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ORIGINAL ARTICLE

# FIUVV: Associations and Outcome

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**Abstract** To investigate the ultrasound characteristics, associations and obstetric outcomes in pregnancies with intra-abdominal umbilical vein varix of the fetus. This was a retrospective cohort study conducted over 2 years from March 2019 to February 2021. The data collected were demographic characteristics, varix characteristics, obstetric complications (fetal growth restriction/IUFD) and neonatal outcomes. Descriptive statistics (means, standard deviations, and percentages [%]) were calculated using SPSS, version 21.0 (SPSS Inc, Chicago, USA). Over the period of 2 years, six cases of FIUVV were diagnosed putting the incidence of FIUVV at 5/10000 pregnancies. The incidence of isolated FIUVV was 4.4/10000 cases. Mean gestational age at diagnosis was 25 weeks 3 days with earliest diagnosis at 19w1D. Mean varix size was 11.85 mm ± 2.28 mm (range 8.9–14.8 mm). No incidence of turbulence or thrombus formation within the varix was seen in the current study. One case had absent DV with anomalous drainage of the umbilical vein in to the IVC along with pleural effusion, polyhydramnios and increased nuchal fold thickness. Perinatal death after planned LSCS at term was noted in this pregnancy. One case had rapid dilatation of the varix from 9.5 at 19 weeks to 15.4 mm at 27 weeks. The patient reported sudden IUFD at 33 weeks. The association of FIUVV with the adverse obstetrical outcomes was seen in some cases during the current study. Increased surveillance to look for rapid dilatation/ turbulence/ thrombosis may prevent adverse perinatal outcomes.

**Keywords** FIUVV · Umbilical vein · Aneuploidy · Fetal malformations · IUFD

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## Introduction

The Focal dilatation of the intra-abdominal, subhepatic portion of the umbilical vein in a fetus is termed as fetal intra-abdominal umbilical vein varix (FIUVV). This condition is a rare abnormality and has a varying reported prevalence of 0.6/1000 to 2.8/1000 deliveries [1, 2]. Isolated FIUVV has an even lower reported prevalence of 1/2300 [3]. In earlier studies, very strong associations of FIUVV with other fetal malformations and poor perinatal outcomes were reported [4], but recent systematic reviews [1] and retrospective studies [2, 3, 5] have shown a lower overall incidence of associated major structural malformation (9–28% of cases) & a lower association with aneuploidies (0–5% of cases). Isolated FIUVV cases are associated with better perinatal and long term outcomes [3]. With recent advancements in screening modalities such as color Doppler and 3D–4D ultrasound (Fig. 1, 2), and with stress on earlier screening of fetuses, this condition is now being diagnosed

in early anatomy scans. Management depends on associated malformations, associated aneuploidies and the presence or absence of turbulence/ thrombus in the dilated vein. We present the retrospective analysis of data on incidence, associations and outcome of FIUVV cases at our Center of Fetal medicine.

### Aims and Objective

To investigate the ultrasound characteristics, associations and obstetric outcomes in pregnancies with intra-abdominal umbilical vein varix of the fetus.

## Materials and Methods

Our study is a retrospective cohort study conducted over a period of 2 years from March 2019 to February 2021. All cases with a diagnosis of fetal intra-abdominal vein varix, during the study period were included in the study. Both singleton and multiple pregnancies were included in the study. All scans were performed using a convex abdominal transducer at a frequency of either 3.5 or 5 MHz with one of the following ultrasound models (Voluson E6 BT18, Voluson S10 expert, GE Medical Systems, Zipf, Austria). The FIUV varix diameter was measured from one outer edge to the opposite inner edge with electronic calipers on axial images immediately cephalad to the insertion of the umbilical vein into the fetal abdomen. In cases with a suspected umbilical vein varix, color-flow Doppler imaging and a detailed fetal anatomic survey were done to look for other associated conditions. Invasive testing was offered only when FIUVV was associated with other major or minor structural abnormalities or in the presence of hydrops. Cases with intermediate/high risk in aneuploidy screening were also offered invasive testing.

Apart from routine demographic characteristics, data was collected on the status of aneuploidy screening, gestational age at the time of diagnosis, size of varix at the time of diagnosis, progression of the varix size, turbulence & thrombus formation, and, association with any other major or minor structural malformations if present. The following outcome parameters were noted- gestational age at delivery, birth weight, sex of the baby, mode of delivery, NICU admission and perinatal mortality.

Statistics: Descriptive statistics (means, standard deviations, and percentages [%]) were calculated using SPSS, version 21.0 (SPSS Inc, Chicago, USA). P values were not calculated because of too small sample size.

