The results of fetal echocardiography in a tertiary center and comparison of low- and high-risk pregnancies for fetal congenital heart defects

Üçüncü basamak bir merkezde fetal ekokardiyografi sonuçları ve fetal konjenital kalp hastalıkları için düşük ve yüksek risk gruplarının karşılaştırılması

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Abstract

Objective: Fetal echocardiography (FE) is considered for fetal, maternal or hereditary reasons in pregnants with suspect of intrauterine heart disease (IUHD). However, in few studies it was reported that most of the fetuses with IUHD are in the low-risk group (suspicion of IUHD during 2nd trimester ultrasound, lack of good vision of the heart, self-referral). Our aim is to examine retrospectively the reasons for referral of pregnants, the results of FE, distribution of pregnants having fetuses with IUHD according to low- and high- risk factors and to evaluate reliability of FE.

Methods: Our study group consisted of 1395 fetuses and 1370 pregnants underwent FE between 1999 and 2006. These cases included self-referred women and the pregnants having previous child or family history of cardiac anomaly or referred by obstetricians. The prevalence of IUHDs in low- and high- risk pregnancies was compared by Chi-Square test.

Results: The low risk group included 453 patients and the remaining 917 women were in the high- risk group. Intrauterine heart diseases were detected in 152 (10.9%) of 1395 fetuses. The prevalence of IUHDs was 19% in the low- risk group and 7% in the high-risk group. Of the152 fetuses 56.6% were in the low-risk group and 43.4% were in the high- risk group. The sensitivity of FE for diagnose of IUHDs was 97%, the specificity was 100%.

Conclusion: Fetal echocardiography is highly reliable method for diagnosing of IUHDs. The most IUHDs occur in the low- risk group.

(Anadolu Kardiyol Derg 2010; 10: 263-9)

Key words: Fetal echocardiography, congenital heart disease, indication, low-risk and high- risk factors

Özet

Amaç: Fetal, maternal ve herediter nedenlerle FE yapılan gebeler, konjenital kalp hastalıklı (KKH) fetusa sahip olma olasılığı yüksek olan gebelerdir. Ancak yapılan çok az sayıdaki çalışmada KKH'lı fetusların çoğunun düşük riskli (ikinci trimester ultrasonunda KKH şüphesi, kalbin iyi görüntülenememesi, gebelerin kendi istediğiyle başvurması) gebelik grubuna dahil olduğu bildirilmiştir. Bu çalışmada bölümümüzde son yıllarda FE'si yapılan gebelerin başvuru nedenlerini, ekokardiyografi sonuçlarını ve fetuslarında KKH'ı olan gebelerin düşük ve yüksek risk faktörlerine göre dağılımlarını ve FE sonuçlarımızın güvenilirliğini retrospektif olarak değerlendirdik.

Yöntemler: Çalışmamızda Ekim 1999-Haziran 2006 tarihleri arasında Ünitemizde 1536 gebeye FE yapıldı. Postnatal ekokardiyografi sonucu bilinen 1243 normal kalp bulguları olan fetus ile postnatal ekokardiyografisi ve/veya otopsisi bilinen 152 intrauterin kalp hastalıklı (IUKH) fetus olmak üzere toplam 1395 fetus ve 1370 gebe çalışma grubumuzu oluşturdu. Bu olgular, kadın hastalıkları ve doğum uzmanları tarafından yönlendirilen, kendi isteğiyle başvuran ve ailesinde veya daha önceki gebeliklerinde KKH'ğı olan gebelerden oluşmaktadır. Düşük ve yüksek riskli gebelerdeki IUKH'ğı prevalansı Ki-Kare testiyle karşılaştırılmıştır.

Bulgular: Düşük risk grubunda 453 (%33.1), yüksek risk grubunda 917 (%66.9) gebe yer almaktaydı. 1395 fetusun 152'sinde (%10.9) IUKH saptandı. IUKH sıklığı düşük riskli gebeliklerde %19, yüksek riskli gebeliklerde %7 idi. 152 fetusun %56.6'sı düşük risk, %43.4'ü yüksek risk grubuna dahil gebeliklerde yer alıyordu. IUKH'lı fetusların %54.6'sındaki başvuru nedeni düşük risk grubundaki ikinci trimester ultrasonunda KKH'ğı şüphesi idi. IUKH'larının tanısındaki duyarlılığımız %97, özgüllüğümüz %100 idi.

