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Original Article

Impact of the type of ductus venosus agenesis and the presence of associated anomalies on prognosis

Züat Acar [a †], Yusuf Başkiran [b]

[a] Department of Gynecology and Obstetrics, İstanbul Tema Hospital, Bahat Clinic ,İstanbul , Türkiye

[b] Department of Gynecology and Obstetrics, Yuzuncu Yil University, Faculty of Medicine, Van, Türkiye

ABSTRACT

Objective: The Ductus Venosus (DV) connects the umbilical vein to the inferior vena cava. With a portocaval pressure gradient, the well-oxygenated blood in the ductus venosus accelerates towards the left sidewall of the inferior vena cava, directing the blood preferentially towards cephalic and coronary circulation through the foramen ovale (1). DV serves as a shunt, expanding to protect the heart and brain in hypoxic conditions. Ductus Venosus Agenesis (DVA) is a rare congenital abnormality with a prevalence of 0.03-0.07%. The type of DVA, along with any additional anatomical or chromosomal anomalies in fetuses with DVA, significantly affects the postnatal prognosis. Some fetuses with DVA develop normally, while others may experience growth retardation, heart defects, or other complications. In this study, we aimed to evaluate the frequency of associated anomalies in DVA cases, examine the impact of each type of DVA (intrahepatic and extrahepatic venous drainage) on prognosis, and contribute to the literature on this rare disease.

Materials and Methods; We conducted a retrospective study of all cases diagnosed prenatally with DVA at a tertiary center between 2016-2019. Our study reviewed obstetric data, associated anomalies, other systemic anomalies, type of DVA, chromosomal or genetic anomalies, and perinatal and postnatal outcomes. Postnatal infants were followed up to the 6th month.

Results; We identified 16 cases with ductus venosus agenesis. The type of DVA (intrahepatic-extrahepatic shunt), presence of chromosomal anomalies, accompanying ultrasonographic findings, and perinatal outcomes were recorded. Generally, in 7 out of the 16 cases, the umbilical vein drained into the portal system (44% - intrahepatic), and in 9 cases, it drained into the systemic venous system.

Conclusion; DVA is a rare congenital abnormality with potentially significant implications for affected fetuses and infants. Early diagnosis, careful monitoring, and appropriate management strategies are crucial to optimize outcomes for these patients. There's a need for future research to better understand the underlying etiology and pathophysiology of DVA and to develop more effective treatment options for affected individuals.

Keywords: ductus venosus agenesis; extrahepatic; intrahepatic; chromosomal anomaly; neonatal outcomes

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Introduction

The fetal ductus venosus (DV) is a pivotal structure connecting the umbilical vein to the inferior vena cava at the heart's entrance. The portocaval pressure gradient facilitates acceleration of well-oxygenated blood in the DV towards the left sidewall of the inferior vena cava, ensuring blood preferentially flows cephalad and to the coronary circulation via the foramen ovale [1]. Acting as a shunt, the DV expands to protect the heart and brain under hypoxic conditions. 20-30% of well-oxygenated blood from the umbilical vein is delivered to the left atrium via the DV, inferior vena cava (IVC), and foramen ovale [2]. Under normal circumstances, two-thirds of umbilical venous flow nourishes the liver, while the remaining third passes through the DV. In hypoxic situations, there's an increase in the DV shunt, ensuring vital organs, notably the heart and brain, receive adequate oxygen and glucose [3]. Ductus Venosus Agenesis (DVA) is a rare congenital abnormality with a prevalence of 0.03-0.07%, characterized by the absence of the DV during fetal development, responsible for transporting oxygen-rich blood from the umbilical vein to the inferior vena cava [3,4]. In fetuses with DVA, the umbilical venous return occurs through two distinct pathways: extrahepatic and intrahepatic.

Extrahepatic; Drainage from the umbilical vein bypasses the liver (connecting directly to the iliac vein, inferior vena cava, renal vein, right atrium, or, rarely, the left atrium or coronary sinus).

Intrahepatic; The umbilical vein drains into the liver (connecting to the portal sinus as usual) [5].

Fetuses with DVA may exhibit a range of clinical manifestations, including cardiac and non-cardiac anomalies, intrauterine growth restriction (IUGR], and even fetal death in severe cases [6]. The etiology of DVA remains unclear, but genetic factors and environmental influences may play a role [7]. Prenatal diagnosis is typically made during the first trimester ultrasound examination [8].

Management of DVA is contingent on the severity of the condition, presence of associated anomalies, and the gestational age at diagnosis. Postnatal management of infants with DVA is determined by the severity of the condition and the presence of associated anomalies [9]. Given the elevated risk of IUGR and other complications in fetuses with DVA, it is crucial to closely monitor fetal growth and well-being [10]. In certain situations, such as hydrops fetalis or significant cardiac dysfunction, intrauterine intervention may be considered [11].

