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DATA NOTE

The relationship between umbilical-portal-systemic venous shunt and outcome in 11 fetuses [version 1; peer review: 2 approved with reservations]

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V1 First published: 18 Oct 2021, 10:1058
<https://doi.org/10.12688/f1000research.55600.1>
 Latest published: 18 Oct 2021, 10:1058
<https://doi.org/10.12688/f1000research.55600.1>

Abstract

Objective: To investigate the relationship between congenital umbilical-portal-systemic venous shunt (UPSs) and fetal outcome.

Methods: The ultrasonographic and genetic characteristics of 11 cases of UPSs were retrospectively analyzed and followed up to postnatal.

Results: Four cases of ductus venosus -- systemic shunt (DVSS), one case of extrahepatic portal -- systemic shunt (EHPSS), and one case of umbilical systemic shunt (USS) combined with intrahepatic portal-systemic shunt (IHPSS), six cases of intrahepatic portal-systemic shunt (IHPSS) were observed. chromosomal abnormalities were observed in 9.1% (1/11), other ultrasonic abnormalities in 54.5% (6/11), cardiothoracic ratio increase in 45.5% (5/11), fetal growth restriction in 36.4% (4/11), edema was in 9.1% (1/11) and live birth was in 72.7% (8/11).

Conclusion: The incidence of IHPSS is the highest and the outcome is the best. Shunt of DVSS and IHPSS can be closed spontaneously after birth. When the prenatal diagnosis is congenital UPSs, chromosomal abnormalities and other ultrasonic abnormalities should be required further examination, and the growth and development of the fetus should be closely monitored.

Keywords

umbilical-portal-systemic venous shunt; fetus; the outcome

Open Peer Review

Approval Status ? ?

	1	2
version 1		
18 Oct 2021	view	view

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2. **Johannes van der Merwe** , University Hospitals Leuven, Leuven, Belgium

Any reports and responses or comments on the article can be found at the end of the article.

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Author roles: Fang L: Conceptualization, Data Curation, Formal Analysis, Investigation, Methodology, Project Administration, Writing – Original Draft Preparation, Writing – Review & Editing; Xueyan W: Data Curation, Formal Analysis, Project Administration; Yangxue X: Data Curation, Formal Analysis, Investigation, Methodology, Software; Xiaohang Z: Investigation, Methodology; Suzhen R: Investigation, Methodology; Lan Z: Investigation; Deying H: Investigation

Competing interests: No competing interests were disclosed.

Grant information: The author(s) declared that no grants were involved in supporting this work.

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How to cite this article: Fang L, Xueyan W, Yangxue X *et al.* **The relationship between umbilical-portal-systemic venous shunt and outcome in 11 fetuses [version 1; peer review: 2 approved with reservations]** F1000Research 2021, 10:1058 <https://doi.org/10.12688/f1000research.55600.1>

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Introduction

Congenital portosystemic shunt (CPSS) is associated with some complications, such as cholestasis, hyperammonemia, pulmonary arterial hypertension, hepatopulmonary syndrome, and benign and malignant liver tumors, in childhood. Some types of CPSS including extrahepatic, persistent intrahepatic shunt and ductus venosus must be inhibited by interventional radiology or surgery.¹

Due to the low incidence, there is limited prenatal information on the relationship between umbilical-porta-systemic shunt and its prognosis. In the past, portal systemic shunts were divided into extrahepatic and intrahepatic shunts. They have been used to study fetal umbilical-portal system shunt and pediatric congenital portal systemic shunt.^{2–6} The recent systematic reclassification of the term “umbilical-porta-systemic venous shunt (UPSVS)” has been considered as the best choice for fetal prognosis analysis. This classification is based on the theory of UV-PV-DV as an intact structure.

