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Current follow-up results of Cyanotic Congenital Heart Diseases detected during Pregnancy in a specific Region

Gebelikte Belirli Bir Bölgede Tespit Edilen Siyanotik Konjenital Kalp Hastalıklarının Güncel Takip Sonuçları

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Abstract

Aims: Congenital heart disease (CHD) is the main cause of death in infants among congenital anomalies. Fetal echocardiography is important for the diagnosis and treatment plan of congenital heart diseases in the prenatal period. This study aimed to retrospectively screen the follow-up and treatment results of cyanotic CHD patients detected on fetal echocardiography.

Material and Method: Fetal echocardiography results were scanned from the hospital record system. Data of fetuses with major cardiac anomalies and cyanotic CHD were examined retrospectively.

Results: Fetal echocardiography was performed on 420 pregnant women between July 2020 and April 2023. Major cardiac anomalies and cyanotic heart disease were detected in the fetuses of 40 pregnant women (9.5%) out of 420. The median age of the pregnant women was 29 (19-41 years). The median gestational age at check-up was 23 weeks (22-28 weeks). 9/40 pregnant women (22.5%) had risk factors. The most common cyanotic congenital heart diseases were hypoplastic left heart syndrome (HLHS) and unbalanced complete atrioventricular septal defects (AVSDs) with obstructive lesions of the right or left ventricle. Three fetuses (7.5%) with heart failure findings died intrauterine. Two fetuses with HLHS and critical aortic stenosis (AS) died before being operated on. A patient with complete AVSD, hypoplasia of the left heart chambers, AS, and severe aortic coarctation died due to sepsis during the post-operative follow-up period. Chromosome analysis was performed in 8 patients. Down syndrome was detected in 3 of the patients with complete AVSD. 22q11 deletion and DiGeorge Syndrome were detected in 2 patients with tetralogy of Fallot.

Conclusions: Congenital heart diseases and rhythm problems can be safely detected with fetal echocardiography. It is beneficial to perform a fetal echo scan at the appropriate gestational week, especially in fetuses with risk factors and in whom the four chambers view cannot be seen.

Keywords: fetal echocardiography, prenatal screening, cyanosis, congenital heart disease

Öz

Aim: Konjenital kalp hastalığı (KKH), konjenital anomalili bebeklerde önde gelen ölüm nedenidir. Fetal ekokardiyografi konjenital kalp hastalıklarının prenatal dönemdeki tanı ve tedavi planı açısından önemlidir. Bu çalışma ile fetal ekokardiyografide saptanan siyanotik KKH hastalarının takip ve sonuçlarının retrospektif olarak taranması amaçlandı.

Gereçler ve Yöntem: Fetal ekokardiyografi sonuçları ekokardiyografi kayıt sisteminden tarandı. Major kardiyak anomali ve siyanotik KKH olan fetusların verileri geriye dönük incelendi.

Bulgular: Temmuz 2020-Nisan 2023 tarihleri arasında 420 gebeye fetal ekokardiyografi yapıldı. 420 gebenin 40'ının (%9,5) fetusunda majör kalp anomalisi ve siyanotik kalp hastalığı tespit edildi. Gebelerin ortalama yaşı 29 (19-41 yıl) idi. Ortalama gebelik yaşı 23 hafta (22-28 hafta) idi. Gebe kadınların 9/40'ında (%22,5) risk faktörleri vardı. En sık görülen siyanotik konjenital kalp hastalıkları hipoplastik sol kalp sendromu (HSKS) ve sağ veya sol ventrikülün obstrüktif lezyonlarıyla birlikte dengesiz tam atriyoventriküler septal defektlerdi (AVSD). Kalp yetmezliği bulguları olan 3 fetüs (%7,5) intrauterin dönemde kaybedildi. HLHS'li ve kritik aortik darlığı (AD) olan iki fetüs ameliyat edilmeden önce öldü. Komplet AVSD, sol kalp boşluklarında hipoplazi, AD ve ciddi aort koarktasyonu olan bir hasta, ameliyat sonrası takip sırasında sepsis nedeniyle kaybedildi. 8 hastaya kromozom analizi yapıldı. Komplet AVSD'li hastaların 3'ünde Down sendromu saptandı. Fallot tetralojili 2 hastada 22q11 delesyonu ve DiGeorge Sendromu tespit edildi.

Sonuç: Fetal ekokardiyografi ile konjenital kalp hastalıkları ve ritm problemleri güvenli olarak tespit edilebilmektedir. Özellikle risk faktörleri olan, dört boşluk net görülemeyen gebelerde uygun gebelik haftasında fetal eko taraması yapılmasında fayda vardır.

Anahtar Kelimeler: fetal ekokardiyografi, prenatal tarama, siyanoz, konjenital kalp hastalığı

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INTRODUCTION

Congenital heart disease (CHD) is the main cause of death in infants with congenital anomalies.[1] By identifying congenital heart diseases intrauterine, early diagnosis and treatment are possible by evaluating the heart structure, functions, and rhythm. One of the most effective screening methods is fetal echocardiography.

