Prevalence and distribution of structural heart diseases in high and low risk pregnancies

Yüksek ve düşük riskli gebeliklerde yapısal kalp hastalıklarının sıklığı ve dağılımı

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ABSTRACT

Objective: To establish and compare the frequency of intrauterine congenital heart defects in high-risk and low-risk pregnancies for congenital heart diseases.

Methods: Records of 3782 patients who underwent fetal echocardiography at the Pediatric Cardiology Unit were reviewed for reasons of referral and results of echocardiography retrospectively. The categorical variables between the groups were analyzed using a Chi-square test.

Results: Structural heart defects were found in 213 (5.6%) fetuses in both high and low risk groups. Most common defects were ventricular septal defect (36.2%) and atrioventricular septal defect (14.1%). Frequency of congenital heart diseases was 7.8% (169 fetuses) in high-risk group: 4.1% were complex, 2.3% significant and 1.4% were minor. In low-risk group, the frequency was 2.7% (44 fetuses): 0.6% were complex, 0.8% significant and 1.3% were minor. In this group, rates of congenital defects were high regarding particular reasons: intrauterine fetal death in previous pregnancy (6.3%), abnormal first or second trimester screening tests (4.3%), and multiple gestations (3.4%). The sensitivity and specificity of fetal echocardiography according to transthoracic echocardiography were found to be 86% and 99%, respectively.

Conclusion: Congenital heart diseases rate, as expected, was found to be higher in high-risk group. However, regarding intrauterine fetal death in previous pregnancy, abnormal first or second trimester screening tests and multiple gestation, no statistically significant difference was observed between low-risk and high-risk groups. Therefore, we suggest the routine use of fetal echocardiography in cases we have mentioned above if the staff and equipment of the pediatric cardiology clinic are eligible. *(Anadolu Kardiyol Derg 2011; 2: 125-30)*

Key words: Congenital heart disease, fetal echocardiography, high-risk pregnancy, low-risk pregnancy

ÖZET

Amaç: Doğuştan kalp hastalıkları için yüksek ve düşük risk taşıyan gebelerde intrauterin kalp hastalığı sıklığını belirlemek ve karşılaştırmak.

Yöntemler: Üniversitemiz Tıp Fakültesi Pediatrik Kardiyoloji Ünitesinde fetal ekokardiyografi yapılan 3782 gebenin kayıtları ve ekokardiyografi sonuçları retrospektif olarak değerlendirildi. Gruplar arasındaki değişkenler Ki-kare testi kullanılarak analiz edildi.

Bulgular: Yüksek ve düşük riskli gruplardaki tüm fetüslerin 213'ünde (%5.6) yapısal kalp hastalığı bulundu. En sık patolojiler ventriküler septal defekt (%36.2) ve atriyoventriküler septal defekt (%14.1) idi. Yüksek riskli grupta doğuştan kalp hastalığı sıklığı %7.8 (169 fetüs) bulundu; %4.1'i kompleks, %2.3'ü önemli, %1.4'ü minör patolojiydi. Düşük riskli grupta bu oran %2.7 (44 fetüs) idi; %0.6'sı kompleks, %0.8'i önemli ve %1.3'ü minör patolojiydi. Bu grupta bazı nedenlerle başvuranlarda yapısal kalp hastalığı sıklığı yüksek bulundu; önceki gebelikte intrauterin fetal ölüm (%6.3), anormal birinci ve ikinci üç aylık dönem tarama testleri (%4.3) ve çoğul gebelik (%3.4). Fetal ekokardiyografik incelemenin duyarlılığı %86, özgüllüğü %98 bulundu.

Sonuç: Doğuştan kalp hastalığı sıklığı beklenildiği gibi yüksek riskli grupta daha yüksek bulundu. Düşük riskli grupta yer almalarına rağmen önceki gebelikte intrauterin fetal ölüm, anormal birinci ve ikinci üç aylık dönem tarama testleri ve çoğul gebelik nedeniyle başvuranlardaki kalp hastalığı sıklığı ile yüksek riskli gruptaki kalp hastalığı sıklığı arasında istatistiksel olarak anlamlı bir fark bulunmadı. Bu nedenle kardiyoloji kliniğinin bu konuda uzman kardiyoloğu ve ekipmanı yeterli ise yukarıdaki nedenlerle başvuran gebelere rutin fetal ekokardiyografik çalışma yapılmasını öneriyoruz. *(Anadolu Kardiyol Derg 2011; 2: 125-30)*