According to Achiron and Kivilevitch,⁷ the UPSVs are divided into three types: Type I, umbilical–systemic shunt (USS), with the blood flow from the umbilical vein entered directly into the systemic veins; Type II, ductus venosus–systemic shunt (DVSS), with the DV blood flow shunted from its normal path into the systemic veins; Type III, portal–systemic shunt, which divided into two subgroups: Type IIIa, intrahepatic portal–systemic shunt (IHPSS), with an intrahepatic shunt between the IHPVS and the hepatic vein; and Type IIIb, extrahepatic portal–systemic shunt (EHPSS), with an extrahepatic shunt between the portal system and systemic veins (IVC, iliac vein, renal vein). According to previous studies, the incidence of trisomy 21 in UPSVS was 10.4%.⁸ Achiron *et al.* observed that DVSS and IHPSS had the best prognosis, with spontaneous shunt closure after birth.⁷ Berg *et al.*⁹ observed that cases with extrahepatic shunt were more likely to develop into cardiac decompensation. Delle *et al.*¹⁰ observed a causal relationship between IHPSS and FGR.

The purpose of this study was to review our experience with fetal UPSVS and analyze its clinical and prognostic characteristics for better prenatal counseling with UPSVS.

Methods

Retrospective analysis was performed on 11 cases of UPSVSs admitted to the prenatal diagnosis center of our hospital from December 1, 2019, to December 1, 2020. According to the UPSVS classification criteria, four cases were DVSS, and six cases were IHPSS, including one case of USS combined with IHPSS and one case of EHPSS. All patients signed an informed consent form, performed routine ultrasound examinations of the fetus, placenta and amniotic fluid, and then performed detailed examinations and records of each fetus's heart, celiac vessel and middle cerebral artery, focusing on observation of the umbilical vein and ductus venosus, main portal vein, left and right branch morphology, internal echo and surrounding structures, observed whether there are abnormal ducts between the umbilical vein, ductus venosus, portal vein, hepatic vein and other systemic veins, and follow up until the shunt is closed after birth. The karyotype and low-coverage massively parallel copy number variation sequencing (CNV-seq) of the fetus were further examined by amniocentesis. Statistical methods: Descriptive statistics were used to retrospectively analyze the clinical features and pregnancy outcomes of 11 cases. SPSS20.0 software was used for statistical analysis of data. Measurement data was expressed as mean ($\pm$ SD), and the Bonferroni adjustment method in ANOVA was used for pairwise comparison. $p < 0.05$ indicates that the difference is statistically significant. Counting data are expressed as percentages.

Results

According to the UPSVS classification criteria, four cases of DVSS, six cases of IHPSS, one case of USS combined with IHPSS and one case of EHPSS were recorded.

The four cases of DVSS

In two cases, the ductus venosus entered the middle of the inferior vena cava (Cases 2 and 4) and was observed at the gestational age of 23 weeks and 24+4 weeks, respectively. In one case, observed at 18 weeks of gestation, the ductus venosus was inserted into the hepatic segment of the inferior vena cava (Case 1, [Figure 1](#)). In one case, observed at 23 +4 weeks, the ductus venosus was inserted into the middle hepatic vein (Case 3). Three cases received amniocentesis to do karyotype and CNV-seq test, and trisomy 21 was observed in Case 1; the other two cases had normal results. Two cases terminated their pregnancies: Case 1 terminated pregnancy because of trisomy 21, Case 3 terminated because of other associated structural abnormalities, including multiple hemivertebrae with scoliosis, and the left and right branches of the portal vein are not detected on ultrasound. Two cases were delivered prematurely (Cases 2 and 4), of which Case 4 had fetal growth restriction. The ductus venosus of the two cases had closed one month after birth, and the growth and development were normal.

Figure 1. I represents DV: ductus venosus, IVC: inferior vena cava, ductus venosus enters the hepatic segment of inferior vena cava. II represents: MHV: middle hepatic vein, LPVsb: left upper branch of portal vein; LPVlb: left lower branch of portal vein; the left upper branch and left lower branch of the portal vein enter into the middle hepatic vein. III indicates: MHV: middle hepatic vein, LPV: left portal vein, left portal vein enters into middle hepatic vein. IV (A) indicates: the confluence point of left outer lower branch of portal vein and middle hepatic vein, (B): the confluence point of left inner portal vein and the right hepatic vein.