Sonuç: IUKH'larının tanısında FE çok güvenilir bir yöntemdir. KKH'nın büyük bir kısmı düşük risk gurubuna dahil gebeliklerde yer almaktadır.

(Anadolu Kardiyol Derg 2010; 10: 263-9)

Anahtar kelimeler: Fetal ekokardiyografi, konjenital kalp hastalığı, endikasyon, düşük risk ve yüksek risk faktörleri

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Accepted/Kabul Tarihi: 28.01.2010

doi:10.5152/akd.2010.068

Anadolu Kardiyol Derg
2010; 10: 263-9

Introduction

Congenital heart diseases (CHD) are the most common cardiac malformations with high mortality and morbidity (1, 2). The progress in ultrasound imaging technology provides significant improvement for prenatal diagnose of intrauterine heart diseases (IUHDs) (3-6). Fetal echocardiography (FE) is a method, which takes long time, requires high skilled and experienced investigators and is costly. There is no chance to perform FE to all pregnants in developing countries. Fetal echocardiography is performed in a few pediatric centers in our country. As a result of this, it is very important to define the pregnants who need FE and the centers performed FE.

The pregnants who undergo FE by fetal, maternal and hereditary reasons are at high risk for having a fetus with CHD. However, it has been reported that most of the fetuses with CHD are in the low risk group (suspicion of CHD during 2nd trimester ultrasound, lack of good vision of the heart, self referral) in few studies in which the mothers having the fetus or child with CHD were evaluated (7, 8).

In this study, we evaluated reasons for referral of the pregnants who underwent FE, the results of FE and categorized the pregnants having the fetus with CHD according to high- and low-risk groups by reason for referral.

Methods

Study patients

The patients in our study consist of the pregnants referred by obstetricians, having previous child or family history of cardiac anomaly and who are self-referral. We recorded the ages and referral reasons of the patients, referring hospitals, number and properties of previous pregnancies, used medicines, whether or not pregnants or their partners have experienced any diseases, if there are any other organ anomalies of fetus, chromosomal disorders, findings of other pregnancies and heart findings of them. In our study, all these data were retrospectively examined.

Fetal echocardiography

Fetal echocardiography was made by the same doctor and a Trinitron GE Vivid Five performance echocardiographic scanner with 2.5-5 MHz transducers (Cardiovascular Ultrasound Systems, General Electric, Horten, Norway). The fetal examination included the standard techniques to evaluate the position and axis of the heart and for scanning plans and conventional Doppler and M-mode measurements (9, 10). The structural disorders of the heart were evaluated by a two-dimensional ultrasound imaging technique and rhythm and dimensions of heart by M-mode technique were evaluated. Echocardiography procedure was repeated several times to pregnants having unclear ultrasound imaging, dysrhythmia, fetuses with CHD and those with polypregnancies.

Outcome

We suggested all pregnants with normal FE to come again for postnatal echocardiographic control or if it is not possible to inform us when they are evaluated postnatally by any pediatric cardiologist and instruct us about of result. Also, we recommended to the pregnants having fetuses with CHD to deliver in our center. Cases whose postnatal echocardiographic findings and/or the autopsy results could not be obtained were not included in this study.

We told to the parents that pregnancies of the pregnants younger than 24 weeks old with complex CHD might be terminated (6). If the parents with complex cardiac anomaly do not want to terminate the pregnancy with complex cardiac anomaly or if the fetus is older than 24 weeks or has cardiac anomaly other than complex CHD, we informed the parents about the centers performing medical and surgical treatment of CHDs. The postmortem results of cases whose pregnancies were terminated were recorded.

Statistical analysis

The pregnants referred by several reasons were grouped according to basic reason. The percentages for describing numbers of the pregnants were calculated (6-8). All statistical analyses were done using SPSS for Windows Version 17.0 software (Chicago, IL, USA). The prevalence of IUHDs in low- and high-risk pregnancies was compared using the Chi-square test. Statistical significance was inferred at $P<0.05$. Reliability of FE was evaluated by sensibility and specificity formulas.

