ISSN: 2717-8161 RESEARCH ARTICLE

New Trend Med Sci 2025; 6(1): 8-16. https://dergipark.org.tr/tr/pub/ntms

Sonographic features and perinatal outcomes in fetuses with ductus venosus agenesis: Single center experience

Verda Alpay[1*], Selçuk Atalay[2], Fırat Ersan[1], İzel Günay[3]

[1]Department of Obstetrics and Gynecology, Division of Perinatology, Başakşehir Çam and Sakura City Hospital, Istanbul, Türkiye
[2]Department of Obstetrics and Gynecology, Division of Perinatology, Ordu University Training and Research Hospital, Ordu, Türkiye
[3]Department of Obstetrics and Gynecology, Başakşehir Çam and Sakura City Hospital, Istanbul, Türkiye

Article History
Received 24 Sep 2024
Accepted 10 Jan 2025
Published Online 31 Jan 2025

****Corresponding Author***
Verda Alpay
Department of Obstetrics and Gynecology
Division of Perinatology
Başakşehir Çam and Sakura City Hospital
Istanbul, Türkiye
Phone: +90 5332523100
E-mail: verda_alpay@yahoo.com

Doi:10.56766/ntms.1555333

Authors' ORCIDs
Verda Alpay
https://orcid.org/0000-0002-5937-0220
Selçuk Atalay
https://orcid.org/0000-0001-7702-5773
Fırat Ersan
https://orcid.org/0000-0001-5337-0169
İzel Günay
https://orcid.org/0009-0007-5650-5998

Abstract: The purpose of this study is to evaluate the prenatal sonographic features and postnatal outcomes in fetuses with ductus venosus agenesis (DVA) in a tertiary center. We performed a retrospective study of 15 consecutive cases of DVA diagnosed in our perinatology department between January 2020 and October 2023. All clinic records, fetal echocardiograms, any accompanying anomalies, obstetrical ultrasounds, and postnatal echocardiograms were reviewed. Of the 15 cases detected, umbilical vein had extrahepatic type connection in 8 fetuses (53.3%) and intrahepatic type connection in 7 fetuses (46.7%). 11 patients had associated anomalies including hydrops (n=3, 20%), cardiac (n=6, 40%), extracardiac structural (n=7, 46.7%) and chromosomal anomalies (n=3, 20%). In our patient group, only 4 cases (26.7%) presented with isolated DVA, of which 3 had intrahepatic type connection. Prenatal genetic testing including karyotype and microarray was performed in 8 patients (53.3%) and 3 (20%) of them had abnormal results. 4 women (26.7%) underwent legal termination of pregnancy. There were 2 (13.3%) neonatal deaths, and the remaining 9 cases (60%) were alive at last follow-up. DVA is associated with cardiac, extracardiac, and genetic anomalies independent of the site of umbilical venous connection. Postnatal outcomes in cases with DVA depend on the presence of additional anomalies. Fetuses with DVA and extrahepatic connection have additional risk for cardiac failure, hydrops and portal venous system agenesis which worsen the outcomes. DVA cases with intrahepatic connection associated with no or minor anomaly tend to have more favorable outcomes. ©2025 NTMS.

Keywords: Ductus Venosus Agenesis; Portosystemic Shunt; Intrahepatic Drainage; Extrahepatic Drainage; Hydrops.

1. Introduction

Human fetal circulation depends on three physiological shunts which are specific to fetal life and essential for the adaptation of fetal circulation throughout intrauterine life: the ductus arteriosus, the foramen ovale and the ductus venosus (DV)[1]. The first two have been extensively studied over time but DV has recently become a subject of interest with the improvement of ultrasound techniques such as Doppler ultrasound which led a more detailed examination of fetal venous circulation, even in the first trimester[2]. DV is an

Cite this article as: Alpay V, Atalay S, Ersan F and Günay İ. Sonographic features and perinatal outcomes in fetuses with ductus venosus agenesis: Single center experience. *New Trend Med Sci.* 2025; 6(1):8-16. Doi:10.56766/ntms.1555333.

hourglass-shaped structure between umbilical vein and inferior vena cava and plays a key role in the redistribution of fetal blood flow by directing 20-30% of highly oxygenated blood to the systemic circulation[3,4]. Abnormal ductus venosus blood flow is found to be associated with chromosomal abnormalities and congenital cardiac defects[5,6]. Furthermore, observation of typical triphasic flow pattern over the DV may be used for the surveillance of wellbeing in growth restricted fetuses[7].