Although the incidence of congenital heart disease varies between countries, in a recent study conducted in middle Anatolia, the prevalence was 27.8 per 10,000 live births.[2] Besides, CHD is identified in approximately 1 percent of births, and accounts for 30 to 50 percent of deaths related to congenital anomalies in the United States.[3] In children with an isolated cardiac abnormality, the commonness of associated abnormalities also relies on the type of CHD. Cyanotic congenital heart diseases seem to have more adverse neurodevelopmental outcomes compared to acyanotic CHD.[4]

Fetal echocardiography is carried out in fetuses at a great risk of CHD and in fetuses who have or are doubted of having a pathology on routine ultrasound screening. However, even in low-risk patients, fetal echocardiography can also be performed in case of suspicion after routine screenings.[5]

Fetal cardiac anomalies can be divided into major and minor anomalies.[6] Major cardiac anomalies are cyanotic (heart defects with right-left shunt) like single ventricle, critical pulmonary and/or aortic stenosis, severe aortic coarctation, hypoplastic left heart syndrome (HLHS), dextro-transposition of great artery (D-TGA), etc. It includes heart diseases that require intervention as soon as birth, where prostaglandin-E1 (PGE1) infusion is frequently needed, or where normal physiology is disrupted, although there is no need for urgent intervention.

In this study conducted in the Eastern Mediterranean region, current fetal echocardiography results were scanned in a specific region, and data regarding cyanotic CHD were analyzed. There are very few recent studies in this region in the literature. This study was planned to retrospectively scan the fetal echocardiography results in the last 2 years and evaluate cyanotic congenital heart diseases, which are major cardiac structural anomalies, and follow-up treatment results.

MATERIAL AND METHOD

The study was carried out with the permission of Mersin University Clinical Researches Ethics Committee (Date: 01.11.2023, Decision No: 748). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

The data of pregnant women who were cared for in the pediatric cardiology clinic and underwent fetal echocardiography between July 2020 and April 2023 were examined retrospectively.

Fetal echocardiography at a median week of 22 weeks (19-35 weeks of gestation) in the intrauterine period had been done. In the postnatal period, echocardiographic examination was repeated in fetuses with cyanotic CHD.

Fetal echocardiography was performed with the Vivid E9 Pro Ultrasound System (GE Medical Systems, Canada) with a 4C-RS convex ultrasound probe in the 1.6 to 4.6 MHz range. It was performed with 2D, M-mode, color Doppler, and pulse wave (PW) Doppler imaging methods. Four-chamber, five-chamber, three-vessel, ductal arch, and aortic arch positions were evaluated in two-dimensional imaging.

Transthoracic echocardiography, performed via Vivid E9 Pro Ultrasound System (GE Medical Systems, Canada) by using 3 and 6 MHz transducers as 2D, M-mode and colored Doppler, conventional continuous-wave (CW) and pulse wave (PW) Doppler visualizing methods. Two experienced pediatric cardiologists carried out all the studies.

Patients who were diagnosed in our center and came for follow-up and check-ups regularly were included in the study. Patients without complex congenital heart diseases were not included in the study. Those with simple CHD with left-right shunt diseases were not included in the study. Patients who were not initially diagnosed in our center and did not attend regular follow-ups were excluded from the study.

Statistical Method

Descriptive statistical methods were used to analyze the data expressed as numbers and percentages. Analysis of the data collected in the study was carried out using SPSS Statistics for Windows 16.0 (SPSS Inc., Chicago, IL, USA).

RESULTS

A total of 420 pregnant women were examined between the specified dates. Major cardiac anomalies with cyanotic heart disease were detected in the fetuses of 40 pregnant women out of 420 (9.5%). The median age of the pregnant women was 29 years (19-41 years). The median gestational age at check-up was 23 weeks (22-28 weeks). 9/40 pregnant women (22.5%) had risk factors. Two of the pregnant women had diabetes mellitus diagnosed during pregnancy. Maternal obesity was present in five pregnant women. Only one pregnant woman had a twin pregnancy. One pregnant woman had in vitro fertilization (IVF) with external assistance. None of the pregnant women had a history of CHD in their family, siblings, and/or first-degree relatives such as parents.

When the most common cyanotic heart diseases are summarized, there were 7 patients (17.5%) with HLHS, 6 patients (15%) with unbalanced complete atrioventricular septal defect (AVSD) with right or left ventricular outflow tract obstructions, 4 patients (10%) with tricuspid atresia, 4 patients with tetralogy of Fallot, and 5 patients (%12.5) with critical aortic valvular stenosis (AS) and/or severe aortic coarctation (AC). The distribution of all other diseases is summarized in **Table 1**.

Table 1. Characteristics of Cyanotic Congenital Heart Diseases diagnosed in Fetal Period.