- One case of EHPSS
- In Case 5, at 24+4 weeks of gestation, ultrasound showed fetal edema including abdominal effusion and skin thickening, widened hepatic veins, and increased cardiothoracic ratio, suggesting congestive heart failure. The umbilical vein was directly connected to the ductus venosus, the left and right branches of the portal vein and the main portal vein are not shown. The splenic vein was thin, and did not appear to enter the portal vein, the superior mesenteric vein was unclear. The distal end of the hepatic vein was widened and tortuous, seeming to be connected to the distal end of the hepatic artery, suggesting hepatic arteriovenous fistula. The pregnant woman finally chose to terminate the pregnancy without a chromosome examination.

One case of USS

Case 8 displayed USS combined with IHPSS, see IHPSS for details.

Six cases of IHPSS

The location of shunt in six cases is shown in Table 1. Amniocentesis was performed in two cases. The results showed no abnormality in karyotype or gene copy number variation. Two cases had fetal growth restriction (Cases 7 and 10). Ultrasound revealed cardiothoracic ratio increased in three cases (Cases 7, 8 and 10), congestive heart failure with possible cerebral edema in one case (Case 10). In Case 10, MRI revealed: cerebral vein, superior sagittal sinus, right transverse sinus and enlarged sigmoid sinus. Finally, one case underwent full-term delivery, five cases underwent premature delivery, due to congestive heart failure with possible cerebral edema (Case 10), increased cardiothoracic ratio (Cases 7 and 8), breech presentation combined with premature rupture of membranes (Case 9), fetal growth restriction with oligohydramnios (Case 11). All six cases had live births. Follow-up of those six cases showed that the shunts were closed within half a year after birth, and blood ammonia, liver function, growth and development were normal.

Table 1. Clinical features and outcomes of the cases (n = 11).

	Classification	GA	Shunt	FGR	Cardiac anomalies	Edema	Anomalies associated	Karyotype	CNV-seq	Pregnancy outcome	Shunt closure	Growth and development after birth
Case1	DVSS	18W	DV-IVC	No	No	No	Absence of nasal bone	47, XN+21	Normal	TOP	/	/
Case2	DVSS	23W	DV-IVC	No	No	No	No	Normal	Normal	Premature delivery by cesarean section	1 month after birth	Normal
Case3	DVSS	23+4W	DV-MHV	No	No	No	Multiple hemivertebrae with scoliosis	/	/	TOP	/	/
Case4	DVSS	24+4W	DV-IVC	Yes	No	No	Polydactylism	Normal	Normal	Premature delivery by cesarean section	1 month after birth	Normal
Case5	EHPSS	24+4W	UV-DV	No	Congestive heart failure	Yes	No	/	/	TOP	/	/
Case6	IHPSS	26+4W	LPV-LHV	No	No	No	No	Normal	Normal	Term delivery by cesarean section (breech presentation)	4 months after birth	Normal
Case7	IHPSS	35+4W	LPV-MHV, LPV-RHV	Yes	CTR: 0.42	No	No	/	/	Premature delivery by cesarean section	4 months after birth	Normal
Case8	IHPSS	36+5W	LPV-MHV(2 branches), combined with UV-MHV (multiple branches)	No	CTR: 0.46	No	No	/	/	Premature delivery by cesarean section	1 month after birth	Normal
Case9	IHPSS	30+1W	LPV-MHV	No	No	No	No	/	/	Premature delivery via vaginal delivery (PPROM)	6 months after birth	Normal
Case10	IHPSS	35+1W	LPV-MHV LPV-RHV LPV-LHV	Yes	Congestive heart failure	No	Possible encephaledema	Normal	Normal	Premature delivery by cesarean section	6 months after birth	Normal
Case11	IHPSS	34+4W	LPV-LHV	Yes	CTR: 0.42	No	No	Normal	Normal	Premature delivery by cesarean section (oligoamnios)	6 months after birth	Normal