Ductus venosus agenesis (DVA) is a recently described group of anomalies in which the common characteristic is the absence of normal connection between umbilical vein-portal system and inferior vena cava[8]. The evaluation of DV in the late first trimester as a part of routine ultrasonography led to an increase in the number of DVA cases published in the literature. Despite this and common use of better technologies, DVA is a rare condition, and the true prevalence is unknown[2]. There are several classifications of this anomaly, to simplify we use the one that divides the cases into two large subgroups according to the drainage site of the umbilical vein: intrahepatic and extrahepatic[8,9]. In the intrahepatic type, umbilical vein drains into portal sinus without giving rise to the DV and the blood circulation occurs passing through the liver. In the extrahepatic type, umbilical vein bypasses the liver, does not connect to portal system, and drains to superior vena cava, inferior vena cava, iliac veins or directly to right atrium[9,10]. While extrahepatic type DVA is more often associated with congestive cardiac failure, portal system agenesis and hydrops, intrahepatic type DVA tends to show better neonatal outcomes as it is rarely associated with major structural anomalies compared with extrahepatic type[10,11]. In cases presenting with DVA as an isolated finding, the prognosis is usually good[4,12]. Here, we present prenatal features, association with other structural and genetic abnormalities and postnatal outcomes of 15 cases of DVA followed up in our institution.

2. Material and Methods

This was a retrospective study of a series of cases with DVA diagnosed prenatally in Başakşehir Çam and Sakura City Hospital perinatology department between January 2020 and October 2023. All patients referred in our department for tertiary review of suspected fetal anomalies have a detailed morphology scan, fetal echocardiography, and Doppler flow studies, as appropriate. The DV is evaluated in all patients referred for suspected anomalies, detailed morphological scan and as a part of fetal wellbeing assessment, using color or power Doppler in transverse or sagittal plane. If DV is not visualized at its insertion between portal system and vena cava inferior, the diagnosis of DVA is confirmed and then the site and type of umbilical venous drainage is determined. All ultrasound examinations were performed on ARIETTA 850 (Hitachi Medical Corporation, Tokyo, Japan) device (3.5 mHz abdominal transducer). All clinic records, including fetal echocardiograms, obstetrical ultrasounds and postnatal echocardiograms were reviewed. Fetal echocardiographic data included site of connection of the umbilical vein, any accompanying structural or functional cardiac anomalies and presence of hydrops. Results of genetic testing (both pre- and postnatal if present), the outcomes of pregnancies and for live births, status of the baby at last follow-up were recorded. Patients' characteristics and clinical features were summarized using standard descriptive statistics. Statistical analyses were performed using IBM SPSS statistical software, version 21 (IBM, SPSS Corp., Armonk, NY, USA). This study was approved by Istanbul Başakşehir Çam and Sakura City Hospital Clinical Research and Ethics Committee (ethical approval no: 2023/522, date: 25.10.2023) and was conducted in accordance with the World Medical Association's Declaration of Helsinki (including the 2013 amendments). In addition, informed consent was obtained from all participants before the enrollment.

3. Results

During the study period, a total of 15 cases with prenatally diagnosed DVA were collected. The gestational age at diagnosis ranged from 12 to 33 weeks. In 2 cases, the reason for referral was cystic hygroma in the first trimester and DVA was the accompanying finding. 8 of the cases were referred to our tertiary center for suspected anomalies or intrauterine growth restriction and DVA was detected during targeted ultrasound. In the remaining 5 cases, DVA was an incidental finding during routine second trimester ultrasound scan. The prenatal findings and postnatal outcomes of the cases are summarized in Table 1. Prenatal ultrasound studies revealed intrahepatic type connection in 7 cases (46.7%) and extrahepatic type connection in 8 fetuses (53.3%). Among 8 cases with extrahepatic connection, umbilical vein drained directly to inferior vena cava in 5 cases (62.5%), into right atrium in 2 cases (25%) and to vena azygos in 1 case (12.5%). In our patient group, only 4 cases (26.7%) presented with isolated DVA. 3 of 4 fetuses with isolated DVA had intrahepatic type connection with clearly detectable left portal vein, they were all survivors and reported to be healthy at discharge. However, the remaining fetus with isolated DVA had extrahepatic type connection with umbilical vein draining directly into inferior vena cava. The patient delivered at 25 weeks of gestation due to preterm premature rupture of membranes and the newborn died at day 3 because of extreme prematurity. 11 patients had associated anomalies including hydrops (n=3, 20%), cardiac (n=6, 40%), extracardiac structural (n=7, 46.7%) and chromosomal anomalies (n=3, 20%). Cardiac anomalies constitute the most common associated group of structural anomalies in our study. The majority of cardiac diagnoses were ventricular septal defects. Two cases presented with pericardial effusion, one of them had confirmed Turner syndrome. Other detected cardiovascular anomalies were tricuspid