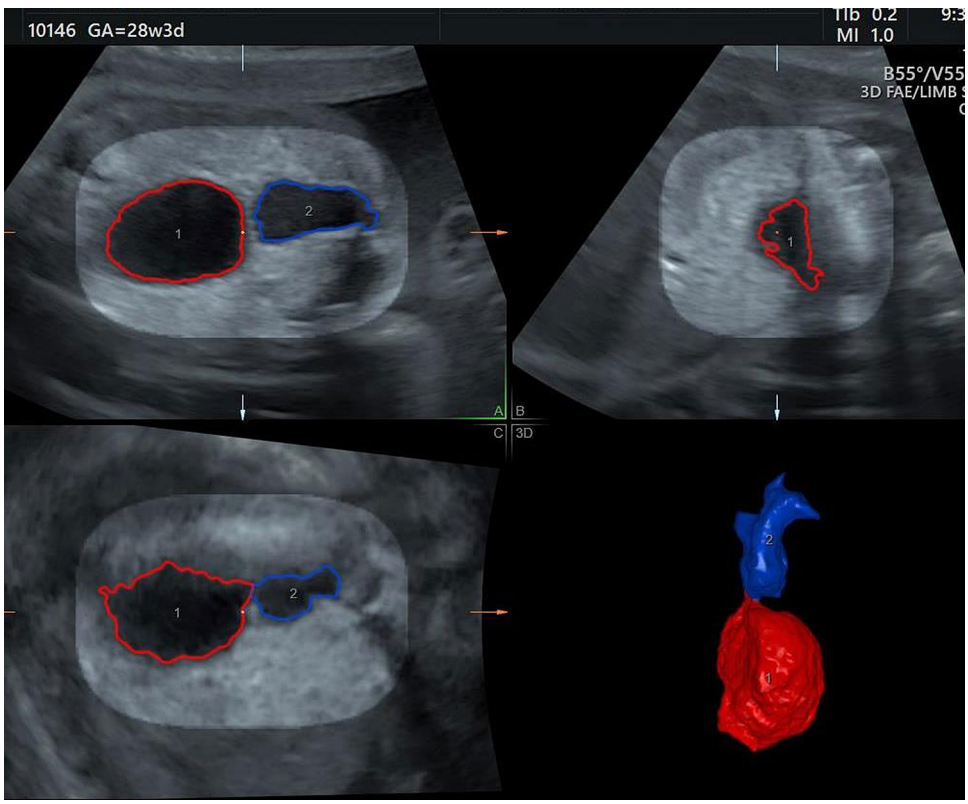


**Fig. 1** Sono AVC with inversion mode (3D rendering view) demonstrating cast of the umbilical vein varix (UVV)2 and fetal urinary bladder 1 and their mutual relationship

