Özgün Araştırma / Original Article

Jinekoloji - Obstetrik ve Neonatoloji Tıp Dergisi
The Journal of Gynecology - Obstetrics and Neonatoloogy

Fetal Anomalies in Pregnancies with Pathological Patterns of Umbilical Artery Doppler Velocimetry

Patolojik Umbilikal Arter Doppler Akım Paterni Tesbit Edilen Gebeliklerde Görülen Fetal Anomaliler

Esma Sarıkaya[1,2], Özay Oral[3]

[1]Centre for Reproductive Medicine, Zekai Tahir Burak Women's Health Research and Education Hospital, Ankara, Turkey

[2]Yıldırım Beyazıt University Ankara, Turkey

[3]Koşuyolu Women's Health Center Istanbul, Turkey

ÖZET

Amaç: Çalışmamızda; 20. gestasyonel haftanın üzerinde patolojik umbilikal arter Doppler paterni (diastol sonu akım kaybı veya ters akım) ile birlikte görülen konjenital anomalilerin araştırılması amaçlanmıştır.

Materyal ve Metod: 20. gebelik haftası üzeri umbilikal arter Doppler incelemesinde diastol sonu akım kaybı olan 29, ters akım olan 15 hasta çalışmaya dahil edilmiştir. Olgularda saptanan kromozomal ve konjenital anomaliler kaydedilmiştir. Konjenital anomali, umbilikal arter Doppler kelimeleri girilerek Medline ve PubMED de yer alan 1987 ve 2010 yıllarını kapsayan literatürler gözden geçirilmiştir.

Bulgular: Umbilikal arterde patolojik Doppler akımı en sık intrauterin gelişme geriliğinin hipertansiyon ile birlikte olduğu vakalarda (%68.8) sonra %58.8 sıklıkla sadece intrauterin gelişme geriliği olanlarda, %40 oranında da sadece hipertansiyon olanlarda tesbit edilmiştir. Patolojik Doppler akımı mevcut olan 44 hastanın 3'ünde amniyotik sıvı indeksi ve uterin arter dalga formları normaldi ve hipertansiyon komplikasyonu yoktu. Bu hastalardan 1 tanesinde Trizomi 18 (%2.2), 1 konjenital ihtiyoz (%2.2), ve 1 fetal hidrops (%2.2) tesbit edildi.

Sonuç: Gelişmekte olan ülkelerde oturmamış antenatal tarama programları ve fetal anomaliler de gebelik terminasyonuna çeşitli kültürel yaklaşımlar nedeniyle birçok anomalili bebek gebeliğin 3. trimesterine ulaşabilmektedir. Oligohidramnios ve hipertansiyon gibi komplikasyonlar yokken patolojik umbilikal arter Doppler akımı görülen özellikle ileri yaş olgularda genetik sonogram bu gebeliklerin yönetiminde gereklidir.

Anahtar Kelimeler: Doğumsal anomaliler, Doppler

ABSTRACT

Aim: Our aim was to evaluate the associated congenital anomalies with pathological patterns of umbilical artery Doppler (absent or reversed end-diastolic velocity (AREDV)) at a gestational age > 20 weeks.

Material and Methods: Fourty four fetuses with absent (n=29) or reversed (n=15) end-diastolic velocity in the umbilical artery (UA) at a gestational age > 20 weeks were considered. Presence of chromosomal or congenital abnormalities were recorded. A computerized literature search through Medline and PubMED was performed, applying the words "congenital anomaly, umbilical artery Doppler ultrasound " cited between the year 1987 and 2010.

Results: Pathological patterns of umbilical artery doppler were most frequently encountered in subjects with significant intrauterine growth retardation (IUGR) associated with hypertension (68,8%), followed by IUGR alone (58,8%), and hypertensin alone (40%).