atresia, total anomalous pulmonary venous connection and left persistent vena cava superior. Extracardiac structural anomalies were present in 7 patients (46.7%) including cystic hygroma, unilateral renal agenesis, cleft lip, ventriculomegaly, hepatosplenomegaly, ileal atresia, and intrauterine growth restriction. Except the patient with co-existing ileal atresia, all cases with extracardiac anomalies were extrahepatic type DVA cases. In the case with hepatosplenomegaly, there was also hepatic calcifications, and, in this case, umbilical vein had an extrahepatic course draining directly into vena azygos. In one case with intrahepatic type DVA, the only associated anomaly was single umbilical artery. In our series, there were 3 cases presented with hydrops, all of them had DVA with extrahepatic type connection and all of them had termination of pregnancy due to associated anomalies. Prenatal genetic testing including karyotype and microarray was performed in 8 patients (53.3%) and 3 (20%) of them had abnormal results. Confirmed genetic diagnoses were Noonan syndrome, Turner syndrome and 3p deletion syndrome. The remaining 5 cases had normal karyotype and microarray results. 4 women (26.7%) underwent legal termination of pregnancy, all of them had extrahepatic type DVA and multiple structural anomalies, two of them were diagnosed with confirmed genetic anomalies (Noonan syndrome and 3p deletion syndrome). In our study group there were 2 (13.3%) neonatal deaths, one at day 3 due to extreme prematurity and the other at day 10 due to prenatally diagnosed tricuspid atresia, pulmonary stenosis and coarctation of aorta. The remaining 9 cases (60%) were alive at last follow-up (follow-up duration between 2 months and 2 years). 6 of these survivors had intrahepatic type DVA prenatally, the diagnosis is confirmed, and varying degrees of portal system components are demonstrated in the postnatal period, none of them had portal agenesis. The other 3 survivors had extrahepatic type DVA with co-existing structural anomalies, all detected sonographic findings in the prenatal period are confirmed postnatally. One of them has co-existing total anomalous pulmonary venous connection and is waiting to be operated at 3 years old. The other one with co-existing hepatosplenomegaly was thought to have portal agenesis in the prenatal period, hepatosplenomegaly is still present, and the infant is following up by pediatric haemato-oncology due to pancytopenia. However, portal system was partially visualized in the postnatal period.

Table 1: Prenatal features, associated anomalies, and outcomes in 15 fetuses with ductus venosus agenesis (DVA).

Cases	Gestational age at diagnosis	Type of DVA-Umbilical vein insertion	Cardiac anomalies	Associated extracardiac findings	Hydrops	Prenatal genetic testing-Karyotype	Outcome
1	12	Extrahepatic-Inferior vena cava	None	Cystic hygroma, polyhydramnios	Yes	CVS / AS Noonan syndrome	TOP at 28 weeks
2	23	Extrahepatic-Inferior vena cava	None	None	No	N/A	PPROM at 25 weeks Neonatal death at day 3 due to extreme prematurity
3	22	Intrahepatic-Left portal vein	Pericardial effusion, ventricular septal defect	None	No	AS Turner's syndrome (45,X)	Live birth at 38 weeks Alive at 1,5 years
4	22	Intrahepatic-Portal system	None	None	No	AS Normal	PROM at 32 weeks Live birth at 32 weeks 5 days Alive at 16 months old
5	20	Extrahepatic-Inferior vena cava	Total anomalous pulmonary venous connection	Left renal agenesis, hydroureteronephrosis in the right kidney	No	N/A	Live birth at 38 weeks Alive at 14 months old Postnatal karyotype normal
6	22	Intrahepatic-Left portal vein	None	Single umbilical artery	No	N/A	Live birth at 38 weeks Alive at 9 months Postnatal karyotype normal Postnatal ultrasound: Portal system visualized.