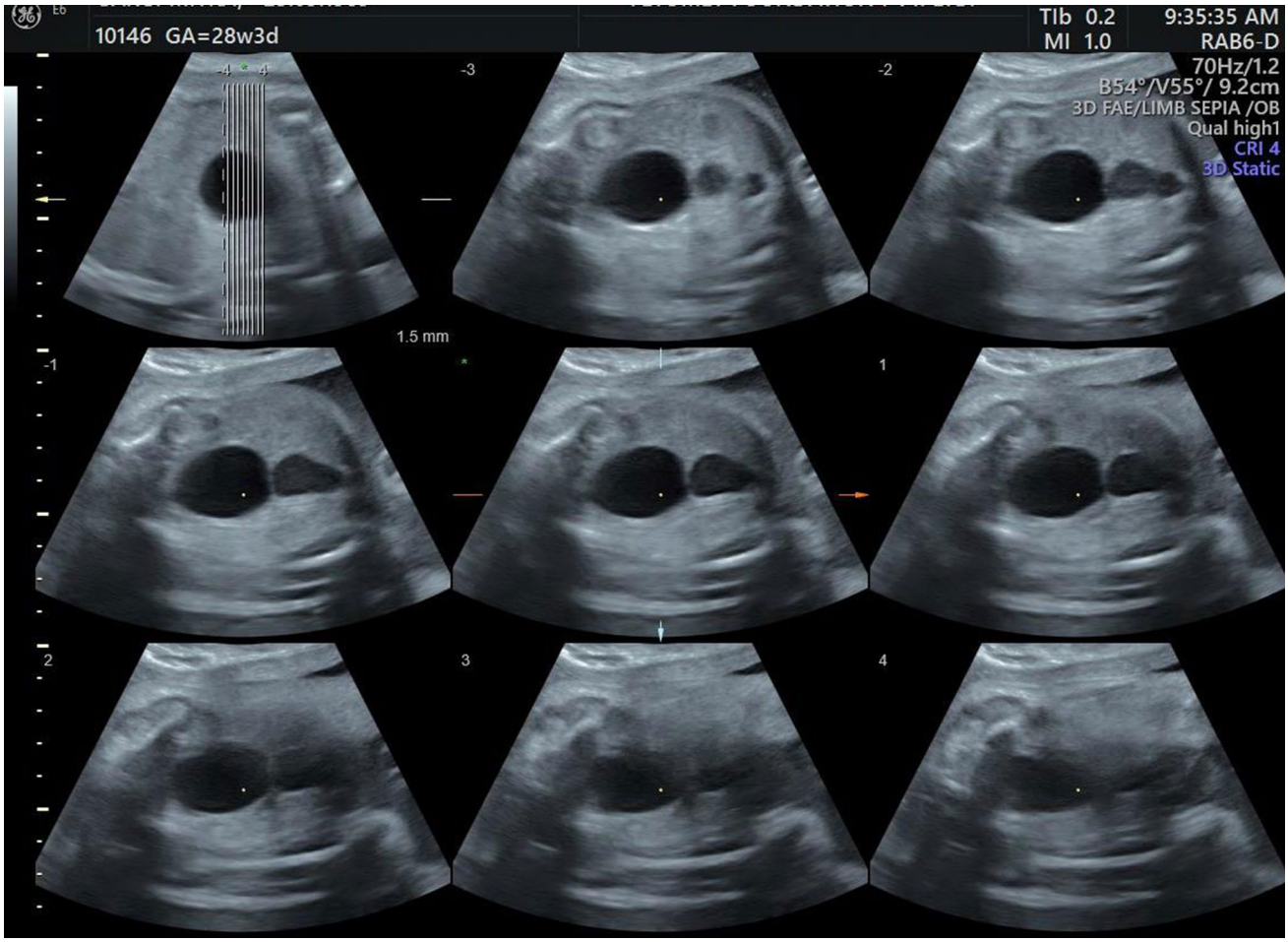


**Fig. 2** Multiplanar reconstruction in tomographic ultrasound imaging (TUI) mode demonstrating the spatial relationship of umbilical vein varix to the anterior abdominal wall (at the level of cord insertion) and fetal urinary bladder posteriorly

## Results

Over the period of 2 years from 1st April 2019 to 31st march 2021 11,462 obstetric patients were scanned at our center out of which 6,769 belonged to second and third trimester and 1069 were twin pregnancies. During this period six cases of FIUVV were diagnosed at our center making the incidence of FIUVV 5/10000 pregnancies and 8.9/10000 s-third trimester obstetric cases. As FIUVV is more commonly diagnosed in the late second or early third trimester its incidence also increases with gestational age. None of the cases were diagnosed before 19th week of gestation. The incidence of isolated FIUVV was 4.3/10000 pregnancies at our center. Out of six FIUVV cases, one pregnancy was dichorionic diamniotic twin pregnancy making its incidence 9.3/10000 twin pregnancies and 0.87/10000 pregnancies. The demographic data of cases is summarized in Table 1.

Mean maternal age in the FIUVV cases was $32.67 \pm 3.361$ years ranging from 29 to 38 years. There were three second gravidas with a history of previous miscarriages seen in two cases and one carried previous pregnancy till term and delivered a healthy baby. Only one case has conception through assisted reproductive technique rest were natural pregnancies.

**Aneuploidy screening and genetic testing:** Out of six cases, only one case had no aneuploidy screening. In the rest of the five cases, four were screened by combined first trimester screening and one by quadruple marker test in the second trimester. In those FTS cases, one test came out as intermediate risk for Trisomy 21 for which noninvasive prenatal testing was done which showed low risk for aneuploidies. Invasive testing was not offered in isolated FIUVV cases. It was recommended in the case with hydrops and absent ductus venosus. The test was refused by the patient because of financial and cultural beliefs (Fig. 3).

**Table 1** Demographic and other characteristics

| S. no. | Parameter | Outcome |
|---|---|---|
| 1 | Age | Mean ± SD: 32.67 ± 3.361 years |
| 2. | Parity | N (%) |
| | Primigravida | 3 (50%) |
| | Second gravida | 3 (50%) |
| | Living issues | 2 (33.33%) |
| 3. | Conception | |
| | Natural | 5 (83.33%) |
| | ART | 1 (16.67%) |
| 4. | Gestation | |
| | Single | 5 (83.33%) |
| | Multiple (DCDA) | 1 (16.67%) |
| 5. | Associated disorders | |
| | Diabetes | 1 (16.67%) |
| | Hypothyroidism | 2 (33.33%) |

## Varix Details and Fetal Survey

Mean gestational age at the time of diagnosis was 25 weeks 3 days ranging from 19w1d to 30w4d. Mean varix size was 11.85 mm ± 2.28 mm at the time of diagnosis. The smallest varix size noted was 8.9 mm and the largest was 14.8 mm (Table 2). In most of the cases, the size of the varix remained constant during gestation except for two cases. The first showed a decrease in size from 24 at 28 weeks 6 days to 16 mm at 34 weeks 3 days. In the second case the varix size increased from 9.5 at 19 weeks to 15.4 mm at 27 weeks. No hydrops or turbulence/thrombus were noted. The patient was lost to follow up and reported at 33 weeks with loss of fetal movements.

Fetal growth restriction and turbulence within the varix or thrombus formation was not seen in any of the FIUVV affected pregnancies in the current study. Only in one of the cases fetal hydrops with pleural effusion, polyhydramnios, increased nuchal fold thickness and absent ductus venosus with an anomalous connection of umbilical vein with inferior vena cava was noted (Figs. 4 and 5). In twin gestation, the co-twin of the affected fetus showed echogenic intracardiac focus. The rest of the anatomy of both the twins was normal.

