portion
    D. Dilated more than 5mm