Results

Between October 1999 and June 2006, 1536 pregnants underwent FE. Because the results of postnatal echocardiography of 146 fetuses with normal heart and 20 fetuses with CHD were not obtained they were excluded from the study. Twenty-five of the remaining 1370 pregnants were polypregnancies (3 of them had structural CHD). Thus, our study group consisted of 1395 fetuses (1243 fetuses with normal heart, 152 fetuses with IUHD). The results of postnatal echocardiography and/or reports of fetal and natal autopsies of all the patients were obtained.

Of 152 fetuses with IUHD, 144 had structural CHD, 5 had "noncompaction" of left ventricle and 3 had rhabdomyoma.

The referral reasons of the pregnants underwent FE were shown in Table 1. The most common referral reason was history of fetus or child with a cardiac anomaly in previous pregnancy or pregnancies. Most of these pregnants were mothers of children followed upin our unit. Second frequent referral reason was diagnose or suspicion of CHD during 2nd trimester ultrasound performed by obstetricians. Most of these pregnants were referred from the of obstetrics and gynecology clinic of our hospital. Self-referral pregnants were health professionals.

Intrauterine heart diseases were determined in 152 (10.9%) of 1370 fetuses belong to 1395 pregnants. Prevalence of IUHD according to referral reasons, is shown in Table 1. Of IUHDs, 94.7% (n=144) had structural CHDs and 5.3% (n=8) had other diagnosis ("noncompaction" of left ventricle and rhabdomyoma).

When the pregnants were classified according to low- and high-risk factors, 453 (33.07%) pregnants were in low-risk group

Table 1. Referral reasons of pregnants and prevalence of intrauterine heart diseases

Referral reason	n	%	IUHD, n	%
Previous child or fetus with CHD	274	20.00	13	4.7
Suspicion or diagnosis of CHD during 2nd trimester ultrasound	256	18.69	83	32.4
Self referral	193	14.09	3	1.6
Maternal metabolic disease (diabetes mellitus, homocysteinemia)	127	9.27	9	7
Fetal dysrhythmia	75	5.47	13	17.3
Advanced maternal age	71	5.18	2	2.8
Bad obstetric history	56	4.09	2	3.5
Polyhydramniosis, oligohydramniosis, IUGR	43	3.14	1	2.3
Maternal another diseases	32	2.34	-	
Previous child with other cardiac anomaly than CHD	29	2.12	-	
Non immune hydrops	26	1.90	5	19.2
Fetal anomaly	25	1.82	6	24
Previous child with other anomalies than heart	25	1.82	2	8
Poly pregnancy	25	1.82	3	12
Previous child with the other diseases (PKU, immune deficiency)	22	1.61	-	
Maternal using of medicine	21	1.53	-	
Maternal CHD	16	1.17	4	25
Fetal chromosomal anomaly	10	0.73	2	20
Paternal CHD	7	0.51	2	28.5
Immune hydrops	7	0.51	-	
Maternal SLE or Sjögren disease (presence of autoantibody)	7	0.51	-	
Single umbilical artery	4	0.29	1	25
Lack of good vision of the heart during 2nd trimester ultrasound	4	0.29	-	
Increased nuchal translucency	3	0.22	-	
Rubella antibody positivity	2	0.15	-	
Familial history of CHD (out of parents and sibling)	2	0.15	1	50
Unknown reason	8	0.58)	-	
TOTAL	1370	100.00	152	

CHD - congenital heart disease, IUGR - intrauterine growth retardation, IUHD - intrauterine heart disease, PKU - phenylketonuria, SLE - systemic lupus erythematosus

and 917 (66.93%) of them were in high-risk group (Table 2). The low-risk group included 256 pregnants having suspicion of CHD during 2nd trimester ultrasound and 4 cases having lack of good vision of the heart. Overall 193 women were self-referred. The majority of high-risk group included pregnants having hereditary risk factors (n=415).

The distribution and prevalence of main cardiac anomalies of 144 pregnants with structural CHD are shown in Table 3. The most frequent structural CHDs were ventricular septal defect (VSD) (16.7%), atrioventricular septal defect (AVSD) (13.9%), hypoplastic left heart syndrome (11%), double-outlet right ventricle (DORV) (9%) and the malformations having univentricle morphology (7.6%).

