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ORIGINAL ARTICLE

Intrahepatic persistent fetal right umbilical vein: a retrospective study

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ABSTRACT

Introduction: To appraise the incidence and value of intrahepatic persistent right umbilical vein (PRUV).

Methods: This was a single-center study. Records of all women with a prenatal diagnosis of intrahepatic PRUV were reviewed. The inclusion criteria were women with gestational age greater than 13 weeks of gestation. Exclusion criteria were fetuses with situs abnormalities, due to the hepatic venous ambiguity, and extrahepatic PRUV. The primary outcome was the incidence of intrahepatic PRUV in our cohort. The secondary outcomes were associated malformations.

Results: 219/57,079 cases (0.38%) of intrahepatic PRUV were recorded. The mean gestational age at diagnosis was 21.8 ± 2.9 weeks of gestations. PRUV was isolated in the 76.7%, while in 23.3% was associated with other major or minor abnormalities. The most common associated abnormalities were cardiovascular abnormalities (8.7%), followed by genitourinary abnormalities (6.4%), skeletal abnormalities (4.6%), and central nervous system abnormalities (4.1%). Within the cardiovascular abnormalities, the most common one was ventricular septal defect (six cases).

Conclusion: In most cases PRUV is an isolated finding. Associated minor or major malformations are presented in the 23.3% of the cases, so this finding should prompt detailed prenatal assessment of the fetus, with particular regard to cardiovascular system.

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Abortion; fetal malformation; genetic; MRI; NIPT

Introduction

Persistent right umbilical vein (PRUV) is a pathologic vascular anomaly occurring in embryonic development in which the right umbilical vein persists, and the left vein is occluded. PRUV is the most common anomalies of the Porto-umbilical system [1].

The estimated frequency of PRUV is about 1 in 250–1250 [2]. This anomaly can occur in an isolated form, representing a variant of normality, or can be associated to other major or minor anomalies. The presence of a PRUV can be assessed in the transverse section of the fetal abdomen during routine scan. The umbilical vein courses laterally and to the right of the gallbladder, where it may then fuze with the right portal vein, which courses toward the stomach, in the so-called intrahepatic variant. In the extrahepatic variant, associated with agenesis of ductus venosus (DV), the umbilical vein drains into the right atrium, infracardiac portion of the inferior vena cava, or iliac veins [1,3]. Case series on intrahepatic PRUV published so far included small number of cases, and a recent systematic review by Lide et al. of all published studies included 16 articles for a total of only 240 cases of intrahepatic PRUV [4]. Therefore, the exact incidence and the clinical significance of intrahepatic PRUV is not well known. The primary endpoint of this study is to appraise the incidence and significance of intrahepatic PRUV in a retrospective single-center study.

Materials and methods

Study design and participants

This was a single-center retrospective study. Clinical records of all consecutive pregnant women with a prenatal diagnosis of intrahepatic PRUV, who were referred to our Center (Diagnostica Ecografica e Prenatale di A. Di Meglio, Naples, Italy), were included in this study.

The inclusion criteria were pregnant women with gestational age greater than 13 weeks of gestation. Exclusion criteria were fetuses with situs abnormalities,

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Table 1. Characteristics of the included women.

	$N = 219$
Age	31.6 ± 4.9
Gravidity	1.7 ± 0.9
Singletons	205 (93.6%)
Twins	12 (5.5%)
Triplets	2 (0.9%)
IVF	4 (1.8%)
Gestational age at diagnosis	21.8 ± 2.9

Data are presented as number (percentage) or as mean ± standard deviation.
IVF: *in vitro* fertilization.

due to the hepatic venous ambiguity, and extrahepatic PRUV.

The diagnosis of intrahepatic PRUV was based on the following criteria [4]:

1. Situs solitus
2. Curving of the intrahepatic portion of UV toward fetal left in the standard abdominal circumference plane using gray scale 2D and color Doppler
3. Medial relation of the gall bladder with the UV, between PRUV and stomach

In all cases of PRUV, a detailed anatomy scan was performed, including fetal echocardiography. The status of the DV was also documented in all the cases.

Outcomes

The primary outcome was the incidence of intrahepatic PRUV in our cohort. The secondary outcomes were associated malformations, including cardiovascular abnormalities, and incidence of chromosomal abnormalities.