Yazışma Adresi / Correspondence Address:
Esma SARIKAYA
Zekai Tahir Burak Women's Health Research and Education Hospital, Talatpasa Bulvari Hamamonu 06230 Ankara, Turkey
Tel: 00 90 312 3103100 • Fax: 00 90 312 3124931
e-mail: runakara@gmail.com

Geliş tarihi / Received : 02.05.2014
Kabul tarihi / Accepted : 22.05.2014

In 3 of the 44 patients with AREDV in the UA, amniotic fluid index and the uterine artery waveform was normal and there were no hypertensive complications. Of these patients 1 trisomy18 (2.2%), 1 congenital ichthyosis (2.2%), and 1 fetal hydrops (2.2%), were detected. So our congenital anomaly rate was 6.8% in such cases.

Conclusion: In developing countries, due to poor antenatal care programs and different cultural resources regarding selective termination of pregnancies for fetal anomalies many fetuses with anomalies could reach to the third trimester of pregnancy. Genetic sonogram is essential, when pathological umbilical Doppler velocimetry patterns are associated with advanced maternal age, and absence of oligohydramnios and hypertensive complications in the management of these pregnancies

Key Words: Congenital abnormalities, Doppler

Introduction

When pathological patterns of umbilical artery (UA) Doppler velocimetry (defined by absent or reversed end-diastolic flow velocities (AREDV)) in the third trimester have been associated with advanced maternal age, absence of oligohydramnios and hypertensive complications and presence of structural malformations, the risk of fetal anomaly increases. The most common reported chromosomal abnormality (CA) is trisomy 18 and the most common congenital anomaly is cardiac malformation in these cases. Looking for sonographic markers of these malformations by targeted ultrasonography is recommended in such cases (1).

After 2002 there is no study in the literature about association of fetal anomalies with pathological patterns of UA Doppler velocimetry in the third trimester. After that, studies started to focus on different methods to detect fetal anomalies in earlier gestational weeks and focused on Doppler studies of vessels other than UA. Also an increasing uptake of prenatal diagnosis and use of the genetic sonogram and as a result, selective termination of pregnancies for fetal anomalies (TOPFA) at earlier gestations appears to be the major factors responsible for the accelerated decline in congenital anomalies during second trimester and infant deaths in recent years. Another reason is different types of CA have different degrees of lethality (2,3) .

But the situation is a bit different in developing countries. Detection rate of fetal anomalies by genetic sonogram is affected by resolution of ultrasound scans, expertise of operators and the presence of a sonographic sign associated with the abnormality. Antenatal care programs in developing countries which have been modeled on those in developed countries, have been poorly implemented and largely ineffective. Because existing opportunities for referral are not fully used and inadequate staff training and shortages of equipment inhibit the full provision of services. TOPFA is also a controversial subject in many countries, and the laws, cultures and religions governing it and legal gestation limits vary. Because of the parents' reluctance to terminate the pregnancy,many fetuses with anomalies could reach to the third trimester of pregnancy (4).

Detection of CA by Doppler ultrasound in the first trimester is studied. Some investigators found an association between high resistance to flow in UA and CA (5-11) . However the findings of Bindra study demonstrated that that Doppler sonography cannot exclude CAs before the 20th weeks of gestation (12). But during the second half of pregnancy several investigators have shown an association. It is postulated that in these patients there is a process of obliteration of small arteries in the placenta that is triggered by the abnormal fetus (13,14).

In this study, fetal chromosomal and congenital abnormalities in patients with AERDV in the UA in the third trimester and in the literature wererewieved.

Materials and Methods

This prospective single center cohortstudy protocol was approved by the Hospital Ethics Committee. All the patients gave their informed consent to participate to the study.

The sample included white Caucasian women, many of whom wereof low socioeconomic status and regional patients referred for consultative services. The study group consisted of 1415 patients with singleton pregnancies referred to the high-risk pregnancy unit at 26 to 34 (mean 30) weeks' gestation because of a variety of pregnancy complications (pre-eclampsia, essential hypertension or fetal growth retardation).