**Obstetrical outcome:** The overall Mean gestational age of delivery in all six diagnosed cases was 37w2d and there was no significant difference between good and adverse perinatal outcome groups. The main mode of delivery was lower segment cesarean section for indications enumerated in Table 3. The average birth weight was 2.95 ± 0.6 kg, with mean and standard deviation in surviving and non-surviving groups at 3.25 ± 0.524 kg and

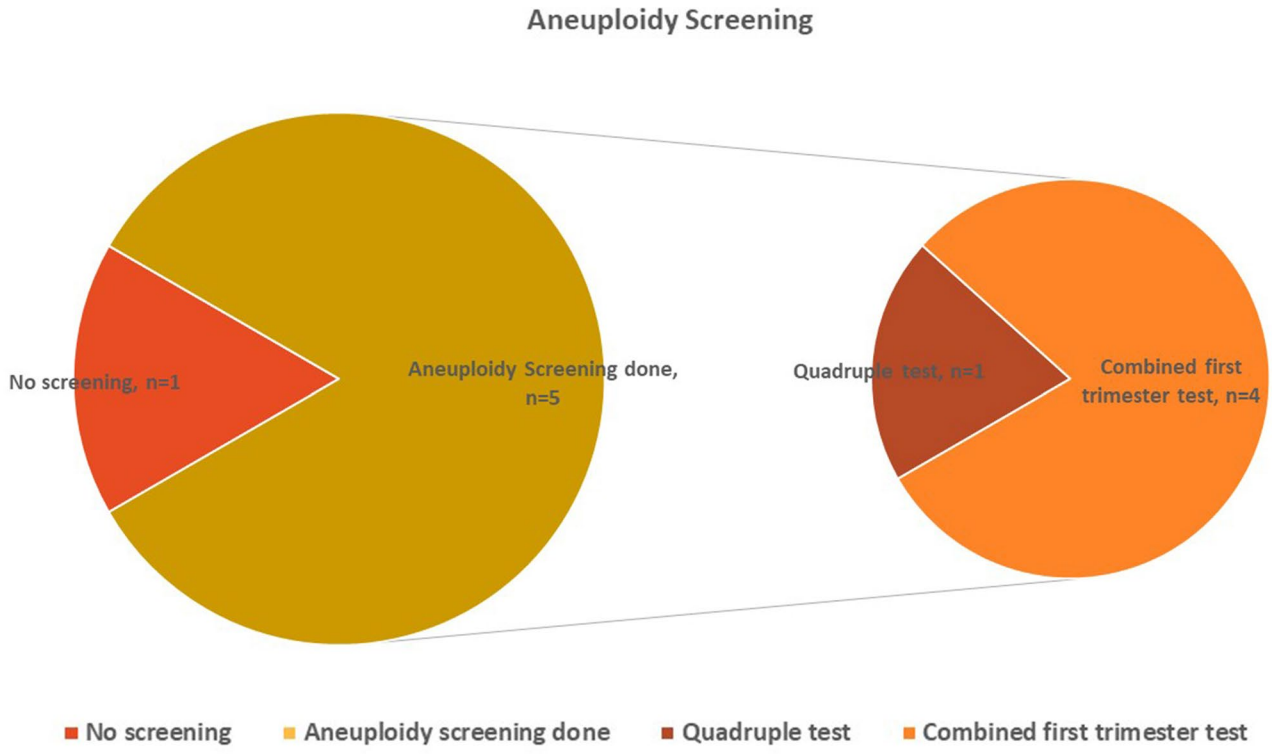


**Fig. 3** Aneuploidy screening status

**Table 2** Varix details

| S. no. | Varix Characteristics | Outcome |
|---|---|---|
| 1. | Gestational age at diagnosis | Mean 25w3d |
| | Range | 19w1d–30w4d |
| | Mean in adverse outcome cases | 24 weeks ± 7 weeks |
| | Mean in good outcome cases | 26w3d ± 4.7 weeks |
| 2. | Varix diameter | Mean- 11.85 mm ± 2.28 mm<br>Range- 8.9–14.8 mm |
| 3. | Turbulence | – |
| 4. | Thrombus | – |
| 5. | Hydrops | 1 (33.33%) |
| 6. | FGR | – |

2.35 ± 0.92 kg respectively. Out of six cases, two were male and four were female making the sex ratio of male: female of 1:2. Two cases of adverse obstetric outcomes were noted in the current study, the first case suffered intrauterine fetal demise at 33 weeks. The pregnancy was terminated by induction of labor with the delivery of a macerated female fetus weighing 1.7 kg. No postnatal autopsy or genetic test was done as it was refused by the patient. In the antenatal period the same case has shown a rapid increase in varix size from 9.5 at 19 weeks to 15.4 mm at 27 weeks. The second case showed hydrops, absent ductus venosus with an anomalous connection of portal vein with IVC in antenatal scans. The patient was counseled about the possibility of adverse perinatal outcomes and the need for invasive genetic testing (no aneuploidy screening test was done by the patient). The patient refused the latter and continued her obstetrical care at another place. The data collected from that centre was studied retrospectively and showed no increase in varix size during the antenatal period. However, no further comments were noted on hydrops and pleural effusion. The patient underwent elective LSCS at term with the delivery of a male child weighing 3 kg. The baby failed to cry after birth and succumbed immediately after. (Table 3).