7	22	Extrahepatic-Right atrium	None	Early onset fetal growth restriction, bilateral anophthalmia, ascites	Yes	AS 3P deletion	TOP at 25 weeks
8	22	Intrahepatic-Portal system	Tricuspid atresia, ventricular septal defect, pulmonary stenosis, coarctation of the aorta	None	No	N/A	Live birth at 40 weeks Neonatal death at day 10
9	24	Extrahepatic-Right atrium	None	Fetal growth restriction, severe ventriculomegaly, non-visualization of stomach, esophageal atresia, cleft lip, interruption of inferior vena cava, azygos continuation, single umbilical artery, bilateral talipes, lumbosacral hemivertebrae	No	N/A	TOP at 25 weeks
10	21	Intrahepatic-Left portal vein	None	None	No	AS Normal	Live birth at 37 weeks Alive at 8 months Postnatal ultrasound: Left portal vein visualized; right portal vein thin. Postnatal diagnosis: Abernethy type 2 syndrome Operation will be planned.
11	22	Extrahepatic-Vena azygos	Pericardial effusion, left persistent superior vena cava	Hepatosplenomegaly, non-visualization of portal system in the liver, diffuse calsifications in the liver, interruption of inferior vena cava, azygos continuation	No	AS Normal	Live birth at 39 weeks Alive at 8 months Postnatal ultrasound: Portal system partially visualized, hepatosplenomegaly. Pancytopenia detected, close follow-up by pediatric hematology-oncology.
12	22	Intrahepatic-Portal system	None	None	No	N/A	Live birth at 39 weeks Alive at 3 months
13	33	Extrahepatic-Inferior vena cava	Tricuspid atresia, hypoplastic right heart	None	No	N/A	Live birth at 37 weeks Alive at 1,5 months Operated once due to cardiac anomaly, waiting for the second operation.

14	22	Intrahepatic-Left portal vein	Ventricular septal defect	İleal atresia	No	AS, Normal	Live birth at 38 weeks Alive at 2 weeks
15	13	Extrahepatic-Inferior vena cava	None	Cystic hygroma	Yes	CVS Normal	TOP at 13 weeks

CVS: chorion villus sampling, AS: amniocentesis, TOP: termination of pregnancy, N/A: not assessed, PROM: premature rupture of membranes.

4. Discussion

The ductus venosus is located between umbilical vein and inferior vena cava and plays a critical role in the redistribution of blood flow by shunting placental oxygenated blood in the fetal systemic circulation[13]. 20-30% of highly oxygenated blood in the umbilical vein directly reaches the left atrium through ductus venosus. The remaining oxygenated blood in the umbilical vein is dispersed to the left lobe of fetal liver via left portal vein and overall portal blood flow is directed to the right lobe of the liver[14]. In cases of fetal hypoxia or reduced placental return, the percentage of blood flow shunted through ductus venosus is increased[15]. Embryologically, the right umbilical vein obliterates at day 33-34 while the left umbilical vein persists and gives rise to left portal vein and DV in the liver[3]. The etiology of the fetal venous system anomalies is not clearly defined, but failure of development of these primitive veins is thought to be associated with anomalies of umbilical-portal circulation, as well as DVA[8,14]. Another possible explanation of DVA may be secondary occlusion of already formed vessel due to thromboembolism or a systemic event[16]. Whichever is the etiopathogenesis, in case of DVA, umbilical vein which carries the blood returning from the placenta takes an alternative route to fetal heart[8]. The lack of flow regulation in this alternative route may contribute to fetal cardiac volume overload, congestive heart failure and eventually hydrops fetalis[17].

Although the definite incidence of DVA in the general population is unknown, the estimated prevalence varies between 1/556 and 1/2500[18,19]. However, in high-risk populations such as fetuses referred to maternal-fetal units with cardiomegaly, hydrops, cardiac or extracardiac anomalies, the prevalence increases up to 6/1000 cases[20]. The prognosis of DVA depends on site of connection, associated malformations, and chromosomal anomalies[11].

In our study, most cases of DVA were diagnosed in the second trimester during anatomical screening or in association with other malformations. Only 2 cases (13.3%) were diagnosed in the first trimester, and they were both associated with cystic hygroma. One of these cases was diagnosed with Noonan syndrome after prenatal genetic testing. Iliescu et al. have evaluated the potential of first and second trimester screening in the diagnosis of DVA. In 6114 consecutive low risk pregnancy, they identified 11 cases of DVA and 10 of these cases (91%) were identified during first trimester screening[19]. This proves the need for a careful and detailed examination in the first trimester as the early the detection of DVA is possible and may have an important impact during follow-up.

In our cohort, a total of 15 cases of DVA were detected, out of which 7 fetuses (46.7%) had intrahepatic venous drainage without liver bypass and 8 (53.3%) had extrahepatic venous drainage with liver bypass. In a similar study, Dhingra et al. presented 8 cases of DVA, out of which 2 (25%) with intrahepatic and 6 (75%) with extrahepatic drainage[12]. They suggested that DVA with intrahepatic shunt may be a more common condition but is less frequently reported as it requires a more rigorous examination particularly with color flow mapping of the fetal portal venous system. Extrahepatic shunt is more easily noticed due to abnormal course of intraabdominal umbilical vein which can also be detected on gray scale mode. Berg et al. reported 19 cases of DVA with intrahepatic connection and only 4 cases of DVA with extrahepatic connection. The authors explained this high rate of intrahepatic type connection by the Doppler assessment of the DV which is an integral part of routine fetal examination in their institution[21]. According to the recent literature about DVA, intrahepatic type connection occurs more frequently, but more easily escapes diagnosis even in the presence of coexisting anomalies due to the need of Doppler examination[9]. In our institution, Doppler examination of DV is a routine part of fetal assessment in the second trimester anatomical screening or in fetuses referred to our center due to suspected anomalies and fetal growth restriction. This may explain the relatively high proportion of DVA cases with intrahepatic connection in our series.