Fourty four patients with absent (n=29) or reversed (n=15) end-diastolic velocity in the UA at a gestational age > 20 weeks were considered.

A detailed medical history was taken from all participants, who also received a complete clinical examination. Age, menstrual pattern, and history of drug intake were recorded. After delivery, all babies underwent a complete physical examination by a pediatrician from Neonatology Unit of same hospital. Presence of chromosomal or congenital abnormalities were recorded.

Ultrasound Examination

Doppler analysis of maternal/fetal circulation, fetal biometric measurements and assesment of amniotic fluid volume were performed immediately upon arrival of patients to the hospital by the same obstetrician with a two-dimensional pulsatile echo Doppler (Acuson 128*P/10) equipment fitted with 3.5 and 5.0-MHz transducers with power and color Doppler options. The high pass filter was set at 125 Hz. UA flow velocity waveforms were obtained from the UA, as previously described and the systolic –diastolic ratio was calculated using on-screen software (15).

We performed detailed ultrasonography for markers of CAs especially in cases who have inappropriately normal amniotic fluid index (AFI) and no hypertensive complications.

A maximal vertical amniotic fluid pocket of <2 cm was evaluated as oligohydramnios.

The pregnancy duration was determined from the last menstrual period and confirmed by ultrasonic measurements.

A computerized literature search through Medline and PubMED was performed, applying the words "congenital anomaly, umbilical artery Doppler ultrasound" cited between the year 1987 and 2010.

Results

In our study AREDV in the UA were most frequently encountered in subjects with significant intrauterine growth retardation (IUGR) associated with hypertension (68,8%), followed by IUGR alone (58,8%), and hypertensin alone (40%).

In 3 of the 44 patients with AREDV in the UA, AFI and the uterine artery waveform werenormal and there were no hypertensive complications. Two fetuses were found to be grossly anomalous on ultrasound examination. Neonatal examination confirmed these findings. The characteristics of patients with fetal anomaly were revealed in Table1. In one of these 3 patients trisomy18 (2.2%), in another, congenital ichthyosis (2.2%), and in the other fetal hydrops with unknown etiology

(2.2%), were detected. So our congenital abnormality rate was 6.8% in patients with AREDV in the UAs. The mean maternal age of affected children was 28.6 years.

In fetus with trisomy 18, associated sonographic markers included a biometric measurement below the fifth percentile, micrognathia and overlapping fingers. Sonography at the 26th week of gestation revealed anomalies of the fetal face. However, prenatal diagnosis was not established in the fetus with congenital ichthyosis. Because of the uncorrectable fetal conditions and the parents' reluctance to terminate the pregnancy, no interventions were undertaken and eventually fetus with hydrops and trisomy 18 died in utero. In ichthyosis case, sonography at the 26th week of gestation revealed anomalies of the fetal face; however, the diagnosis of harlequin ichthyosis was not established prenatally. This pregnancy was complicated by premature rupture of membranes, oligohydramnios and growth retardation. AEDV in the UA Doppler was found at 32th week of gestation. The male child was born alive at the 34th week of the third pregnancy, with a birth weight of 2300g.

Reported anomalies in the literature in patients with AERDV in the UA were trisomy 18, trisomy 13, trisomy 21 and triploidies, nonimmune fetal hydrops and congenital heart (Table 2) (16-31).

Table1: Characteristics of patients with fetal anomaly

Case	Patient age (years)	Triple test	Fetal anomaly	Outcome
1	29	normal	congenital ichthyosis	alive
2	26	normal	fetal hydrops	died in utero
3	31	normal	Trisomy18	died in utero

Table 2: Reported structural or chromosomal abnormalities in patients with AERDV in the umbilical artery.