a.LPV-LHV: Left portal vein to left hepatic vein (shunt between the left branch of the portal vein and the left hepatic vein).
b.LPV-MHV: Left portal vein to middle hepatic vein (shunt between the left branch of the portal vein and the middle hepatic vein).
c.LPV-RHV: Left portal vein to right hepatic vein (shunt between the left branch of the portal vein and the right hepatic vein).
d.UV-MHV: Umbilical vein to middle hepatic vein (shunt between umbilical vein and middle hepatic vein).
e.UV-DV: Umbilical vein to ductus venosus (shunt between umbilical vein and ductus venosus).
f.DV-IVC: Ductus venosus to inferior vena cava (shunt between ductus venosus and inferior vena cava).
j. DV-MHV: Ductus venosus to middle hepatic vein (shunt between Ductus venosus and the middle hepatic vein).
h.FGR: Fetal growth restriction.
i.GA: Gestational age.
j.TOP: Termination of pregnancy.
CTR: cardiothoracic ratio.

Table 2. Clinical features and outcomes of 11 cases.

	Total (n = 11)	DVSS (n = 4)	IHPSS (n = 6)	EHPSS (n = 1)	p < 0.05
Age	29.360 ± 5.005	27.250 ± 4.787	31.500 ± 4.848	25	p = 0.305
GA	27.655 ± 6.158	22.300 ± 2.942	31.733 ± 5.088	24.6	p* = 0.028
Chromosome abnormality	9.1% (1/11)	33.33% (1/3)	0%	/	
Other Ultrasonic Abnormalities	54.5% (6/11)	75% (3/4)	33.3% (2/6)	100%	
CTR enlargement	45.5% (5/11)	0%	66.7% (4/6)	100%	
Edema	9.1% (1/11)	0%	0%	100%	
FGR	36.4% (4/11)	25% (1/4)	50% (3/6)	0%	
Live birth	72.7% (8/11)	50% (2/4)	100%	0%	

* Represents p-value: * p < 0.05.

Results are shown in [Tables 1](#) and [2](#).

- **What's known/what's new statements**
- **What's already known about this topic?**

UPSVSs are divided into three types in recent research. Limited prenatal information is available on the relationship between umbilical–portal–systemic venous shunt and outcome due to the low incidence.

What does this study add?

We collected 11 cases of fetus from different UPVSV types, and analyze the clinical and prognostic characteristics in details to enable better prenatal counseling with UPSVS.

Ethics statement

The report was ethically approved by the institutional review board (Chongqing Health Center of Women and Children) and written informed consent was obtained from the mothers to publish this paper.

Data availability

Underlying data

Dryad: Underlying data for 'The relationship between umbilical–portal–systemic venous shunt and outcome in 11 fetuses'.

<https://doi.org/10.5061/dryad.crjdfn34g>

Data are available under the terms of the [Creative Commons Zero "No rights reserved" data waiver](#) (CC0 1.0 Public domain dedication).

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[PubMed Abstract](#) | [Publisher Full Text](#)

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Current Peer Review Status: ? ?

Version 1

Reviewer Report 27 June 2022

<https://doi.org/10.5256/f1000research.59190.r140424>

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Johannes van der Merwe

University Hospitals Leuven, Leuven, Belgium

The manuscript describes the clinical outcomes of a small series of prenatal diagnosed UPSVS cases. The manuscript is overall sound and the topic is relevant. The biggest criticism of this manuscript is that it seems to add no new insights to this rare finding. Structured comments:

1. General:

- The manuscript is sometimes difficult to read due to syntax issues and vocabulary choice. The manuscript could benefit from formal copyediting.
- Structurally some headings and subheadings have been omitted.

2. Introduction:

- Adequate although the authors don't reflect on recent publications. A lot have been published in this field in the last 2-3 years.