There were 8 cases with no structural CHDs, 5 of them had"noncompaction" of left ventricle and 3 had rhabdomyoma. Three patients with "noncompaction" were diagnosed prenatally and the other 2 cases postnatally (11). The diagnosis of 3 cases with "noncompaction" and 2 - with rhabdomyoma were confirmed with postnatal echocardiography. As a result, total number of IUHDs was 152 and the number of postnatal echocardiography was 116. Of IUHDs, 3.3% were cases with diagnosis of "noncompaction" and 1.9% - rhabdomyoma.

When we categorized the structural CHDs according to severity, 57% (n=82) of cases were defined as complex, 35.4% (n=51)-as significant and 7.6% (n=11)-as having minor cardiac anomalies (Table 4).

Thirty-six pregnancies in complex group and younger than 24 weeks were terminated by parents' acceptance (Table 3). Postnatal echocardiography was performed in 108 cases. Five of these patients (1 with AVSD, 1 -hypoplastic left heart syndrome, 1-critical AS, 2- the critical CoAs) died in neonatal stage despite surgical interventions or angioplasty procedures were made. The autopsy results of these patients were recorded.

Echogenic focus was detected in 17 fetuses with normal heart (15- left ventricle, 2-right ventricle). Of 2 fetuses consid-

Table 2. Distribution of pregnants according to low and high risk factors

Risk factors	n	%
Low risk		
Suspicion of CHD during 2nd trimester ultrasound	256	18.69
Self referral	193	14.09
Lack of good vision of the heart by ultrasound	4	0.29
Total	453	33.07
High risk		
Maternal factors	276	20.15
Maternal metabolic disease	127	9.27
Advanced maternal age	71	5.18
Maternal the other diseases	32	2.34
Maternal using of medicine	21	1.53
Maternal CHD	16	1.17
Maternal autoantibody positivity (SLE, Sjögren disease)	7	0.51
Rubella antibody positivity	2	0.15
Fetal factors	218	15.90
Dysrhythmia	75	5.47
Polyhydramniosis, oligohydramniosis, IUGR	43	3.14
Non immune hydrops	26	1.90
Fetal anomaly	25	1.82
Poly pregnancy	25	1.82
Chromosomal anomaly	10	0.73
Immune hydrops	7	0.51
Single umbilical artery	4	0.29
Increased nuchal translucency	3	0.22
Hereditary factors	415	30.30
Previous child or fetus with CHD	274	20.00
Poor obstetric history	56	4.09
Previous child with other cardiac anomaly than CHD	29	2.12
Previous child with other anomalies than heart	25	1.82
Previous child with the other diseases (FKU, immune deficiency, etc)	22	1.61
Paternal CHD	7	0.51
Familial CHD (out of parents and sibling)	2	0.15
Unknown reason	8	0.58
TOTAL	917	66.93
GENERAL TOTAL	1370	100.00

CHD – congenital heart disease, IUGR- intrauterine growth retardation, PKU- phenylketonuria, SLE- systemic lupus erythematosus

ered as having normal heart, one had intermediate type of AVSD (small primum type of ASD and small inlet type of VSD) and the other had tetralogy of Fallot (TOF) postnatally. In addition, one case with prenatal VSD that was closed spontaneously and one case with sustained sinus bradycardia and heart failure prenatally were diagnosed as "noncompaction" (12).

Prenatal diagnoses of these cases, were in agreement with postnatal and autopsy diagnoses. Sensitivity of FE was 97% and specificity was 100% in our study.

Eighty-six (56.6%) of 152 fetuses with IUHD were in low- risk pregnancies, 66 (43.4%) were in high-risk pregnancies. The prevalence of IUHD was 86 (19%) in 453 low- risk pregnants and 66 (7.1%) in 917 high-risk pregnants. The prevalence of IUHDs was significantly higher in low-risk group ($p<0.001$) (Table 5).

The distribution of IUHD according to referral groups of IUHDs is shown in Table 6: 83 (54.6%) of 152 pregnants having fetuses with IUHD were in the group with suspected CHD's during second trimester ultrasound.

Discussion

In our study, intrauterine heart diseases were detected in 152 (10.9%) of 1395 fetuses. When fetuses with IUHDs were compared according to high- and low-risk pregnancies, we found that IUHD prevalence was 19% in low risk group, but only 7% in high-risk group ($p<0.001$). Of the 152 fetuses, 56.6% were in the low-risk group and 43.4% were in the high-risk group. However, the most frequent referral reason among the pregnants who underwent FE was history of previous child or fetus with cardiac anomaly in the high-risk group (20%) The sensitivity of FE for diagnose of IUHDs was 97%, the specificity was 100%.