In the cases with adverse obstetrical outcomes, the association with (1) diagnosis at earlier gestational age, (2) significant increase in size and (3) hydrops was noted

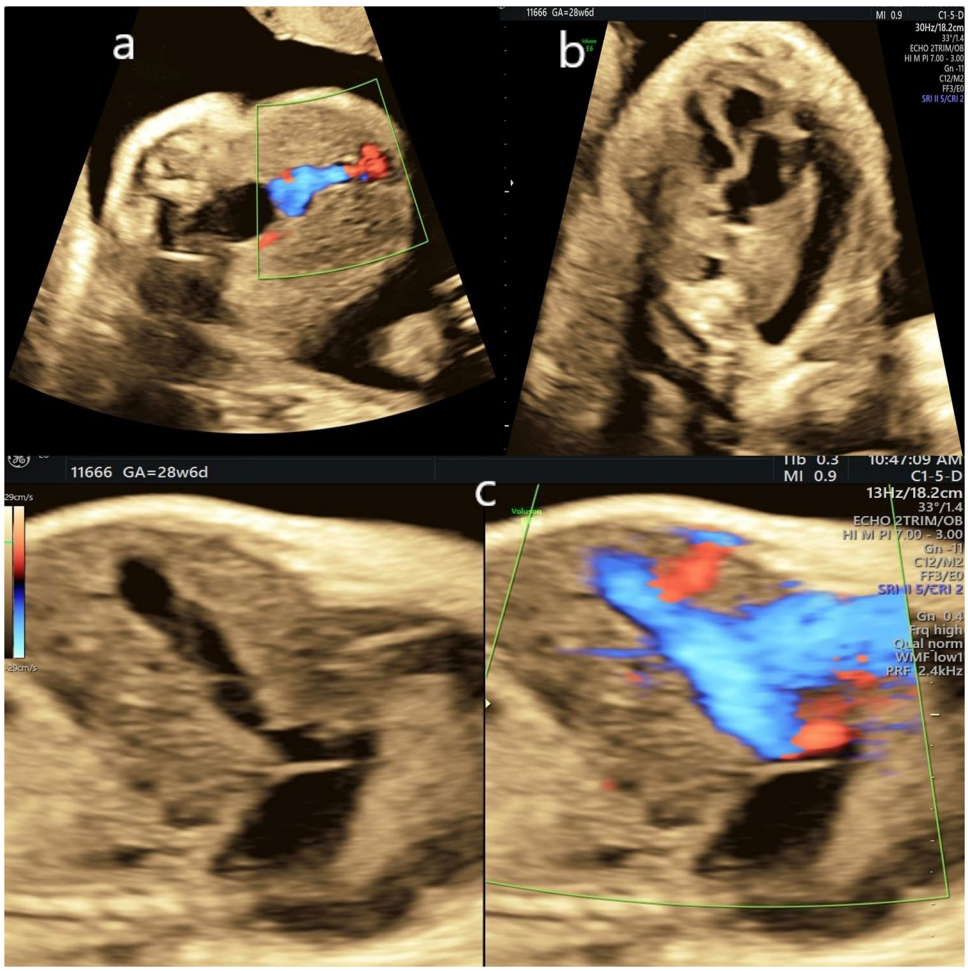


**Fig. 4** 2D and color flow imaging of a fetus showing **a** FIUVV, **b** Pleural effusion, c Absent Ductus venosus with Umbilical vein directly draining into inferior vena cava (aberrant course) leading to volume overload