3. Case descriptions

- The case descriptions could benefit from ultrasound images being added of the EHPSS case and at least one example case of the IHPSS case.

4. Discussion – what the study adds.

- The authors provoke no new discussion on this topic. Nor is there any reflection on current literature or systematic reviews on this pathology. It is unclear to the reader what future direction should be taken with this pathology. Some examples of recent publications that could help:

Van Houdt M, van der Merwe J, Gewillig M, De Catte L. Prenatal 3D-ultrasound diagnosis of isolated intrahepatic portal-systemic shunt with intact ductus venosus: A case report and literature review. *Radiology Case Reports*. 2021 May 1;16(5):1173-8.

Nagy RD, Cernea N, Dijmarescu AL, Manolea MM, Zorilă GL, Drăgușin RC, Vrabie SC, Dîră LM, Sîrbu OC, Novac MB, Drăgoescu NA. Ductus Venosus Agensis and Portal System Anomalies—Association and Outcome. *Biology*. 2022 Apr 1;11(4):548.

Erenel H, Karsli MF, Ozel A, Korkmaz SO, Sen C. Ductus venosus-systemic shunt. Report of six cases and systematic review of the literature. *The Journal of Maternal-Fetal & Neonatal Medicine*. 2020 Mar 18;33(6):1015-23.

Kivilevitch Z, Kassif E, Gilboa Y, Weisbuch T, Achiron R. The intra-hepatic umbilical-Porto-systemic venous shunt and fetal growth. *Prenatal Diagnosis*. 2021 Mar;41(4):457-64.

Pacheco D, Brandao O, Montenegro N, Matias A. Ductus venosus agenesis and fetal malformations: what can we expect?—a systematic review of the literature. *Journal of Perinatal Medicine*. 2018 Dec 1;47(1):1-1.

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Is the rationale for creating the dataset(s) clearly described?

Yes

Are the protocols appropriate and is the work technically sound?

Yes

Are sufficient details of methods and materials provided to allow replication by others?

Yes

Are the datasets clearly presented in a useable and accessible format?

Partly

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Fetal Medicine

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Author Response 07 Oct 2022

Liu Fang, Chongqing Health Center for Women and Children, Chongqing, China

It's my great honor to receive your review. Thank you for your detailed review and the added references. Because the manuscript was submitted as datasets, discussion on this topic was omitted. It took me some time to collect more interesting cases, and I will submit a new view soon. Hope to discuss further with you in the field of fetal diseases. Best regards.

Competing Interests: No competing interests were disclosed.

Reviewer Report 03 February 2022

<https://doi.org/10.5256/f1000research.59190.r119590>

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Bijoy K. Balakrishnan

Department of Feto-Maternal Medicine, CIMAR Cochin and Edappal Hospitals Pvt Ltd, Cochin, Kerala, India

Thank you for the opportunity to review this article. The cases that have been discussed are quite interesting and will provide necessary insight for clinicians while counselling their patients with UPVSS. However, it would have been more interesting if more pictures were provided and video clips were added as supplementary material for the readers to access. I myself would be interested in viewing the case of EHPSS and the cases with multiple shunts between the LPV and the hepatic veins. Once they are submitted I will provide a detailed review of the portal system and an easy method to screen for portal system anomalies.

Is the rationale for creating the dataset(s) clearly described?

Yes

Are the protocols appropriate and is the work technically sound?

Yes

Are sufficient details of methods and materials provided to allow replication by others?

No

Are the datasets clearly presented in a useable and accessible format?

Partly

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Fetal medicine specialist

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Author Response 06 May 2022

Liu Fang, Chongqing Health Center for Women and Children, Chongqing, China

Thank you for your review, we are still collecting cases. EHPSS cases are relatively rare, so it takes some time to summarize the cases. At present, A case of USS has given birth, the prognosis is good. We will collect more data for publication, and would like to discuss further with you in the field of fetal diseases.

Competing Interests: Non-Financial Competing Interests

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