Irrespective of the type of connection, DVA is significantly associated with cardiac, extracardiac structural and chromosomal anomalies[12,21]. In our study, 4 fetuses had isolated DVA (26.7%) and 11 fetuses (73.3%) had associated chromosomal anomalies and major or minor structural malformations including cardiac, skeletal, gastrointestinal, central nervous and genitourinary system. Cardiac anomalies were the most common associated malformations and comprised ventricular septal defects, total anomalous pulmonary venous connection, tricuspid atresia, pulmonary stenosis, and aortic coarctation. Genitourinary system anomalies included unilateral renal agenesis and hydronephrosis. Gastrointestinal malformations included ileal atresia, esophageal atresia, and hepatosplenomegaly. The only central nervous system anomaly detected in our cohort was severe ventriculomegaly. Musculoskeletal system malformations comprised spinal deformities, hemivertebrae and bilateral clubfoot. Other vascular

anomalies including interruption of vena cava inferior and vena azygos continuity, single umbilical artery and left persistent vena cava superior along with facial anomalies such as cleft lip and palate were also diagnosed. Although a wide range of malformations occur in association with DVA, none of these anomalies is disease specific. In our series, among 8 fetuses with extrahepatic connection, 7 (87.5%) had associated anomalies, whereas among 7 fetuses with intrahepatic connection, 4 (57%) had associates minor or major anomalies and 3 fetuses (43%) had isolated DVA. Contratti et al. suggested that particularly fetuses with extrahepatic connection have higher incidence of complex malformations, chromosomal anomalies, and hydrops[14]. Additionally, fetuses with extrahepatic drainage and liver bypass tend to develop congestive heart failure which unfavorably affects the outcome even if the fetal anatomy is normal[21]. The exact mechanism triggering heart failure in the fetus is not well established, the possible explanation is that the umbilical vein bypassing the liver and draining directly into the heart may cause an increased preload, progressive cardiac decompensation, and high central venous pressure[3]. The leading clinical sign in this situation is cardiomegaly and the chronic volume overload may lead to fetal hydrops[22,23]. In a meta-analysis of 35 cases of DVA draining directly into the heart, a higher incidence of cardiomegaly and hydrops was detected[24]. It may also occur in form of edema restricted only to one compartment, such as pericardial, pleural spaces or subcutaneous tissue[2]. Nevertheless, these signs are usually not observed in DVA with intrahepatic drainage, in the presence of connection between umbilical vein and portal system[4,8]. In our study, 3 of the 4 cases (75%) with hydrops/effusions had DVA with extrahepatic connection. The remaining case presenting with pericardial effusion had DVA with intrahepatic connection, was diagnosed with Turner's syndrome in the prenatal period and we linked the presence of pericardial effusion to Turner's syndrome rather than DVA. None of our cases presented with cardiomegaly. DVA without liver bypass seems to have a better prognosis especially if it is not associated with other malformations and chromosomal anomalies[21]. The association with other abnormalities may be the most important prognostic factor in DVA[8,25].

DVA is known to be associated with chromosomal abnormalities with a reported incidence between 17-24%[14,23]. Abnormal connection of the umbilical vein into the inferior vena cava has been reported to increase the risk trisomy 21[26]. However, according to the literature, most frequent chromosomal abnormalities associated with DVA are Turner's syndrome and Noonan syndrome[3,18,23]. Additionally, DVA has been reported in the context of various syndromes such as VACTERL, Beckwith-Wiedemann syndrome, Jacobsen syndrome, Pierre Robin sequence, Pallister-Killian syndrome, Smith-Lemli-Opitz syndrome and Wolf-Hirschhorn syndrome[10,27]. However, genetic abnormalities associated with DVA are thought to be underdiagnosed using conventional cytogenetic studies[28]. Advanced genetic studies, namely chromosomal microarray (CMA) and exome sequencing (ES) allow more detailed analysis of fetal genome and thus, enhance prenatal diagnosis of genetic abnormalities in cases of DVA[27,28]. In our study, 8 out of 15 cases (53%) had invasive genetic testing. In total 20% of cases (3/15) and 37.5% of tested cases (3/8) received a genetic diagnosis thought to be associated with DVA. Confirmed abnormal results were as follows: Turner's syndrome (1), Noonan syndrome (1) and 3p deletion syndrome (1). Genetic abnormalities detected in our series are consistent with the literature. McBrien et al. reported results of 14 cases with DVA and in their series, the incidence of genetic abnormalities was 43% in total and genetic diagnoses were trisomy 21, PHACE syndrome and RASA1 related disorder beside Noonan syndrome[25]. Therefore, fetal genetic assessment including CMA and ES must be indicated in fetuses with prenatally diagnosed DVA especially in the presence of associated anomalies[11,28,29].