Anahtar kelimeler: Doğuştan kalp hastalığı, fetal ekokardiyografi, yüksek riskli gebelik, düşük riskli gebelik

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Introduction

Fetal echocardiographic examination (FE) has been in use since the 1980s (for the last 20-25 years) in pregnant women expecting births with potentially high risk of congenital heart diseases (CHD) (1, 2). Incidence of CHD was reported as approximately 4-10/1000 live births (3, 4). Results of FEs suggest that frequencies of structural heart diseases in prenatal and postnatal periods are rather different from each other. Complex heart defects or chromosome anomalies associated with heart defects may result in early fetal loss or still birth. Today, FE is recommended to all patients with high-risk pregnancies for fetal CHD (5). The frequency of CHD in low-risk pregnancies and in the screening groups were found to be higher than the live birth rate (6, 7).

The aim of this study was to establish and compare the frequency of intrauterine CHD in high-risk and low-risk pregnancies for congenital heart diseases.

Methods

Study population

The medical records of consecutive 3782 fetuses undergoing FE were retrospectively assessed in the Pediatric Cardiology Department of the Faculty of Medicine from January 1997 to December 2007.

We performed 4917 FEs on these fetuses; FE was performed once on 2827 (74.7%), and twice on 813 (21.5%). One hundred and forty two fetuses underwent FE 3 or 4 times. Of the 3782 fetuses, 1353 (35.8%) were examined with transthoracic echocardiographic examination (TTE), and 26 (0.7%) were dead in the prenatal period, 2377 fetuses lost to follow up. The gestations of 26 (26.5%) out of 98 fetuses with complex heart anomalies were terminated intrauterine.

The pregnant women were grouped into a high-risk group (2172 patients) and a low-risk group (1610 patients) for structural cardiac diseases. The high-risk group comprised pregnant women referred for reasons known to be indications for FE (5). Low-risk group included pregnant women referred by an obstetrician for reasons other than indications of FE (5) or presented on their own will for screening with no obvious high-risk.

Fetal echocardiographic examination

Fetal hearts were examined by two-dimensional, pulsed wave and color Doppler echocardiographic methods using the Sonos 5500 and/or 7500 echocardiography device (Hewlett Packard, USA) and 5MHz sector transducer and/or 3-8 MHz curvilinear transducer. This process took place utilizing the standard transabdominal approach. Two-dimensional imaging was performed for four-chamber, five-chamber, three vessels, ductal arch, aortic arch positions, short and long axis views of great vessels. Pregnancies with a visualization problem for fetal hearts were examined the following day the latest. Cardiac situs, rhythm, venous inflow, atrial and ventricular chambers, atrioventricular and semilunar valves, ventriculo-arterial connections, aortic and the ductal arches were visualized in all cases. The cases that were examined prior to the 24th gestational week were examined for a second time. Pathological cases underwent FE with a mean of 1.5±0.8 (range=1-4) times. All pregnancies were recommended to have their newborns undergo a transthoracic echocardiographic examination, 1353 newborns examined with TTE.

Indications of FE, maternal and gestational age, number of pregnancies, fetal echocardiography findings and follow-up were all recorded.

A modified classification system similar to that of Hunter et al. (8) and Wren et al. (9) was used in categorization of congenital heart defects (Table 1). Category I included cardiac anomalies or groups of anomalies, which were inoperable, incompletely correctable or only managed with palliative care and classified as complex. Category 2 consisted of significant anomalies which had high mortality if not operated on, but which could be corrected, leaving children with biventricular circulation. Category 3 consisted of minor lesions, which did not constitute a threat to life and were considered to be simple. A hyperechogenic focus was not accepted as an anomaly.

Statistical analysis

Statistical analyses were performed using the statistical package SPSS v 15.0 and win EPI (Chicago, IL, USA). The categorical variables between the groups were analyzed using a Chi-square test. Sensitivity and specificity were calculated for fetal echocardiography using transthoracic echocardiography as gold test. The results were reported as number (n) and percentage (%), mean±SD and median (minimum-maximum) values.