When the mothers that have a child with structural CHD become pregnant, we inform them that they have a high risk for a child with cardiac anomaly, and also suggest them to be controlled by FE during each pregnancy. Since many years, it has been challenging issue whether the pregnants would like to know if they have a fetus with cardiac anomaly. Our finding of high prevalence of pregnants who had fetusus with CHD in their previous pregnancies shows women who are faced with this disease with high mortality and morbidity prefer to learn 'good or bad' result when they offered good counseling. Also, our finding supports studies that suggest increased sensitivity of mothers about FE (13).

The majority of self-referred pregnants were health professionals from our or other hospitals. These pregnants with high sociocultural level were referred to eliminate their concerns although their cardiac findings during 2nd trimester ultrasound were normal.

We diagnosed IUHD in 152 cases (10.9%), structural CHD in 144 cases (10.3%) by FE. These rates are higher than the levels reported in literature. Todros et al. (7) detected prevalence of CHD as 4.9% at 4523 pregnants by FE, and Perri et al. (8) reported prevalence to be as 2.7% of 1696 pregnants. This variability in prevalence of prenatal CHD may result from more common FE applications, different health policies or a specific society screening in these countries. The prevalence of IUHD in our study is 2-3 times higher than in the studies mentioned above. Our hospital is a tertiary center with referral of high -risk pregnancies from all over country and this might explain increased number of high-risk pregnancies. Indeed 43.4% of fetuses with IUHD was born from pregnants with high risk.

Table 3. The prevalence of structural CHDs and the results of postnatal echocardiography and autopsy

Results of fetal echocardiography	n	%	Postnatal echocardiography, n	Autopsy F, n	Autopsy PN, n
Ventricular septal defect (VSD)	24	16.7	24	-	
Atrioventricular septal defect (AVSD)	22	13.9	13	9	1
Hypoplastic left heart	16	11.1	11	5	1
Double outlet right ventricle (DORV)	13	9.0	7	6	-
Single ventricle	11	7.6	8	3	-
Single atrium or large atrial septal defect (ASD)	10	6.9	10	-	-
Ebstein anomaly	9	6.3	6	3	-
D-transposition of great arteries (d-TGA)	6	4.2	3	3	-
Tetralogy of Fallot (TOF)	4	2.8	4	-	-
Aortic stenosis (AS)	4	2.8	4	-	1
Mitral valvular anomaly	3	2	3	-	-
Pulmonary atresia, VSD	3	2	2	1	-
Coarctation of the aorta (CoA)	3	2	3	-	2
Pulmonary stenosis (PS)	3	2	2	1	-
C-transposition of great arteries (c-TGA)	3	2	3	-	-
Primum atrial septal defect (primum ASD)	2	1.4	2	-	-
Aortic interruption	2	1.4	-	2	-
Truncus arteriosus	2	1.4	1	1	-
Absence of pulmonary artery	2	1.4	1	1	-
Imperforate pulmonary valve	1	0.7	1	-	-
Absence of pulmonary valve	1	0.7	-	1	-
TOTAL	144	100	108	36	5

CHD - congenital heart disease, F-fetal, PN- postnatal

Table 4. Distribution according to severity of structural CHDs

Category	n	%
Complex	82	57.0
Significant	51	35.4
Minor	11	7.6
Total	144	100.0

CHD – congenital heart disease

Table 5. Distribution of IUHDs according to pregnancies with low and high risk factors

	Pregnant		IUHD		Rate of CHDs in risk groups
	n	%	n	%	%
Low- risk group	453	33.1	86	56.6	19.0
High- risk group	917	66.9	66	43.4	7.1
TOTAL	1370	100.0	152	100.0	

Chi -square test value: 42.7, p<0.001
CHD - congenital heart disease, IUHD - intrauterine heart disease

IUHD was observed in 32.4% of pregnants referred by suspicion or diagnosis of CHD during 2nd trimester ultrasound. In Perri's study (7), CHD was detected in 48.7% of 78 pregnants underwent FE because of this indication. We can explain this result by difference in imaging techniques used by obstetricians.