Statistical analysis was performed using Statistical Package for Social Sciences (SPSS) v. 19.0.

Results

From January 2000 to January 2019, out of the 57,079-s trimester ultrasound scans performed, 219 cases (0.38%) of intrahepatic PRUV, and 5 cases (0.01%) of extrahepatic PRUV with agenesis of DV, were recorded. The vast majority of intrahepatic PRUV were singleton pregnancies (93.6%), 12 were twins, and 2 were triplets. In all the 14 cases of multiple gestations, only one fetus was affected. The mean gestational age at diagnosis was 21.8 ± 2.9 weeks of gestations, ranging from 13 to 25 weeks (Table 1).

PRUV was isolated in the 76.7% of the cases, while in 51 cases (23.3%) was associated with other major or minor abnormalities (Table 2). The most common associated abnormalities were cardiovascular abnormalities, reported in the 8.7% of the cases, followed by genitourinary abnormalities (6.4%), skeletal abnormalities (4.6%), and central nervous system abnormalities (4.1%). Within the cardiovascular abnormalities, the most common one, was ventricular septal defect, reported in six cases (Table 3). Single umbilical artery was noticed in 8 cases (3.7%). Only four pregnancies (1.8%) had chromosomal abnormalities, including one 47, XXX; one T(9;13) balanced translocation; one partial monosomy 9p; and one inversion of chromosome 3.

Table 2. Associated abnormalities.

	$N = 219$
Isolated	168 (76.7%)
Overall associated abnormalities	51 (23.3%)
Central nervous system associated abnormalities	
Overall	9 (4.1%)
Agenesis corpus callosum	1 (0.5%)
Colpocephaly	1 (0.5%)
Hydrocephalus	3 (1.4%)
Cerebellar Hypoplasia	3 (1.4%)
Lissencephaly	1 (0.5%)
Choroid plexus cysts	2 (0.91%)
Cord associated abnormalities	
Single umbilical artery	8 (3.7%)
Genitourinary associated abnormalities	
Overall	14 (6.4%)
Unilateral renal agenesis	2 (0.9%)
Hydronephrosis	7 (3.2%)
Cloacal exstrophy	1 (0.5%)
Bladder exstrophy	1 (0.5%)
Multicystic dysplastic kidney (MCDK)	2 (0.9%)
Hyperechogenic kidneys	1 (0.5%)
Gastroenteric associated abnormalities	
Overall	6 (2.7%)
Duodenal atresia	2 (0.9%)
Calcification of glissonian capsule	2 (0.9%)
Hyperechogenic bowel	3 (1.4%)
Stasis Liver	1 (0.5%)
Skeletal abnormalities	
Overall	10 (4.6%)
Unilateral club foot	1 (0.5%)
Bilateral club foot	4 (1.8%)
Bilateral agenesis upper limbs	1 (0.5%)
Sacral hypoplasia	1 (0.5%)
Transverse hemimelia lower limb	1 (0.5%)
Humeral hypoplasia with absent radius	1 (0.5%)
Brachydactyly	1 (0.5%)
Thorax abnormalities	
Overall	3 (1.4%)
Diaphragmatic hernia	1 (0.5%)
Lung hypoplasia	1 (0.5%)
Pleural effusion	1 (0.5%)
Face abnormalities	
Overall	4 (1.8%)
Cleft lip	2 (0.9%)
Micrognathia	1 (0.5%)
Hypotelorism	1 (0.5%)
Hypoplasia nasal bone	1 (0.5%)
Genital abnormalities	
Hypogenitalism	1 (0.5%)
Chromosomal abnormalities	
Overall	4 (1.8%)
47, XXX	1 (0.5%)
T(9;13) balanced translocation	1 (0.5%)
Partial monosomy 9p	1 (0.5%)
Inversion chromosome 3	1 (0.5%)

Data are presented as number (percentage).

Table 3. Incidence of cardiovascular abnormalities.