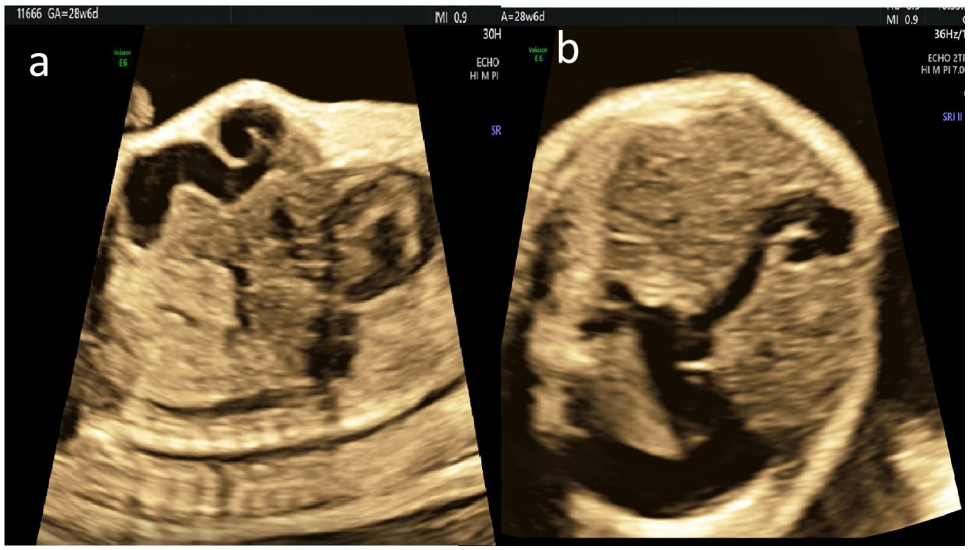


**Fig. 5** **a** Proximally dilated and tortuous extrahepatic course of the umbilical vein. **b** Intrahepatic portion of the umbilical vein is seen draining directly into intrahepatic portion of IVC with right sided pleural effusion secondary to volume overload

**Table 3** Obstetrical outcome

| S. no. | Obstetric parameter | Outcome |
|---|---|---|
| 1. | Mean gestational age of delivery | 37w2d |
| | In good fetal outcome | 38 ± 1.4 weeks |
| | In adverse fetal outcome | 36 ± 4.2 weeks |
| 2. | Mode of delivery | |
| | Vaginal | 1 (16.67%) |
| | LSCS | 5(83.33%) |
| 3. | Indication of termination | |
| | Previous LSCS | 2 (33.33%) |
| | PPROM | 1 (16.67%) |
| | IUFD (delivered vaginally) | 1(16.67%) |
| | Elective LSCS at term | 2 (16.67%) |
| 4. | Average birth weight | |
| | Overall average | 2.95 ± 0.6 kg |
| | Average in good obstetric outcome cases | 3.25 ± 0.524 kg |
| | Average in adverse outcome cases | 2.35 ± 0.92 kg |
| 5. | Sex ratio | 1:2 |
| 6. | Adverse obstetric outcome | 2 (33.33%) |

but due to the small sample size significance of association could not be calculated.

## Discussion

More than 250 cases of FIUVV have been reported in the literature. Most of them were diagnosed in the late second trimester with an average gestational age of diagnosis at around 30 weeks. In the current study, two cases were diagnosed at the time of the TIFFA scan and the overall mean gestational age of diagnosis was 25w3d. The average diameter of the dilated varix at the time of diagnosis ranges from 6 to 13 mm in other studies [1, 3, 6] which is comparable with the current study (8.9–14.8 mm). Most of the pregnancies were singleton but twin gestation with one twin affected has also been reported [2, 5, 7]. Both DCDA and MCDA pregnancies were reported, with adverse outcomes noted in MCDA gestations. The current study has only one DCDA twin gestation with only one twin affected and echogenic intracardiac focus in the left ventricle seen in the co-twin. The pregnancy was terminated at 36 weeks with good neonatal outcomes in both fetuses.

The extrahepatic portion of the umbilical vein is its weakest part thus any condition which causes increased pressure in umbilical vein (e.g., hydrops) may result in dilatation of the vein in that part [8]. The intrahepatic part of the umbilical vein rises steadily from 2 at 15 weeks to 8 mm at term [8]. Two sections are used to analyze the subhepatic intra-abdominal segment of the umbilical vein. The first is the axial section at the level of cord insertion [9]. At this location, FIUVV presents as an anechoic cystic or oval shaped mass oriented obliquely in a cephalocaudal direction between the abdominal wall and the inferior edge of the liver. The mass is vascular on color Doppler examination [9, 10] (Fig. 6). The second section is a sagittal section centered on the umbilical opening which shows its continuity with the umbilical-portal vascular axis [9]. The various diagnostic criteria used are (1) diameter of FIUVV is > 9 mm in the term fetus (2) diameter of the subhepatic segment of the upper umbilical vein exceeding 50% of the diameter of the intrahepatic segment at any time during gestation [8]. More recent studies have used the criteria (3) if the diameter of the umbilical vein was above + 2 SD of the reference range for gestational age [1, 2, 3, 5, and 4] and the diameter of the subhepatic part of the umbilical vein is 1.5 times its intrahepatic portion [10]. The current study has used all of the above-mentioned criteria.