Copel et al. (20) advocate that sensitivity of four-chamber view is higher, whereas other authors consider this approach as low sensitive (4-40%) (14-21). Usually FE studies report that four-chamber view has low sensitivity, obstetric ultrasound studies report high sensitivity. The reported sensitivity of obstetric ultrasound by only four-chamber view was 30-50%. When outflow tracts of aorta and pulmonary artery, three-vessel and trachea view were added to this view sensitivity increased up to 86-99% (22, 23). Our results support the opinion that a standard heart imaging method showing also outflow tracts of main vessels in out-patient obstetric and gynecology clinics must be improved.

In our study, it was shown that 56.6% of fetuses with IUHD were in low-risk group and 54.6% of them were pregnants having suspicion or diagnosis of CHD during 2nd trimester ultrasound. In Todros' s study (8), 70% of fetuses with CHD were in low-risk group and majority them were pregnants having suspicion or diagnosis of CHD during 2nd trimester ultrasound. In Perri's study (7), 89.1% of 46 fetuses with CHD were from pregnancies in low-risk group, 82.6% of them have suspicion or diagnosis of CHD during 2nd trimester ultrasound, and 17.4% of them have lack of good vision of the heart and self- referral. In Perri and Todros' s screening studies (7, 8), majority of fetuses with CHD were in low-risk group, and 70-80% of them were pregnancies having suspicion or diagnosis of CHD. Our rates are lower than reported in these studies because of number of preg-

Table 6. Distribution of IUHDs according to referral groups

Referral reason	CHD	
	n	%
Suspicion of CHD during 2nd trimester ultrasound	83	54.6
Previous child or fetus with CHD	13	8.6
Fetal dysrhythmia	13	8.6
Maternal metabolic disease (diabetes mellitus, homocysteinemia)	9	5.9
Fetal anomaly	6	3.9
Maternal CHD	4	3.3
Polypregnancy	3	2.6
Non immune hydrops	5	2
Self referral	3	2
Paternal CHD	2	1.3
Chromosomal anomaly	2	1.3
Previous child with other anomalies than heart	2	1.3
Bad obstetric history	2	1.3
Advanced maternal age	2	1.3
Single umbilical artery	1	0.7
Familial history of CHD (out of parents and sibling)	1	0.7
Polyhydramniosis, oligohydramniosis, IUGR	1	0.7
TOTAL	152	100.0

CHD - congenital heart disease, IUGR - intrauterine growth retardation, IUHD - intrauterine heart disease

nants in high-risk group is higher. When fetuses with IUHDs were compared according to high-and low-risk pregnancies, we found that IUHD prevalence was 19% in low risk group, but only 7% in high- risk group ($p<0.001$).

The most frequently observed structural CHDs in our study were VSD, AVSD, hypoplastic left ventricle and DORV. In Hoffman's comprehensive screening study (1), the most frequently observed structural CHD was VSD. Perri et al. (7) reported percentage of TOF as 19.6%, VSD as 17.4%, d-TGA as 17.4%, hypoplastic left heart as 15.2% and AVSD as 10.9%.

According to recent data, echogenic focus is a not pathologic symptom and is a normal finding of developing heart (7, 24). We detected 17 echogenic focus and none of them had any CHD or Down syndrome.

Families in 36 (44%) of 82 pregnants having fetuses with CHD were opted to terminate the pregnancy. As long as pregnancies are less than 24 weeks, 50-66% of families having fetuses with complex CHD prefer to terminate the pregnancy (25, 26). When we compare diagnosis of the patients with CHD with postnatal echocardiography and autopsy data, specificity of FE in diagnosis of CHDs was 100% and sensitivity-97%. These values are better than in our first study and similar to results reported in literature (26-28). When prenatal diagnoses were compared with autopsy and postnatal echocardiography results, specificity rates varied between 70-98% (26-29).

We think that the reasons of this improvement are due to increased experience of consultant and advancement in transducer engineering.

Conclusion

Fetal echocardiography is a highly reliable method for diagnosing of IUHDs. Most of the CHDs were determined in pregnancies in low-risk group. Therefore, it should be the mission of gynecologists and obstetricians to determine IUHDs. Pregnant women with a history of previous child with congenital heart defect should be referred for fetal echocardiography.

Conflict of interest: None declared

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