Table 1. Current classification system of significance in the pediatric cardiology database

C	**Complex - absent or hypoplastic chamber or valve, or common valve:** includes complete atrioventricular septal defect, hypoplastic left heart syndrome, pulmonary atresia, tricuspid atresia, truncus arteriosus, double inlet left ventricle, mitral atresia, aortic atresia, congenital corrected transposition of the great arteries
S	**Significant - congenital heart disease requiring operation or intervention, but not included in the complex group:** includes aorto-pulmonary window, critical aortic stenosis, partial atrioventricular septal defect, coarctation, ventricular septal defect (requiring operation), transposition of the great arteries, tetralogy of Fallot, total anomalous pulmonary venous connection (excludes persistent arterial duct and atrial septal defect)
M	**Minor - no intervention:** 4 chambers, 4 valves-includes mainly small ventricular septal defect, less severe aortic stenosis, and pulmonary stenosis

Results

The mean maternal age was 28.9±5.6 years, the gestational age on the first FE was 26.1±5.0 weeks and the number of FE was 1.3±0.4.

Of the cases, 2172 (57.4%) were in high-risk group, and 1610 (42.6%) in low-risk group. The most common indications of FE were CHD in the previous child or the fetus (14.3%) and maternal diabetes (12.2%). Fetal echocardiography indications of high-risk group, reasons for referral by obstetrician in low-risk group, and detection rates for each structural heart disease are presented in Table 2.

The classification of CHDs detected by FE using the Pediatric Cardiology Database is presented in Table 3. Of all fetuses undergoing FE, 213 (5.6%) had cardiac pathology. Structural heart diseases were present in 169 (7.8%) fetuses in high-risk group and in 44 (2.7%) in low-risk group (Table 4). A hyperechogenic focus was observed in 72 fetuses (1.9 %) in both groups.

The frequency of CHD was high in fetuses of pregnant women referred by obstetricians for multiple pregnancy (3.4%), intrauterine fetal loss in previous pregnancy (6.3%) and abnormal screening test results in the first and second trimester (4.3%) in low-risk group (Table 2). No significant difference was observed regarding frequency of CHD between high-risk group and the three referral reasons (intrauterine fetal death in previous pregnancy, abnormal first or second trimester screening tests and multiple gestation) mentioned in low-risk group ($p>0.05$).

Nine membranous ventricular septal defects (VSD) and twenty muscular VSDs spontaneously closed during the intrauterine period and postnatal first months. The rates for spontaneous closure were 75% (9/12) for membranous and 64.5% (20/31) for muscular VSD. Although the first examination was normal in two fetuses, mild pulmonary stenosis (PS) developed in the intrauterine period. Severe PS developed during follow-up in one fetus observed to have a mild PS on the first examination. Two fetuses with prior normal FE, later, developed tricuspid valve anomaly.

Of the 1353 newborns who underwent transthoracic echocardiographic examination (TTE) after birth, 105 (7.8 %) had structural heart disease; 83 (10.4 %) fetuses in high-risk group and 22 (3.9%) in low-risk group (Table 5).

The sensitivity and specificity of fetal echocardiography according to transthoracic echocardiography were found to be 86% and 99%, respectively. Accuracy rate was 98.6%. Sensitivity and specificity were calculated only for complex and significant CHD.

Discussion

In our study, the frequency of structural cardiac anomaly was found 5.6% in all pregnant women; 7.8% in the high-risk and 2.7% in the low-risk group. It was noticed that CHD rate in low-risk group was higher than the reported birth prevalence mentioned in the previous studies.

Table 2. Indications for fetal echocardiography of the high-risk group and the reasons of referral by the obstetrician in low-risk group and the detection rates for each structural heart disease in all pregnant women