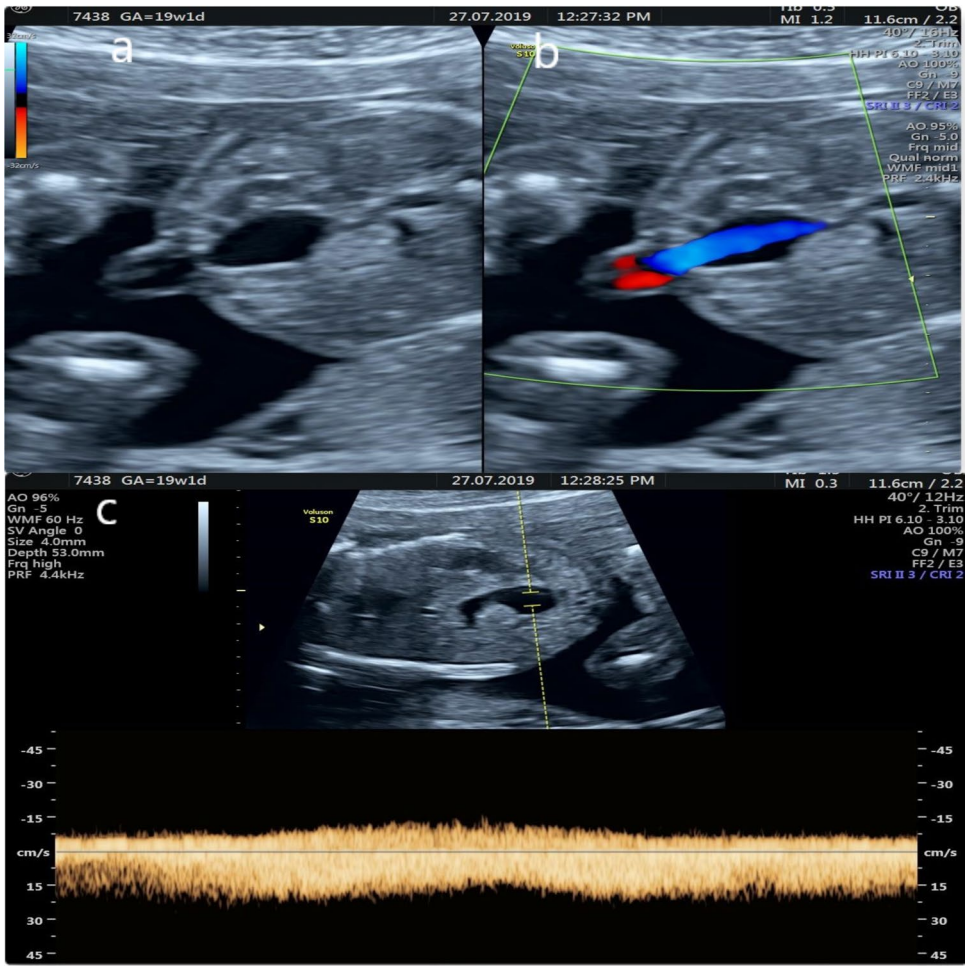


**Fig. 6** **a** & **b**- Axial 2-D image of fetal abdomen at the level of cord insertion showing **a** UVV, **b** Color flow imaging of FIUVV, **c** Coronal section—Pulsed wave Doppler showing continuous monophasic forward flow (venous flow pattern) without pulsations

Once the diagnosis of FIUVV is confirmed, an exhaustive anatomical and chromosomal study of the affected fetus should be conducted to rule out any associated congenital malformation or aneuploidy in the fetus. Recently a detailed systematic review of five cohort retrospective studies of a total of 254 cases was published by E di Pasquo et al [1]. They found that FIUVV was associated with additional ultrasound anomalies (non-isolated FIUVV) in 19% (95% CI 10.9–29.1%) of cases. No case of chromosomal abnormality or IUFD was reported in fetuses with isolated FIUVV. In contrast, in the group of non-isolated FIUVV, the incidence of chromosomal anomalies was 19.6% with trisomy 21 being the commonest followed by deletion 22q. IUFD was 7.3%, with ORs of 14.8 (95% CI 2.9–73.0) and 8.2 (95% CI 1.05–63.1), respectively, when compared with the group of isolated FIUVV.

In another retrospective study by Si Won lee et al. [2], 11 out of 121 cases had associated structural abnormalities like cryptorchidism, hydrops fetalis, atrial septal defect, pulmonary sequestration, renal pelvis dilatation, cerebral ventriculomegaly, single umbilical artery and non-lethal skeletal dysplasia. No karyotype abnormality was noted in any of 121 cases. In the study by Byers et al [5], out of 52 cases, associated anomalies were seen in 28.8% of fetuses and trisomy 21 was diagnosed in two fetuses (5.8%). Recently, Kawamura reported the coexistence of a portosystemic shunt with umbilical vein varix [11]. There are two studies [3, 6] on the fetal outcome in isolated FIUVV. Both showed no association with aneuploidies or IUFD, but there was a 10% risk of fetal growth restriction & preterm birth. In the current study, invasive testing was not offered in isolated FIUVV cases. Five cases had opted for first / second trimester aneuploidy screening, out of which one had intermediated risk for trisomy 21. NIPT was done in the same which showed low risk.