	$N = 219$
Overall	19 (8.7%)
Ventricular septal defect	6 (2.7%)
Atrioventricular canal	3 (1.4%)
Tetralogy of fallot	1 (0.5%)
Right aortic arch	1 (0.5%)
Dextrocardia	1 (0.5%)
Aberrant left subclavian artery	1 (0.5%)
Aberrant right subclavian artery	1 (0.5%)
Atrial septal defect	1 (0.5%)
Hypoplastic left heart	2 (0.9%)
Transposition of the great arteries	1 (0.5%)
Persistent left superior vena cava	1 (0.5%)
Interrupted inferior vena cava with azygos continuation	2 (0.9%)
Dysplastic tricuspid valve	2 (0.9%)
Pericardial effusion	3 (1.4%)
Abdominal aortic aneurysm	1 (0.5%)
Heart failure	1 (0.5%)
Fetal arrhythmias	2 (0.9%)
Aortic valve stenosis	1 (0.5%)

Data are presented as number (percentage).

Discussion

Main findings

In our cohort, the prevalence of intrahepatic PRUV was 0.38%. In the majority of the cases, PRUV was not associated with major or minor abnormalities, i.e. was isolated. Associated minor or major malformations are presented in the 23.3% of the cases, with the cardiovascular abnormalities being the most common associated malformations. PRUV was rarely associated with chromosomal abnormalities, being reported in only 1.8% of the cases. This cohort may be the largest population of fetuses with intrahepatic PRUV published so far.

Prior studies have been published on intrahepatic PRUV (Table 4) [4–17]. A recent systematic review [4], included 240 cases of intrahepatic PRUV. The overall prevalence of intrahepatic PRUV was found to be 212 per 166,548 (0.13%). Of the 240 cases of an PRUV identified by the review, 183 (76.3%) were isolated. In 23.7% of the cases, the authors found minor or major abnormalities, including 19 cardiac abnormalities (7.9%), 9 cases of malformations in the central nervous system (3.8%), 15 cases of abnormalities in the genitourinary system (6.3%), 17 cases (7%) of placental or cord abnormalities, and only three women (1.3%) with genetic abnormalities [4]. Three more studies have been published after the systematic review [5–7]. Krzyżanowski et al. reported on 12 cases of PRUV [5]. They reported an incidence of PRUV of 0.5% (12/2360), with vast majority of the cases (9 cases, 75%) showing PRUV as an isolated finding with favorable prognosis [5]. In referral centers, the prevalence of fetuses with anomalies is usually increased, and this may explain the higher prevalence of PRUV in our cohort. In prior published studies the prevalence of intrahepatic PRUV ranged from 0.03% to 0.51%, with a mean of 0.13% (Table 4).

Table 4. Reported prevalence of intrahepatic persistent right umbilical vein, studies published since 1994.

	Reported prevalence
Hill 1994 [14]	33/15,237 (0.22%)
Kinare 1996 [16]	8/5,754 (0.14%)
Blazer 2000 [13]	69/30,240 (0.22%)
Wolman 2002 [12]	17/8,950 (0.19%)
Viora 2004 [17]	9/34,410 (0.03%)
Yang 2007 [11]	6/1,302 (0.46%)
Weichert 2011 [10]	39/46,653 (0.08%)
Leal 2012 [15]	9/3,576 (0.25%)
Martinez 2013 [9]	22/20,426 (0.11%)
Adiego-Calvo 2016 [6]	56/43,149 (0.13%)
Kumar 2016 [7]	23/20,452 (0.11%)
Krzyżanowski 2019 [5]	12/2,360 (0.51%)
Total	303/232,509 (0.13%)
Toscano 2019	219/57,079 (0.38%)
Total including our cohort	522/289,588 (0.18%)

Adiego-Calvo et al. found 56 records of PRUV, with an overall rate of associated malformation of 17.9% [6]. Kumar et al. found 23 records of PRUV, with an incidence of associated malformation of 52.2%, with cardiovascular malformations being the most common ones [7].

Implications

At the end of the seventh week of gestation, when the embryo is about 6 mm long, the right umbilical vein has normally disappeared [18]. Two types of PRUV have been described in literature. In the type 1, the intrahepatic form, the right umbilical vein is connected to the portal system and the DV is present. In the type 2, the extrahepatic form, the right umbilical vein "jumps" completely the hepatic circulation going to connect directly to the inferior vena cava or to the right atrium.

According with our findings, the prevalence of intrahepatic PRUV was about 0.4%, with an incidence of associated malformation of 23.3%. Although the diagnosis of PRUV can be made by using the B-mode, the routine use of Color-Doppler in the transverse abdominal section may avoid a missing diagnosis. The routine use of Color-Doppler in the transverse abdominal section during the second trimester routine anatomy scan may explain the higher prevalence of PRUV in our cohort compared to prior published studies.