High-risk group	**Total n**	**CHD n (%)**
Maternal indications		
Metabolic disorders (diabetes mellitus)	463	13 (2.8)
Gestational diabetes mellitus	272	4 (1.5)
Type I and II Diabetes mellitus	191	9 (4.7)
Maternal congenital cardiac disease and familial cardiomyopathy	53	2 (3.8)
Exposure to cardiac teratogens	50	0 (0)
Collagen disease with anti Ro/SSA-La/SSB antibodies	18	0 (0)
Medication with NSAI drugs after 25-30 gestational weeks	5	0 (0)
Familial indications		
Previous child or fetus with CHD or congenital AV block	541	18 (3.3)
Chromosomal disease, gene disorders, or syndromes with CHD	20	0 (0)
Paternal congenital cardiac disease	14	0 (0)
Fetal indications		
Extracardiac malformation	290	15 (5.2)
Suspicion of cardiac malformation or disease during an obstetrical scan	256	82 (32)
Arrhythmias	225	8 (3.6)
Polyhydramnios	116	13 (11.2)
Fetal hydrops	85	13 (15.3)
Hydrothorax	14	1 (7.1)
Chromosomal abnormalities	14	4 (28.6)
Nuchal translucency greater than the 99th percentile for crown rump length	8	0 (0)
Total (High-risk group)	**2172**	**169 (7.8)**
Low-risk group	**Total n**	**CHD n (%)**
Screening group	1152	30 (2.6)
Multiple gestation	119	4 (3.4)
Intrauterine fetal death in previous pregnancy	79	5 (6.3)
In vitro fertilization pregnancy	76	2 (2.6)
Abnormal first or second trimester screening tests	70	3 (4.3)
Oligohydramnios	53	0 (0)
CHD in distant relative	51	0 (0)
Late maternal age	10	0 (0)
Total (Low-risk group)	**1610**	**44 (2.7)**

AV - atrioventricular, CHD - congenital heart disease, NSAI - nonsteroidal anti-inflammatory

Table 3. Distribution of pathological abnormalities according to current significance classification system in pediatric cardiology database

Results of Fetal Echocardiography	n	%
Complex	**98**	**2.6**
CAVSD	30	0.8
HLHS	20	0.5
Dysplasia of tricuspid valve	11	0.3
Single ventricle	10	0.3
Truncus arteriosus	6	0.2
DORV+TGA (both of them: dextrocardia)	5	0.1
Tricuspid atresia	4	0.1
DILV	3	0.1
Hypoplastic RV+PS	3	0.1
Mitral atresia, hypoplasia	2	0.1
VSD+PA	2	0.1
Ebstein's abnormality	2	0.1
Significant	**64**	**1.7**
VSD	31	0.8
AS	7	0.2
d-TGA	6	0.2
TOF	7	0.2
CoA	5	0.1
L-TGA	2	0.1
VSD+CoA	2	0.1
TAPVR	1	0.03
DORV	1	0.03
Dextrocardia+Absent pulmonary artery with TOF+AV block	1	0.03
Absent pulmonary artery with TOF	1	0.03
Minor	**51**	**1.3**
Small VSD	46	1.2
PS	4	0.1
Bicuspid aorta	1	0.03
Total	**213**	**5.6**

AS - aortic stenosis, AV - atrioventricular, CAVSD - complete atrioventricular septal defect, CoA - coarctation of aorta, DILV - double inlet left ventricle, DORV - double outlet right ventricle, FO - foramen ovale, HLHS - hypoplastic left heart syndrome, PA - pulmonary atresia, PS - pulmonary stenosis, RV - right ventricle, TAPVR - total anomalous pulmonary venous connection, TGA - transposition of great arteries, TOF - tetralogy of Fallot, VSD - ventricular septal defect

The frequency and distribution of CHD in children were investigated in many studies and prevalence was found to be 4-10/1000 live births (3, 4). The results of FEs suggested that frequencies of CHD in prenatal and postnatal periods were different. Complex heart defects or chromosome anomalies associated with heart defects may result in early fetal loss and stillbirth. For this reason, the total CHD incidence in the fetus has been reported to be as much as five times that found in live-born children (10).