Rochelson et al.	(1987)	4/15 (26%)	3 Trisomy 18, 1 nonimmune fetal hydrops
Brar and Platt	(1988)	3/12 (25%)	1 Trisomy 18, 1 Trisomy 13
Wenstrom et al.	(1991)	10/22 (45.5%)	2 Trisomy 18,1 Trizomy21,1chromosome inversion 2 nonimmune hydrops,1ventriculomegaly,1 extensive body wall disruption
Hecher et al.	(1992)	6/24 (25%)	
Battaglia et al.	(1992)	1/26 (3.8%)	1 nonimmune fetal hydrops
Poulain et al.	(1993)	16/62 (16%)	2 Trizomy 21, 1 Trisomy 13 microdeletion p7 Hydrocephaly+cardiac defect, club foot, duodenal atresia Macrocephaly cystic kidneys fascial abnormality
Snijders et al.	(1993)	14 /113(12%)	10 Triploidy, 3 Trisomy 18, 1 Other
Valsamonico et al.	(1994)	3/31(9.7%)	3 Trisomy?
Rizzo et al.	(1994)	16/192 (8.3%)	2 69 XXX, 9 Trisomy 18, 4 Trizomy21
Tannirandorn et al.	(1994)	5/15 (33%)	2 nonimmune fetal hydrops 2 lethal anomalies 1 Trisomy 18
Aries et al.	(1994)	-	1 Trisomy 18, 1 multiple organ anomalies, Galen venous anomaly
Zelop et al.	(1996)	3/71(4%)	1Tetralogy of Fallot + Dandy Walker 1 nonimmune hydrops, 1 hydrocephaly
Kurkinen-Räty et al	(1997)	13/83(15%)	3 Trizomy 21, 2 Trisomy 13, 3 congenital heart, 1 encephalocele, 4 different combinations
Du et al.	(1999)	9/33 (27.3%)	
Borrel et al.	(2001)	9/11 (81%)	2 trisomy 13, 4 trisomy 18, 1 trisomy 21, 2 congenital heart (pulmonary artery atresia)
Brodszki et al.	(2002)	2/56(3.5%)	-

Discussion

Although in our series the indication for referral wasfor further assesment because of a variety of pregnancy complications, detailed ultrasonography for markers of CAs revealed that in three cases there were fetal anomalies (1 trisomy18 (2.2%), 1 congenital ichthyosis (2.2%), 1 fetal hydrops with unknown etiology (2.2%)). In our study the frequency of structurally or chromosomally abnormal fetuses was 6.8% in patients with AERDV in the UAs at a gestational age > 20 weeks. These rates are in accordance with many earlier papers. Reported anomalies were trisomy 18, trisomy 13, trisomy 21 and triploidies, nonimmune fetal hydrops and congenital heart (Table 2). We could not find any reported congenital ichthyosis in such cases. Only a few cases of prenatal sonographic diagnosis of congenital ichthyosis have been published and these were a flat profile with absent nose; a large mouth, widely gaping open; dysplastic ears; abnormal fixed position of the hands, short foot length, intrauterine growth retardation, echogenic amniotic fluid; and edema of thighs (32).

Targeted sonography could identify abnormal fetal anatomy or abnormal biometric findings in 77-97% of fetuses with trisomy 18 with a false-positive rate of 8.9% in the second trimester. Maternal serum screening protocols are able to achieve detection rates up to 50% of trisomy 18 with a 1% false positive rate in the second trimester (33-35).

The underlying pathophysiology of the AERDV in trisomic fetuses is unclear but it is thought to be due to an immature placenta with inadequate vascular network or reduction in small muscular artery count. Coexisting heart defects, extremely common in trisomies 18 and 13, may play a role in the abnormal flow pattern (5,36-38).

The cross-sectional design of the study implies that we cannot establish a cause-effect relationship butwe try to emphasize that genetic sonogram is essential, when abnormal umbilical Doppler velocimetry patterns are associated with advanced maternal age, absence of oligohydramnios and hypertensive complications. The knowledge of these factors are important in the management of such fetuses especially in developing countries. So at any time of pregnancy even at term, sonologists and obstetricians must be in alert about anomaly possibility of the fetus.

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