Prenatal diagnosis of DVA is strongly linked with high rate of pregnancy termination due to the presence of associated malformations which impact pregnancy outcomes and parental decision making[17]. In our series, 4 women (26.7%) underwent legal termination of pregnancy, all these fetuses had DVA with extrahepatic connection and associated major structural anomalies. Two fetuses had abnormal genetic results (Noonan syndrome and 3p deletion syndrome). Decision for termination of pregnancy should be based upon associated structural or chromosomal anomalies. The prognosis for cases of isolated DVA is usually good, independent of the type of umbilical vein connection site[17]. This information is extremely important and should be emphasized during parental counseling even if precise outcome prediction is challenging. In case of continuation of pregnancy, possibility of rapid deterioration of cardiac status and in utero fetal demise for DVA cases with liver bypass should be kept in mind and close follow-up should be planned for these fetuses until delivery[17].

Our findings are consistent with the literature suggesting that fetuses with intrahepatic connection with no or minor malformation have better outcomes compared to fetuses with extrahepatic connection[12]. In our series, among 7 cases with intrahepatic connection, 5 cases presented with minor or no associated anomalies, all these fetuses survived, all diagnoses were confirmed in the sonographic imaging of portal system during neonatal period, none of them had portal agenesis, various degrees of portal venous system components were demonstrated, and no short-term sequelae was observed. 1 case with DVA and intrahepatic connection had also ventricular septal defect and pericardial effusion, invasive genetic testing resulted as Turner's syndrome, the infant is 1,5 years old and otherwise healthy, her portal system was visualized in the sonography. Similarly, Berg et al.

found that all 13 fetuses with isolated DVA without liver bypass survived and none had long-term sequelae[21].

Extrahepatic connection of umbilical vein is associated with portal agenesis which may unfavorably affect long-term outcomes in 24% of fetuses with DVA and liver bypass[21]. This may cause severe postnatal complications such as congestive heart failure, pulmonary edema, focal nodular hyperplasia, and hepatic tumors[30,31]. In all cases with DVA and extrahepatic connection, agenesis of portal system should be ruled out, as it is the main prognostic factor[9]. However, according to the literature, prenatally suspected cases of portal agenesis may recover in the postnatal period[32]. Presence of portal venous system may predict favorable outcomes if there are no associated anomalies[17]. DVA with intrahepatic connection is associated with portosystemic shunts, rather than portal agenesis[32]. In this condition, intrahepatic portal venous system is normally developed, but there is a connection between portal and hepatic veins, also known as portosystemic shunt[32]. This group of anomalies require postnatal sonographic evaluation because a precise sonographic determination of portal system components in the prenatal period is difficult and that makes parental counseling more challenging[3]. In case of DVA with extrahepatic connection, if the possibility of portal agenesis cannot be ruled out, then long-term sequelae cannot be predictable, and parents must be informed about possible poor prognosis. During the counseling process, the family must be informed about the type of malformation, associated anomalies, postnatal complications, and possible surgical correction. It should also be kept in mind that intrahepatic shunting may be associated with metabolic consequences, potential neonatal hepatic dysfunction and hyperammonemic encephalopathy in the neonate[17,20]. If an intrahepatic shunting is suspected on prenatal ultrasound, the neonate should be monitored for hiperammonemia and liver and followed up until the closure of the shunt is confirmed[9,33]. Once DVA is diagnosed, care must be taken to rule out coexisting venous system anomalies including umbilical, hepatic, portal or caval venous systems since defects in the venous systems can either occur in isolation or in combination[11]. In our opinion, evaluation of an anatomically normal DV should be an integral part of detailed anatomy screening and in case of non-visualization, a thorough assessment of hepatic and portal veins is mandatory. However, some anomalies of portal venous system such as partial portal agenesis or portosystemic shunts can occur even if DV is present and precise diagnosis is not possible during prenatal period[9].

Our study provides significant data about prenatally diagnosed DVA cases to the literature and thus, may help promote antenatal management approaches, parental counseling and decision-making processes keeping in mind that clinical decision should always be made on a case-by-case basis. One strength of our study is that there is no lack of data during follow-up due to centralization of cases in a tertiary referral unit. The retrospective design and limited data on long-term outcomes are among our study limitations. Further studies with larger number of cases and with long-term outcomes are needed to confirm our results.