Table 4. Structural cardiac pathologies detected by fetal echocardiography

Category	High-risk group, n (%)	Low-risk group, n (%)	Total, n (%)	p*
Structural abnormalities	169 (7.8)	44 (2.7)	213 (5.6)	<0.0001
Complex	88 (4.1)	10 (0.6)	98 (2.6)	
Significant	51 (2.3)	13 (0.8)	64 (1.7)	
Minor	30 (1.4) (n=2172)	21 (1.3) (n=1610)	51 (1.3) (n=3782)	

Data are presented as number/percentage
*Chi-Square test

Table 5. Structural cardiac pathologies detected by transthoracic echocardiography

Category	High-risk group, n (%)	Low-risk group, n (%)	Total, n (%)	p*
Structural abnormalities	83 (10.4)	22 (3.9)	105 (7.8)	<0.0001
Complex	29 (3.6)	4 (0.7)	33 (2.4)	
Significant	20 (2.5)	4 (0.7)	24 (1.8)	
Minor	34 (4.3) (n=796)	14 (2.5) (n=557)	48 (3.5) (n=1353)	

Data are presented as number/percentage
*Chi-square test

In a comprehensive study conducted by Tegnander et al. (11), 29460 non-selected fetuses that had been assessed in a prenatal period were followed-up in the prenatal and postnatal periods. Of these, 430 (14.6/1000 prenatal and/or live birth) had CHD. Patients with no structural defects such as arrhythmia or tumor were excluded from the study. The frequency of major CHD was 3.3/1000, and that of minor CHD was 11.3/1000 (11).

Although the frequency of minor cardiac anomaly in this study was as low as 1.4% and 1.3% in the two groups, Tegnander et al. (11) found the frequency of minor CHD to be higher. However, Tegnander et al.(11) assessed prenatal and postnatal diagnoses together. We believe that this difference may have been due to the failure in diagnosing minor anomalies (such as small muscular VSD, mild valvular stenosis) by FE, as opposed to diagnosing them in the postnatal period using TTE. We found the frequency of minor CHD (3.5%) in the postnatal to be higher than the frequency in the prenatal period.

The distribution of CHD in the intrauterine period is different from that of the postnatal period. Isolated VSD is the most frequently encountered type of CHD in the postnatal period. In their study with high-risk 4052 fetuses, Paladini et al. (12) found that although VSD was diagnosed in 83 (20.8%) out of 400 fetuses with structural heart diseases, hypoplastic left heart syndrome (HLHS), which has a very low frequency in the postnatal period, was found in 43 (10.8%) fetuses. In large series of non-selected pregnant women, the distribution of CHD was found to be VSD, atrioventricular septal defect (AVSD), transposition of great arteries and HLHS in decreasing order of frequency (11). We also found isolated VSD as the most common CHD; however,

AVSD and HLHS were of similar frequencies. The prenatal diagnosis of AVSD and HLHS is easier due to co-existing anomalies (such as chromosome anomalies, *hydrops fetalis*). Besides, the diagnosis with four-chamber position enables the obstetricians to recognize these pathologies. However, their prevalence in the postnatal period is lower as these fetuses are lost in the intrauterine or early postnatal periods. Like HLHS, tricuspid valve dysplasia, which has a poor prognosis in the early postnatal period, is also more common in the intrauterine period (13). This anomaly was ranked as fourth in our study.

As FE enables the termination of pregnancies with poor prognosis in the early period, widespread follow-up of this study will provide a decrease in the postnatal prevalence of the serious CHD. The majority of terminated pregnancies are ones that are very serious, easily diagnosed and that have a poor prognosis. The recent significant decrease in the birth of babies with HLHS is an example for this situation (14). Hunter et al. (8) found the termination rate in 1994 as 22.7% and in 1997 as 57%. Therefore, the prevalence of complex and serious CHD was reduced from 3.3/1000 live births to 2.6/1000 live births. Paladini et al. (12) found the termination rate as 37.5% and the rate reached 65.2% in pregnant women diagnosed before the 25th gestational week. Özkutlu et al. (15) reported the termination rate in complex anomalies as 41.9%. We found the termination rate in fetuses with complex anomalies in our study as 26.5%. It is important to know that additional malformations and chromosome anomalies co-exist in these fetuses when making a decision on termination of such fetuses. The rate of these anomalies was 65% in the study by Tegnander (11); the rate of extracardiac malformations was 29.5%, and that of chromosome anomalies was 25.9% in the study by Paladini (12).

The most common indications of FE in our study were family history for CHD, maternal diabetes and suspected CHD in the obstetric ultrasound imaging, which were consistent with the literature (16). The most frequent indication was CHD in siblings or previous pregnancies. These fetuses were siblings of our patients who were followed-up in our Pediatric Cardiology Clinic. None of the fetuses whose fathers had CHD had any pathology. The reason was thought to be the small number of pregnant women presenting with this indication.

