

Contents lists available at ScienceDirect

Taiwanese Journal of Obstetrics & Gynecology

journal homepage: www.tjog-online.com



Original Article

Are congenital malformations more frequent in fetuses with intrahepatic persistent right umbilical vein? A comparative study



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ARTICLE INFO

Article history: Accepted 11 December 2015

Keywords: congenital heart defects congenital malformation prenatal diagnosis umbilical cord umbilical veins

ABSTRACT

Objective: Persistent right umbilical vein (PRUV) is a vascular anomaly where the right umbilical vein remains as the only conduit that returns oxygenated blood to the fetus. It has classically been described as associated with numerous defects. We distinguish the intrahepatic variant (better prognosis) and the extrahepatic variant (associated with worse prognosis). The objective of this study was to compare rates of congenital malformations in fetuses with intrahepatic PRUV (I-PRUV) versus singleton pregnancies without risk factors.

Materials and Methods: A multicenter, crossover design, comparative study was performed between 2003 and 2013 on fetuses diagnosed with I-PRUV (n = 56), and singleton pregnancies without congenital malformation risk factors (n = 4050).

Results: Fifty-six cases of I-PRUV were diagnosed (incidence 1:770). A statistically significant association between I-PRUV and the presence of congenital malformations (odds ratio 4.321; 95% confidence interval 2.15–8.69) was found. This positive association was only observed with genitourinary malformations (odds ratio 3.038; 95% confidence interval 1.08–8.56).

Conclusion: Our rate of malformations associated with I-PRUV (17.9%) is similar to previously published rates. I-PRUV has shown a significant increase in the rate of associated malformations, although this association has only been found to be statistically significant in the genitourinary system. Noteworthy is the fact that this comparative study has not pointed to a significant increase in the congenital heart malformation rate. Diagnosis of isolated I-PRUV does not carry a worse prognosis.

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Introduction

Persistent right umbilical vein (PRUV) is a vascular anomaly that involves the obliteration of the left umbilical vein, leaving the right umbilical vein as the only conduit that returns oxygenated blood from the placenta. Two variants are described: intrahepatic (I-PRUV), with proper development of ductus venosus; and

extrahepatic, in which the umbilical vein drains directly into the inferior vena cava or right atrium [1].

The first set of cases, published by Jeanty [2] in 1990, presented a rate of associated malformations of 50%, most of them being congenital heart diseases. Therefore, this entity has traditionally been considered a rare anomaly associated with poor prognosis. Recent studies report a better prognosis [3–5], but rates of associated malformations in the latest series show extremely dissimilar results, between 8% and 40.9% [3,6].

I-PRUV is one of the most common fetal venous anomalies, with an estimated incidence varying from 1:250 to 1:1000 pregnancies [2—11]. This study was designed to compare malformations' rate of

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fetuses with I-PRUV with other fetuses from pregnancies without risk factors for associated congenital anomalies.

Material and methods

Data were collected from the pregnant patients with fetal ultrasound diagnosis of I-PRUV from two tertiary centers: Hospital Universitario Puerta de Hierro, Madrid, Spain (since 2003) and Hospital Universitario Miguel Servet, Zaragoza, Spain (from 2007 to May 2013).

First-trimester combined tests for early screening of chromosomal abnormalities was carried out in all patients. Inclusion criteria for cases were: fetus with ultrasound diagnosis of I-PRUV; singleton pregnancy, obstetric referral hospital control, and execution of at least three ultrasound scans (1st, 2nd, and 3rd trimesters). Cases whose data collection could not be completed were excluded. We used the criteria described by Jeanty [4] to diagnose this entity. A case of prenatal diagnosis of I-PRUV is shown in Figure 1.

Patients with singleton pregnancies, whose pregnancies were controlled at Hospital Universitario Miguel Servet in Zaragoza between January 1, 2011 and December 31, 2013, were recruited consecutively for the control group. Those who met the following criteria were excluded: smoking mother; incomplete prenatal screening; maternal congenital malformation; gestational diabetes; maternal conditions that may be associated with congenital malformations such as diabetes, obesity, bariatric surgery, autoimmune disease, hematologic disease, neoplasia, neurological, or psychiatric illness on drug therapy; and documented use of other drugs with teratogenic potential (U.S. Food and Drug Administration category X). After applying these inclusion and exclusion criteria, a database was obtained for the control group of 4050 pregnancies, without risk factor for congenital anomalies.

For the statistical analysis, firstly all the variables analyzed were described, and then a bivariate analysis was conducted, comparing both groups. The variables were described using percentages. In the bivariate analysis, an analysis of contingency tables with odds ratio (OR) calculation was performed, using SPSS

Statistics for Mac OsX. 1999. V19.0. Chicago: IBM. The confidence interval (CI) used was 95%.

Results

During the study period, 43,149 pregnancies were examined, of which 56 fetuses with I-PRUV were identified, corresponding to an incidence rate of 1:770.

The proportion of cases founded was almost identical in both hospitals, 51.8% and 48.2% respectively.

The profile of mothers corresponded in 55.4% of cases to nulliparous women with a mean age of 31.83 ± 4.29 years. The majority of fetuses were male (62.5%), with a male to female ratio of 1.66:1. I-PRUV fetuses were diagnosed between Weeks 19^{+0} and 35^{+2} of gestation (mean gestational age, 20^{+1} weeks).

Of fetuses with I-PRUV, 82.1% showed no associated malformation. In the 10 cases with associated malformations (17.9%) the most frequent were genitourinary (7.1%) and vascular abnormalities of the umbilical cord (3.6%).

Furthermore, 17.9% of I-PRUV fetuses underwent karyotyping, showing no abnormality. The antenatal survey was also completed by echocardiography in 19.6% of cases, diagnosing a ventricular septal defect (as displayed in mid trimester ultrasound) and an aberrant right subclavian artery (Table 1).

The malformation rate presented by I-PRUV cases was compared with the group of 4050 risk factor-free pregnancies. When we classified these malformations into systems, we noted that the proportion of genitourinary system's malformations was 4.67 points higher in fetuses with I-PRUV regarding to those without I-PRUV, followed by umbilical cord (2.34 points), skeletal system (1.49 points) and heart (1.3 points) malformations.

A positive association between the presence of I-PRUV and the presence of any congenital malformations (OR, 4.321; 95%CI, 2.15–8.69)] was found. Malformations of the genitourinary system were the only ones that showed this positive association (OR 3.038; 95%CI 1.08–8.56). We did not observe significant association when congenital heart defects, skeletal, and umbilical cord malformations were compared. No malformation of the central nervous

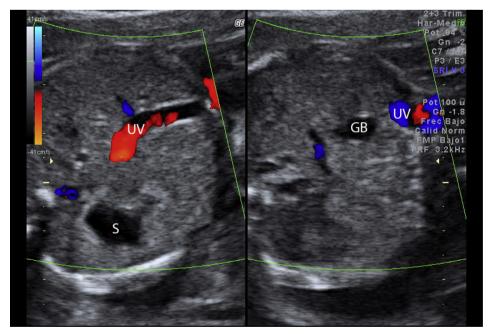


Figure 1. Ultrasound prenatal diagnosis of persistent right umbilical vein. GB = gallbladder; S = stomach; UV = umbilical vein.

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