The prognosis in fetuses with DVA varies depending on the presence of associated anomalies and alternative venous shunts. While some fetuses with DVA develop normally, others may experience growth retardation, heart defects, or other complications. In this study, we aimed to evaluate the frequency of associated anomalies in DVA cases and, in the context of the literature, to explore the impact of

† Corresponding author.
E-mail: drzacar@hotmail.com
Orcid ID: 0000-0002-3485-1554

each type of DVA with intrahepatic and extrahepatic venous drainage on prognosis.

Material and methods

Between 2016 and 2019, we conducted a retrospective study of all cases diagnosed with prenatal DVA at the Istanbul Kanuni Sultan Suleyman Training and Research Hospital. The study was approved by the local ethics committee. Transabdominal ultrasound examinations were performed using a Voluson E6 (GE Healthcare Ultrasound, Milwaukee, WI, USA) ultrasound machine equipped with an RAB 6D (2-7 MHz) probe.

During all ultrasound examinations, general anatomical evaluations, fetal echocardiography, and Doppler studies of the ductus venosus were conducted. A diagnosis of DVA was established when the blood flow between the portal vein and the inferior vena cava couldn't be demonstrated using color Doppler in optimal scanning planes. The connection of the umbilical vein to the portal venous system was classified as intrahepatic, and to the systemic venous system was classified as extrahepatic shunt.

Cases were classified as either isolated or associated with other abnormalities. Genetic counseling was recommended for all cases. Cases with additional anomalies were recommended for karyotype analysis and scheduled accordingly.

In our study, we reviewed obstetric data, associated anomalies, other systemic abnormalities, type of DVA, chromosomal or genetic anomalies, and perinatal and postnatal outcomes. Postnatal infants were followed up until the 6th month. Patients who dropped out of follow-up at any stage of pregnancy and gave birth at another center were excluded from the study.

Results

In our study, we identified 16 cases with ductus venosus agenesis. The type of DVA (intrahepatic-extrahepatic shunt), presence of chromosomal anomalies, accompanying ultrasonographic findings, and perinatal outcomes were recorded (Table-1). One case was observed in a twin pregnancy in a single fetus, while all other pregnancies were singleton.

Overall, of the 16 cases, the umbilical vein connected to the portal system in 7 cases (44% - intrahepatic) and to the systemic venous system in 9 cases (56% - extrahepatic). All three identified chromosomal anomalies (trisomy 21, Turner syndrome, phenylketonuria) were in the extrahepatic drainage group. All pregnancies in the extrahepatic shunt group were either terminated or lost post-delivery. In the intrahepatic drainage group, one baby was lost post-delivery (n:1 - 14%), while the others survived. 25% of the cases (n:4) were isolated, and all isolated cases belonged to the intrahepatic drainage group and resulted in live births. Among ultrasonographic findings, a single umbilical artery was the most frequently observed (n:4 - 25%). Other common findings included signs of cardiac overload, such as cystic hygroma, hydrops, and cardiomegaly.

Discussion

In recent years, studies concerning ductus venosus anomalies have gained momentum. The management of DVA depends on the type of agenesis, the presence of associated anomalies, and the gestational age at diagnosis. When DVA is diagnosed prenatally, due to the elevated risk of IUGR and other complications in these fetuses, it is vital to closely monitor fetal growth and well-being [10].

Postnatal management of infants with DVA is determined by the severity of the condition and the presence of associated anomalies. In cases with portosystemic shunts, surgical intervention may be required to prevent complications like liver dysfunction and pulmonary hypertension [9,11].

Table 1. Classification, concomitant anomalies and prognosis of fetuses in DVA patients

Case	DVA Type	Chromosome	Additional Sonographic Findings	Outcome
1	IHE	Normal	One of the twins dva	Live birth at term
2	EH	Normal	Cystıc hygroma Omphalocele Single umbilikal artery	Termination at 16 weeks
3	EH	Unknown	Cystic hygroma Bilateral talipes	Termination at 18 weeks
4	IH	Normal	Single umbilikal artery Cardiomegaly Blake pouch cyst	Live birt at 36 weeks 21 days NICU-Lives
5	IH	Normal	Ventricular septal defect	Live birt at 32 weeks Postpartum died
6	EH	Phenylketonuria	Cardiac hyperechoic focus	Live birt at term 6 months NICU-Died
7	EH	Unknown	Cleft palate	Live birt at 36 weeks 3 days NICU-Died
8	IH	Unknown	None	Live birth at term 1 month NICU-Lives
9	EH	Unknown	IUGR Umbilical vein varicose	Live birth at 32 weeks Postpartum died
10	EH	Normal	Ventriculomegaly Diaphragmatic hernia	Termination at 28 weeks
11	EH	Turner	Hydrops fetalis Cystic hygroma Single umblical artery	Termination at 19 weeks
12	IH	Unknown	None	Live birth at term
13	EH	Trisomy 21	Increased nb Hyperechoic bowel	Termination at 22 weeks
14	EH	Normal	IUGR, Bilateral uterine artery notch, Single umbilikal artery, Cardiothoracic index increased Shortness of long bones	Live birth at 30weeks 6 months NICU-Died
15	IH	Unknown	Hydrocephalus Shift of the heart axis to the left	Live birt at term 15 days NICU-Lives
16	IH	Normal	None	Live birth at term