Another significant issue in our study was the high frequency of serious and complex heart defects in the high-risk group compared to low-risk group (6.4% vs. 1.4%, $p<0.0001$). This difference may be due to the referred pregnancies to our clinic by obstetricians who could easily diagnose these anomalies themselves during the routine pregnancy screening. The highest rate of indications was with 32% (82/256) for referral by the obstetrician with the suspect of CHD. Simpson et al. (17) showed that there was structural heart disease in 44 out of 275 (16%) cases with suspected CHD that had been referred by an obstetrician. Cooper et al. (16) reported this rate to be as high as 68%. These rates may change with the FE experience of the obstetrician. In their study comparing prenatal and postnatal diagnosis of fetuses with complex CHD, Meyer-Wittkopf et al. (18) found that the sensitivity for these findings among obstetricians was 59%, whereas it was 95% for pediatric cardiologists. Obstetricians use four-chamber position while assessing the fetal heart; however, with this position, only 65% of CHD can be diagnosed. In our study, only 82 out of 354 fetuses (23.2%) that were found to have cardiac pathology were referred by obstetricians with the suspect of CHD. Of all cardiac pathologies that we diagnosed with FE, one fourth were referred for another indication or screening. Of the cases that were referred by obstetricians with suspect of cardiac pathology, only 32% had this anomaly. Perri et al. (6) found that 41 out of 46 fetuses (89%) with intrauterine heart defects diagnosis were not in the high-risk group. It is important to train obstetricians on FE, as fetal heart screening can only be performed by obstetricians today. Due to their rather limited number, it seems almost impossible for pediatric cardiologists to perform fetal heart screenings. We believe that by assessing the frequency of CHD in non-selected groups, it may be possible to extend high-risk groups on whom FE should be performed.

Although the pregnant women referred by an obstetrician for the reasons of intrauterine fetal death, abnormal first and second trimester screening tests and multiple gestations were in low-risk group, there was no significant difference regarding frequency of CHD between high-risk group and these referred reasons (frequencies of CHD were 6.3%, 4.3% and 3.4% respectively). Even if they are not in the high-risk group, all pregnant women should undergo cardiac screening by obstetricians and it would be appropriate to consider cases of intrauterine fetal death, abnormal first and second trimester screening tests and multiple gestations in high-risk groups.

Fetal echocardiography enables us to better understand the development of human heart. The progression of CHD can be monitored by FE. For example, left ventricular dilation and dysfunction in early pregnancy may develop into HLHS (19). Some heart lesions such as aortic coarctation, and right ventricular outflow tract stenosis may be progressive (12, 14, 20, 21) or may manifest during fetal life. Two fetuses in our study with normal initial FE had mild PS and two others, again with normal first FE, had tricuspid valve anomaly. One patient with an initial mild pulmonary stenosis progressed to serious pulmonary stenosis in the follow-up. Therefore, even if the investigations performed in the early periods of pregnancy are normal, FE should be repeated after the 24th gestational week. We believe FE is not a cross-sectional investigation, but rather an important tool in pregnancy management.

Study limitations

Significant limitations of our study were the very small number of fetuses who underwent chromosomal study and autopsy data. Because families did not give authorization and consent for autopsy due to geographic and socio-cultural composition.

Conclusion

We found the frequency of CHD in fetuses in prenatal period to be significantly higher than that in live births. The frequency of CHD in fetuses whom referred by obstetricians for the reasons of intrauterine fetal death in the previous pregnancy, abnormal first or second trimester screening tests, or multiple gestations in low-risk group was found as high as in high-risk group. These pregnant women had no current indications for FE. Therefore, we suggest the routine use of FE in cases we have mentioned above if the staff and equipment of the pediatric cardiology clinic are eligible.

Conflict of interest: None declared.