5. Conclusion

DVA is a rare anomaly, and the routine use of Doppler ultrasound has enabled the diagnosis of DVA as early as 11-14 weeks. Our study results are consistent with the findings and short-term outcomes previously reported about DVA. DVA is significantly associated with cardiac and extracardiac structural malformations, hydrops, and genetic abnormalities. The presence of additional anomalies is the main prognostic factor and may lead to poorer fetal outcomes. Fetuses with DVA and extrahepatic connection have additional risk for cardiac failure, hydrops and portal venous system agenesis which worsen outcomes, even if the fetal anatomy is normal. On the other hand, DVA with intrahepatic connection tend to have more favorable outcomes especially if it is not associated with other malformations and counseling can be reassuring. Detailed anatomical assessment, fetal echocardiography and genetic testing modalities of the current modern era including CMA and ES are recommended when DVA is detected. Ongoing fetal surveillance should be targeted on fetal signs of hydrops and cardiac failure, especially in cases of DVA with extrahepatic connection.

Limitations of the Study

The retrospective design and limited data on long-term outcomes are among our study limitations.

Acknowledgement

None.

Conflict of Interests

No conflict of interest was declared by the authors.

Financial Support

The authors declared that this study received no financial support.

Author Contributions

Idea/Concept: VA. Design: SA, VA. Data Collection/Processing: SA, İG. Analysis/Interpretation: İG, VA. Literature Review: FE. Drafting/Writing: VA, FE. Critical Review: all authors

Ethical Approval

This study was approved approved by Istanbul Başakşehir Çam and Sakura City Hospital Clinical Research and Ethics Committee (ethical approval no: 2023/522, date: 25.10.2023).

Data sharing statement

The data that support the findings of this study are available on request from the corresponding author.

Consent to participate

Informed consent was obtained from all participants before the enrollment.

Informed Statement

None.