In other cases, conservative treatment with regular follow-up to monitor potential complications might be appropriate [12]. Previous studies in the literature have explored the outcomes and effects of DVA in fetuses. Moaddab et al. (2016) found 46.7% normal outcomes, 34.4% chromosomal abnormalities, and 18.9% structural

abnormalities in 259 DVA cases, while Pacheco et al. (2018) identified isolated DVA in 44.6% of the cases and associated anomalies in 55.4%. Maruotti et al. (2018) reported 42.1% normal outcomes, 31.6% chromosomal abnormalities, and 26.3% structural abnormalities in 19 DVA cases [5].

Similarly, Strizek et al. (2019) found 47.9% normal outcomes, 29.2% chromosomal abnormalities, and 22.9% structural abnormalities in 48 cases, while McBrien et al. (2021) reported 44% normal outcomes, 30% chromosomal abnormalities, and 26% structural abnormalities. These studies demonstrate that DVA is associated with diverse outcomes and effects in fetuses (4,11,13].

In our study, of the 16 cases with DVA, the umbilical vein connected to the portal system in 7 cases (44% - intrahepatic) and to the systemic venous system in 9 cases (56% - extrahepatic). The three identifiable chromosomal anomalies were similarly in the extrahepatic drainage group in line with the literature. All pregnancies in the extrahepatic shunt group were either terminated or lost post-delivery. In the intrahepatic drainage group, one baby was lost post-delivery (n:1 - 14%), while the others survived. 25% of the cases (n:4) were isolated, and all isolated cases were in the intrahepatic drainage group and resulted in live births.

The absence of the DV is a rare condition with outcomes varying based on associated factors such as other congenital anomalies, fetal growth restriction, and the presence of portosystemic shunts. Some studies suggest that the prognosis can be positive in cases where no other significant anomaly is present [10, 14]. However, the existence of concomitant malformations or chromosomal abnormalities can significantly worsen the prognosis [4, 11, 13]. Prenatal characteristics and the diameter of portosystemic shunts can also influence outcomes [15,16]. We must bear in mind that the absence of the DV might not always be an isolated finding and can be accompanied by congenital heart disease [17,18], growth retardation, and chromosomal abnormalities [19].

As mentioned in the studies referenced above, research in the literature indicates that while approximately 40-50% of DVA cases do not coexist with another anomaly, the rest are associated with structural or chromosomal abnormalities. A better prognosis is expected in cases without associated anomalies and those without extrahepatic venous drainage.

While studies have clearly demonstrated the incidence of congestive heart failure in DV agenesis with extrahepatic venous drainage, there is limited information regarding the intrahepatic venous drainage portion of DV agenesis [4,19].

In conclusion, DVA is a rare congenital abnormality with potentially significant implications for affected fetuses and infants. Early diagnosis, careful monitoring, and appropriate management strategies are essential to optimize outcomes for these patients. Further research is required to better understand the underlying etiology and pathophysiology of DVA and to develop more effective treatment options for those affected.

Disclosure

Authors have no potential conflicts of interest to disclose.

References

[1] Kiserud T, Acharya G. The fetal circulation. Prenat Diagn. 2004 Dec 30;24(13):1049-59. doi: 10.1002/pd.1062. PMID: 15614842.

[2] Kiserud, Torvid, and Jörg Kessler. "The Ductus Venosus." Doppler ultrasound in obstetrics and gynecology. Cham: Springer International Publishing, 2023. 449-473.

[3] Tchirikov M, Schröder HJ, Hecher K. Ductus venosus shunting in the fetal venous circulation: regulatory mechanisms, diagnostic methods and medical importance. Ultrasound Obstet Gynecol. 2006 Apr;27(4):452-61. doi: 10.1002/uog.2747. PMID: 16565980.

[4] Pacheco, D., Brandao, O., Montenegro, N., & Matias, A. (2018). Ductus venosus agenesis and fetal malformations: what can we expect?–a systematic review of the literature. Journal of Perinatal Medicine, 47(1), 1-11.

