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

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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].

In 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
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

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

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