Many studies have reported obstetric complications like fetal growth restriction (3–5%), oligohydramnios (2–3%) and IUFD (5–7%) associated with FIUVV. Except for IUFD, the risk of other obstetric complications was the same in isolated and non-isolated FIUVV [1, 2, 5, 9]. Several studies have suggested a correlation between earlier diagnosis and the risk of IUFD [7, 10] but recent publications suggested that this may be attributed to turbulence or thrombus formation [12]. In the current study,

one case had IUFD at 33 weeks of gestation. The FIUVV was diagnosed at the gestational age of 19w1d with a rapid increase in the size of the varix. In the neonatal period complications includes consumptive coagulopathy and cerebral hemorrhage have been reported recently [13].

Thrombus formation within the varix seems to be directly related to its size and turbulence (evident by the bidirectional flow in the color doppler) [9]. The thrombus may be seen as an echogenic focus inside varix or as a filling defect in the color Doppler study [9, 14]. Both the phenomenon were not noted in any case in the present study.

The FIUVV diagnosed early in pregnancy (i.e., before 26 weeks) needs increased surveillance during the antenatal period due to complications mentioned before [12, 15]. Some studies had followed antenatal fetal surveillance from 32 weeks of gestation with weekly modified biophysical profile [5] (biweekly NST and weekly AFI). Some recommend attentive sonographic monitoring with frequency ranging from once every 2 weeks to 2 per week depending upon the severity of the situation. The aim of ultrasound monitoring is fetal survey to rule out (1) FGR [16], (2) thrombus formation [14], (3) major dilatation (> 12 mm) (4) turbulence and (5) presence of fetal hydrops [3, 9, 17]. In majority of cases (> 60%) the varix does not increase in size or increases only 1–3 mm parallel to linear increase in umbilical vein diameter. In around 28% cases there is increase of 4–9 mm during antenatal period which is independent of gestational age at diagnosis [8, 12]. A very few cases have reported regression in the size of varix [3, 9]. Although no regression was seen in any of varices in current study, rapid increase was noted in one case which suffered IUFD at 33 weeks.

Beraud et al [9] described an anatomically peculiar form of FIUVV where the venous dilation is associated with a malformation of the umbilical-portal system. The dilated venous segment did not end at the portal sinus but at the caudal part of the superior mesenteric vein, just opposite the confluence with the splenic vein. There is no round ligament and the falciform ligament is short. This condition presents relatively early in pregnancy (mean 23 weeks), rapidly rises and is frequently associated with turbulence and thrombus formation. Six cases have been reported with such anomaly in literature [9]. In this study one case had an absent ductus venosus with umbilical vein anomalously draining into the inferior vena cava.

The earlier studies have recommended and practiced an earlier delivery once fetal lung maturity is confirmed [3, 4, 12]. But the current recommendations practiced are to monitor the pregnancy beginning from diagnosis of varix till term where induction or cesarean delivery is done as per other obstetric indications. Earlier delivery is only indicated for fetal distress, hydrops or presence of thrombus [1, 2, 3, 5]. Although all of the studies stress on close fetal monitoring to look for complication and decide for the optimal time of delivery, fetal demise has been noted in all of them despite of monitoring [1, 2, 3, 5, 8, 18].

## Conclusion and Recommendation

The principal finding from this study is that adverse obstetrical outcome is expected in cases of FIUVV when it is diagnosed earlier in pregnancy, shows rapid increase in size or is associated with other structural malformations. The significance of associations could not be calculated because of small sample size. In spite of all the limitations the data from our experience and the literature is sufficient to stress on major points in management of FIUVV cases

- After the diagnosis of FIUVV is confirmed, detailed anatomical scan should be done to rule out major anomalies, precordial veins abnormalities and soft markers,
- The couple should be counselled by a fetal medicine expert to explain the ultrasound findings and their effects on pregnancy outcomes. The need of enhanced fetal surveillance should be conveyed to the patient,
- In all cases of non-isolated FIUVV genetic counseling should be offered. Amniocentesis or NIPT should be done to rule out aneuploidies,
- In isolated cases of FIUVV anatomical variations should be ruled out early to prognosticate the antepartum, intrapartum and post-partum period,
- Serial monitoring starting early in third trimester with non-stress test coupled with ultrasound examination and Doppler should be carried out,
    - The aim at each surveillance should be to rule out
    - FGR with fetal compromise
    - Hydrops
    - Major increase in Size of varix
    - Turbulence
    - Thrombus formation
- In case of FGR and turbulence intensity of surveillance should be increased.
- Currently there is no indication of preterm delivery based on presence of FIUVV alone. However, delivery should be considered if there is hydrops, decompensated FGR or thrombus in the dilated vein.
- Routine intrapartum care should be given in cases of isolated FIUVV. The lower segment cesarean delivery should be considered for other obstetric conditions.

## Limitations

As with all retrospective studies the current study will have an inferior level of evidence compared with prospective studies. It will also be prone to recall bias and misclassification bias. As the control group was recruited by convenience sampling, they are thus not representative of the general population and prone to selection bias. Also, the small sample size of the study makes the survey unreliable due to high variability. A longer analysis on a large sample is needed to study the association of controls with the outcome. Also, long term studies are needed to study any delayed consequences affecting the adult life of these fetuses.

### Declarations

**Conflict of interest** None.

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