[5] Contratti, G., Banzi, C., Ghi, T., Perolo, A., Pilu, G., Visentin, A. (2001). Absence of the ductus venosus: report of 10 new cases and review of the literature. Ultrasound in Obstetrics and Gynecology: The Official Journal of the International Society of Ultrasound in Obstetrics and Gynecology, 18(6), 605-60

[6] Maruotti, GM, Saccone, G., Ciardulli, A., Mazzarelli, LL, Berghella, V., Martinelli, P. (2018). Absent duktus venosus: iki tersiyer merkezden vaka serileri. The Journal of Maternal-Fetal & Neonatal Medicine , 31 (18), 2478-2483.

[7] Berg C, Kamil D, Geipel A, Kohl T, Knöpfle G, Hansmann M, et all. Absence of ductus venosus-importance of umbilical venous drainage site. Ultrasound Obstet Gynecol. 2006 Sep;28(3):275-81. doi: 10.1002/uog.2811. PMID: 16826563.

[8] Seckin KD, Karslı MF, Baser E, Yeral MI, Tasin C, Ozgu Erdinc AS, et all. Obstetric outcomes in pregnancies with normal nuchal translucency and abnormal ductus venosus Doppler in the first trimester ultrasonography. J Obstet Gynaecol. 2016 May;36(4):440-3. doi: 10.3109/01443615.2015.1060210. Epub 2015 Oct 12. PMID: 26457755.

[9] Kamimatsuse A, Onitake Y, Kamei N, Tajima G, Sakura N, Sueda T, et all. Surgical intervention for patent ductus venosus. Pediatr Surg Int. 2010 Oct;26(10):1025-30. doi: 10.1007/s00383-010-2662-x. PMID: 20661579.

[10] Strizek B, Zamprakou A, Gottschalk I, Roethlisberger M, Hellmund A, Müller A, et all. Prenatal Diagnosis of Agenesis of Ductus Venosus: A Retrospective Study of Anatomic Variants, Associated Anomalies and Impact on Postnatal Outcome. Ultraschall Med. 2019 Jun;40(3):333-339. English. doi: 10.1055/s-0043-115109. Epub 2017 Sep 21. PMID: 28934814.

[11] Moaddab A, Tonni G, Grisolia G, Bonasoni MP, Araujo Júnior E, Rolo LC, et all.. 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 Nov;29(22):3606-14. doi: 10.3109/14767058.2016.1144743. Epub 2016 Mar 3. PMID: 26809266.

[12] Sothinathan U, Pollina E, Huggon I, Patel S, Greenough A. Absence of the ductus venosus. Acta Paediatr. 2006 May;95(5):620-1. doi: 10.1080/08035250500477560. PMID: 16825145.

[13] 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 Jan;41(1):15-20. doi: 10.1002/pd.5827. Epub 2020 Nov 3. PMID: 32920862.

[14] Dauvillée J, Ingargiola I, Jouret M, Biard JM, Steenhaut P, Bernard P. Fetal umbilical-systemic shunt with a positive issue. J Gynecol Obstet Hum Reprod. 2020 Apr;49(4):101656. doi: 10.1016/j.jogoh.2019.101656. Epub 2019 Nov 21. PMID: 31760176.

[15] Shen O, Valsky DV, Messing B, Cohen SM, Lipschuetz M, Yagel S. Shunt diameter in agenesis of the ductus venosus with extrahepatic portosystemic shunt impacts on prognosis. Ultrasound Obstet Gynecol. 2011 Feb;37(2):184-90. doi: 10.1002/uog.7702. Epub 2010 Jun 2. PMID: 20521238.

[16] Erenel H, Karsli MF, Ozel A, Korkmaz SO, Sen C. Ductus venosus-systemic shunt. Report of six cases and systematic review of the literature. J Matern Fetal Neonatal Med. 2020 Mar;33(6):1015-1023. doi:

10.1080/14767058.2019.1569611. Epub 2019 Jan 28. PMID: 30691333.
[17] Vigneswaran TV, Homfray T, Allan LD, Simpson JM, Zidere V. Persistently elevated nuchal translucency and the fetal heart. J Matern Fetal Neonatal Med. 2018 Sep;31(18):2376-2380. doi: 10.1080/14767058.2017.1342804. Epub 2017 Jul 4. PMID: 28614966.
[18] Berg C, Lachmann R, Kaiser C, Kozlowski P, Stressig R, Schneider M, et all. Prenatal diagnosis of tricuspid atresia: intrauterine course and outcome. Ultrasound Obstet Gynecol. 2010 Feb;35(2):183-90. doi: 10.1002/uog.7499. PMID: 20101636.
[19] Deter RL, Dicker P, Lee W, Tully EC, Cody F, Malone FD, et all. Growth patterns and cardiovascular abnormalities in SGA fetuses: 2. Normal growth and progressive growth restriction. J Matern Fetal Neonatal Med. 2022 Jul;35(14):2818-2827. doi: 10.1080/14767058.2020.1807506. Epub 2020 Sep 13. PMID: 32924675.