References

1. Allan LD, Tynan MJ, Campbell S, Wilkinson JL, Anderson RH. Echocardiographic and anatomical correlates in the fetus. Br Heart J 1980; 44: 444-51.
2. Kleinman CS, Hobbins JC, Jaffe CC, Lynch DC, Talner NS. Echocardiographic studies of the human fetus: prenatal diagnosis of congenital heart disease and cardiac dysrhythmias. Pediatrics 1980; 65: 1059-67.
3. Nora JJ, Berg K, Nora AH (Eds). Cardiovascular Diseases: Genetics, Epidemiology and Prevention. Oxford Monographs on Medical Genetics, no.22. Oxford University Press: Oxford, 1991.
4. Hoffman JI. Incidence of congenital heart disease. I: Postnatal incidence. Pediatr Cardiol 1995; 16: 103-13.
5. Allan L, Dangel J, Fesslova V, Marek J, Mellander M, Oberhansli I, et al. Recommendations for the practice of fetal cardiology in Europe. Cardiol Young 2004; 14: 109-14.
6. Perri T, Cohen-Sacher B, Hod M, Berant M, Meizner I, Bar J. Risk factors for cardiac malformations detected by fetal echocardiography in tertiary center. J Matern Fetal Neonatal Med 2005; 17:123-8.
7. Todros T, Faggiano F, Chiappa E, Gaglioti P, Mitola B, Sciarrone A. Accuracy of routine ultrasonography in screening heart disease prenatally. Prenat Diagn 1997; 17: 901-6.
8. Hunter S, Heads A, Wyllie J, Robson S. Prenatal diagnosis of congenital heart disease in the northern region of England: benefits of a training program for obstetric ultrasonographers. Heart 2000; 84: 294-8.
9. Wren C, Richmond S, Donaldson L. Temporal variability in birth prevalence of cardiovascular malformations. Heart 2000; 83: 414-9.
10. Drose JA. Scanning: Indications and Technique. In: Drose JA, editors. Fetal Echocardiography. Philadelphia; W.B. Saunders Company; 1998. p.15-57.
11. Tegnander E, Williams W, Johansens OJ, Blaas HG, Eik-Nes SH. Prenatal detection of heart defects in a non-selected population of 30149 fetuses - detection rates and outcome. Ultrasound Obstet Gynecol 2006; 27: 252-65.
12. Paladini D, Russo MG, Teodoro A, Pacileo G, Capozzi G, Martinelli P, et al. Prenatal diagnosis of congenital heart disease in the Naples area during the years 1994-1999 - the experience of a joint fetal-pediatric cardiology unit. Prenat Diagn 2002; 22: 545-52.
13. Hinojosa Cruz JC, Luis Miranda RS, Veloz Martinez MG, Puello Tamara E, Arias Monroy LG, Barra Urrutia A, et al. Diagnostic and frequency of fetal heart disease by echocardiography in pregnancies with high-risk factors. Gynecol Obstet Mex 2006; 74: 645-56.
14. Allan L. Screening the fetal heart. Ultrasound Obstet Gynecol 2006; 28: 5-7.
15. Özkutlu S, Ayabakan C, Karagöz T, Önderoğlu L, Deren O, Çağlar M, et al. Prenatal echocardiographic diagnosis of congenital heart disease: comparison of past and current results. Turk J Pediatr 2005; 47: 232-8.
16. Cooper MJ, Enderlein MA, Dyson DC, Roge CL, Tarnoff H. Fetal echocardiography: retrospective review of clinical experience and an evaluation of indications. Obstet Gynecol 1995; 86: 577-82.
17. Simpson LL. Indications for fetal echocardiography from a tertiary-care obstetric sonography practice. J Clin Ultrasound 2004; 32: 123-8.
18. Meyer-Wittkopf M, Simpson JM, Sharland GK. Incidence of congenital heart defects in fetuses of diabetic mothers: a retrospective study of 326 cases. Ultrasound Obstet Gynecol 1996; 8: 8-10.
19. Danford DA, Cronican P. Hypoplastic left heart syndrome: progression of left ventricular dilatation and dysfunction to left ventricular hypoplasia in utero. Am Heart J 1992; 123: 1712-3.
20. Axt-Flinder R, Kreiselmair P, Schwurze A, Krapp M, Gembruch U. Development of hypoplastic left heart syndrome after diagnosis aortic stenosis in the first trimester by early echocardiography. Ultrasound Obstet Gynecol 2006; 28: 106-9.
21. Maeno Y, Himeno W, Fujino H, Sigahara Y, Furui J, Mizumoto Y, et al. Progression of congenital heart disease in prenatal period. Pediatr Int 1999; 41: 709-15.