References

1. Kiserud T, Acharya G. The fetal circulation. *Prenat Diagn.* 2004;24(13):1049-59
2. Pacheco D, Brandão O, Montenegro N, Matias A. Ductus venosus agenesis and fetal malformations: what can we expect?-a systematic review of the literature. *J Perinat Med.* 2018;47(1):1-11.
3. Maruotti GM, Saccone G, Ciardulli A, Mazzarelli LL, Berghella V, Martinelli P. Absent ductus venosus: case series from two tertiary centres. *J Matern Fetal Neonatal Med.* 2018;31(18):2478-2483.
4. Born M. The ductus venosus. *Rofo*. 2021;193(5):521-26.
5. Matias A, Montenegro N. Ductus venosus blood flow in chromosomally abnormal fetuses at 11 to 14 weeks of gestation. *Semin Perinatol.* 2001;25(1):32-37.
6. Chelemen T, Syngelaki A, Maiz N, Allan L, Nicolaides KH. Contribution of ductus venosus Doppler in first-trimester screening for major cardiac defects. *Fetal Diagn Ther*. 2011;29(2):127-34.
7. Society for Maternal-Fetal Medicine Publications Committee; Berkley E, Chauhan SP, Abuhamad A. Doppler assessment of the fetus with intrauterine growth restriction. *Am J Obstet Gynecol.* 2012;206(4):300-308.
8. Garcia-Delgado R, Garcia-Rodriguez R, Romero Requejo A, et al. Echographic features and perinatal outcomes in fetuses with congenital absence of ductus venosus. *Acta Obstet Gynecol Scand.* 2017;96(10):1205-13.
9. Strizek B, Zamprakou A, Gottschalk I, et al. Prenatal diagnosis of agenesis of ductus venosus: A retrospective study of anatomic variants, associated anomalies and impact on postnatal outcome. *Ultraschall Med.* 2019;40(3):333-39.
10. Chan ES, Suchet I, Yu W, Somerset D, et al. Absence of ductus venosus: A comparison of 2 distinctive fetal autopsy cases and embryologic perspectives. *Pediatr Dev Pathol.* 2024;27(2):139-47.
11. Rajachander N, Andrew C, Shalini CNS, Gopal S. Ductus venosus agenesis: Ultrasound diagnosis and outcome. *J South Asian Feder Obstet Gynae*. 2021;13(3):156-62.
12. Dhingra B, Makam A. Agenesis of ductus venosus: a case series. *J Fetal Med.* 2020;7(2):149-54.
13. Kiserud T. The ductus venosus. *Semin Perinatol.* 2001;25(1):11-20.
14. Contratti G, Banzi C, Ghi T, Perolo A, Pilu G, Visentin A. Absence of the ductus venosus: report of 10 new cases and review of the literature. *Ultrasound Obstet Gynecol*. 2001;18(6):605-609.
15. Tchirikov M, Eisermann K, Rybakowski C, Schröder HJ. Doppler ultrasound evaluation of ductus venosus blood flow during acute hypoxemia in fetal lambs. *Ultrasound Obstet Gynecol.* 1998;11(6):426-31.
16. Fasouliotis SJ, Achiron R, Kivilevitch Z, Yagel S. The human fetal venous system: normal embryologic, anatomic, and physiologic characteristics and developmental abnormalities. *J Ultrasound Med.* 2002;21(10):1145-58.
17. Moaddab A, Tonni G, Grisolia G, et al. Predicting outcome in 259 fetuses with agenesis of ductus venosus - A multicenter experience and systematic review of the literature. *J Matern Fetal Neonatal Med*. 2016;29(22):3606-14.
18. Staboulidou I, Pereira S, Cruz Jde J, Syngelaki A, Nicolaides KH. Prevalence and outcome of absence of ductus venosus at 11(+0) to 13(+6) weeks. *Fetal Diagn Ther*. 2011;30(1):35-40.
19. Iliescu DG, Cara ML, Tudorache, et al. Agenesis of ductus venosus in sequential first and second trimester screening. *Prenat Diagn.* 2014;34(11):1099-105.
20. Acherman RJ, Evans WN, Galindo A, et al. Diagnosis of absent ductus venosus in a population referred for fetal echocardiography: association with a persistent portosystemic shunt requiring postnatal device occlusion. *J Ultrasound Med*. 2007;26(8):1077-82.
21. Berg C, Kamil D, Geipel A, et al. Absence of ductus venosus-importance of umbilical venous drainage site. *Ultrasound Obstet Gynecol.* 2006;28(3):275-81.
22. Jaeggi ET, Fouron JC, Hornberger LK, et al. Agenesis of the ductus venosus that is associated with extrahepatic umbilical vein drainage: prenatal features and clinical outcome. *Am J Obstet Gynecol.* 2002;187(4):1031-37.
23. Volpe P, Marasini M, Caruso G, et al. Prenatal diagnosis of ductus venosus agenesis and its association with cytogenetic/congenital anomalies. *Prenat Diagn.* 2002;22(11):995-1000.
24. Sau A, Sharland G, Simpson J. Agenesis of the ductus venosus associated with direct umbilical venous return into the heart--case series and review of literature. *Prenat Diagn.* 2004 Jun;24(6):418-23.
25. McBrien A, Caluseriu O, Niederhoffer KY, Hornberger LK. Prenatal features, associated co-morbidities and clinical course of agenesis of the ductus venosus in the current era. *Prenat Diagn*. 2021;41(1):15-20.
26. Achiron R, Gindes L, Gilboa Y, Weissmann-Brenner A, Berkenstadt M. Umbilical vein anomaly in fetuses with Down syndrome. *Ultrasound Obstet Gynecol.* 2010;35(3):297-301.
27. Lapresa Alcalde MV, Cubo AM, Martín Seisdedos MC, Cortejoso Hernández J, Doyague Sanchez MJ, Sayagués JM. Ductus venosus agenesis as a marker of Pallister-Killian Syndrome. *Medicina (Kaunas).* 2019;55(7):374.
28. Mash Y, Bardin R, Gilboa Y, et al. Agenesis of the ductus venosus and its association with genetic abnormalities. *Prenat Diagn.* 2024;44(13):1585-92.

29. Nagy RD, Cernea N, Dijmarescu AL, et al. Ductus venosus agenesis and portal system anomalies-association and outcome. *Biology (Basel).* 2022;11(4):548.
30. Acherman RJ, Rollins RC, Castillo WJ, Evans WN. Stenosis of alternative umbilical venous pathways in absence of the ductus venosus. *J Ultrasound Med.* 2010;29(8):1227-31.
31. Thakur V, Jaeggi ET, Nield LE. A unique foetal case of left ventricular non-compaction associated with arrhythmia, structural cardiac anomalies, and agenesis of the ductus venosus. *Cardiol Young.* 2016;26(2):368-70.
32. Achiron R, Kivilevitch Z. Fetal umbilical-portal-systemic venous shunt: in-utero classification and clinical significance. *Ultrasound Obstet Gynecol.* 2016;47(6):739-47.
33. Han BH, Park SB, Song MJ, et al. Congenital portosystemic shunts: prenatal manifestations with postnatal confirmation and follow-up. *J Ultrasound Med.* 2013;32(1):45-52.

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