Conclusions

In summary, in the majority of cases intrahepatic PRUV was isolated with no minor or major associated abnormalities. Associated minor or major malformations are

presented in the 23.3% of the cases, so this finding should prompt detailed prenatal assessment of the fetus, with particular regard to cardiovascular system.

Disclosure statement

No potential conflict of interest was reported by the authors.

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References

[1] Canavan TP, Hill LM. Neonatal outcomes in fetuses with a persistent intrahepatic right umbilical vein. J Ultrasound Med. 2016;35(10):2237–2241.
[2] Kirsch CF, Feldstein VA, Goldstein RB, et al. Persistent intrahepatic right umbilical vein: a prenatal sonographic series without significant anomalies. J Ultrasound Med. 1996;15(5):371–374.
[3] Sadler TW. Cardiovascular system. In: Langman medical embryology. 12th ed. Baltimore (MD): Lippincott Williams & Wilkins; 2012. p. 162–200.
[4] Lide B, Lindsley W, Foster MJ, et al. Intrahepatic persistent right umbilical vein and associated outcomes: a systematic review of the literature. J Ultrasound Med. 2016;35(1):1–5.
[5] Krzyżanowski A, Swatowski D, Gęca T, et al. Prenatal diagnosis of persistent right umbilical vein – incidence and clinical impact. A prospective study. Aust N Z J Obstet Gynaecol. 2019;59(1):77–81.
[6] Adiego-Calvo I, Saviron-Cornudella R, Martinez-Payo C, et al. Are congenital malformations more frequent in fetuses with intrahepatic persistent right umbilical vein? A comparative study. Taiwan J Obstet Gynecol. 2016;55(6):782–785.
[7] Kumar SV, Chandra V, Balakrishnan B, et al. A retrospective single centre review of the incidence and prognostic significance of persistent foetal right umbilical vein. J Obstet Gynaecol. 2016;36(8):1050–1055.
[8] Jeanty P. Persistent right umbilical vein: an ominous prenatal finding? Radiology. 1990;177(3):735–738.
[9] Martinez R, Gamez F, Bravo C, et al. Perinatal outcome after ultrasound prenatal diagnosis of persistent right umbilical vein. Eur J Obstet Gynecol Reprod Biol. 2013;168(1):36–39.
[10] Weichert J, Hartge D, Germer U, et al. Persistent right umbilical vein: a prenatal condition worth mentioning? Ultrasound Obstet Gynecol. 2011;37(5):543–548.
[11] Yang PY, Wu JL, Yeh GP, et al. Prenatal diagnosis of persistent right umbilical vein using three-dimensional sonography with power Doppler. Taiwan J Obstet Gynecol. 2007;46(1):43–46.
[12] Wolman I, Gull I, Fait G, et al. Persistent right umbilical vein: incidence and significance. Ultrasound Obstet Gynecol. 2002;19(6):562–564.
[13] Blazer S, Zimmer EZ, Bronshtein M. Persistent intrahepatic right umbilical vein in the fetus: a benign anatomic variant. Obstet Gynecol. 2000;95(3):433–436.
[14] Hill LM, Mills A, Peterson C, et al. Persistent right umbilical vein: sonographic detection and subsequent neonatal outcome. Obstet Gynecol. 1994;84(6):923–925.
[15] Leal DB, Maggiolini M, Bianchi A. Prenatal diagnosis and postnatal follow-up of patients with persistent right umbilical vein. Donald Sch J Ultrasound Obstet Gynecol. 2012;6(1):104–108.
[16] Kinare AS, Ambardekar ST, Bhattacharya D, et al. Prenatal diagnosis with ultrasound of anomalous course of the umbilical vein and its relationship to fetal outcome. J Clin Ultrasound. 1996;24(7):333–338.
[17] Viora E, Sciarrone A, Bastonero S, et al. Anomalies of the fetal venous system: a report of 26 cases and review of the literature. Fetal Diagn Ther. 2004;19(5):440–447.
[18] Kiserud T, Acharya G. The fetal circulation. Prenat Diagn. 2004;24(13):1049–1059.