Fetal Echocardiography Results	Number	PGE1 İnfusion	Survival
Hypoplastic Left Heart Syndrome	7	yes	All exitus
D-TGA	3	yes	
Unbalanced Complete AVSD with LVOT or RVOT obstruction	6	yes if alive	3/6 exitus
Tricuspid atresia with LVOT or RVOT obstruction	4	yes	
Tetralogy of Fallot	4	no	
Aort coarctation (AC)	1	yes	
VSD and AC	1	yes	
critical valvular AS	2	yes	2 exitus
valvular AS with AC	1	yes	
Double inlet single ventricul+ aortic interruption	1	yes	
Single ventricle with PA	2	yes	
VSD and PA	1	yes	
ciritical PS, PA	1	yes	
DORV	2	no	
Trunkus arteriozus	2	no	
Ebstein anomaly	2	no	

AS: Aortic stenosis, DORV: Double outlet right ventricle, D-TGA: D-Transposition of Great arteries, LVOT: Left ventricle outflow tract, PA: Pulmonary Atresia, PGE1: Prostaglandin-E1 infusion, PS: Pulmonary stenosis, RVOT: Right ventricle outflow tract. VSD: Ventricular septal defect.

Additional non-cardiac anomalies were detected in the gastrointestinal, central nervous system, and/or genitourinary system in seven patients (17.5%). Two patients with complete AVSD had major intestinal disorders. Three patients (one with tetralogy of Fallot, one with tricuspid atresia, and one with hypoplastic left heart syndrome) had slightly enlarged lateral ventricules of the brain. The last two patients had moderate to large renal calyceal dilation of whom two had aortic coarctation. No additional major systemic disorders were observed in other patients.

Intrauterine and postnatal outcomes

During the follow-up of the patients, three fetuses (7.5%) of whom one was with unbalanced AVSD and isthmus hypoplasia, one fetus was with complete AVSD and pulmonary atresia, Down syndrome, and major intestinal disorder, and one fetus with critical AS and cardiomyopathy died intrauterine.

While 32 of these patients (80%) were born in a pediatric cardiovascular surgery center (CVC), two pregnant women with HLHS gave birth in their local center, even though the must-to-do conditions were explained. A total of six patients with tetralogy of Fallot, double outlet right ventricle (DORV), Ebstein anomaly, and no additional vascular anomalies gave birth in non-CVC centers.

When the results and prognosis in the postnatal period are evaluated; postnatal echocardiograms of the patients were compatible with prenatal results. The patient with Ebstein's anomaly, who gave birth in a center without CVS, was considered to have functional pulmonary atresia, and PGE1 infusion was started because newborn was significantly cyanotic, and the patient was referred to the surgical center. There were no additional problems in other patients with tetralogy of Fallot. The ventricular septal defect (VSD) of the one patient with DORV was large, and when signs of heart failure still appeared on the 30th postnatal day, the patient was operated for pulmonary banding.

Among the patients referred to the surgical center, 2 with HLHS and critical AS died before being operated on. In sum, all seven patients with HLHS died before or after surgery. A patient with complete AVSD, hypoplasia of the left heart chambers, aortic stenosis, and severe aortic coarctation died due to sepsis during post-operative follow-up. Necessary surgical procedures were performed on other patients during their follow-up, and there were no losses in these patients in the post-operative acute period. The total mortality rate was 12/40 (30%).

Chromosomal Analysis

Chromosome analysis was performed in 8 patients. Down syndrome was detected in 3 of the patients with complete AVSD. 22q11 deletion and DiGeorge Syndrome were detected in 2 patients with tetralogy of Fallot. A total of 3 patients with HLHS were evaluated for chromosomal anomaly upon request of the family, but no anomaly was detected.

DISCUSSION

Cyanotic CHDs, among the major cardiac anomalies, are important heart diseases that need to be followed in the intrauterine and postnatal periods. By making a diagnosis in the intrauterine period with fetal echocardiography, necessary precautions such as pregnancy follow-up and subsequent birth planning can be taken in the pediatric CVS center. Our results show that particularly pronounced complex pathology and cyanotic CHD can be seen in patients, regardless of risk factors such as diabetes mellitus and maternal obesity. Four-chambers view, left and right ventricular outflow-tract views [LVOT and RVOT], and three-vessel-and-trachea views should be routinely performed by ultrasonographers, especially during pregnancy ultrasounds. It has been observed that the prognosis may be worse in cases of stenosis that involve the left heart chambers, aortic valve, and aorta, due to heart failure. This study is important in terms of showing the contemporary fetal echocardiography screening results and effectiveness of the fetal screening. It is also important in that it provides information about the prevalence of major cardiac anomalies by covering a specific region.

Compared to previous CHD incidence/prevalence studies; Although the rate of cyanotic CHD was not very low in this study, not every patient who underwent prenatal screening was sent for cardiac evaluation, and it is thought that the prevalence would be lower if all other pregnant women were included.[7]

The most common cyanotic congenital heart diseases were HLHS and unbalanced complete AVSDs with obstructive lesions of the right or left ventricle. When we look at the literature and especially neonatal studies, in a study conducted in Africa, tetralogy of Fallot and truncus arteriosus are the most common congenital heart diseases.[8] In our study, HLHS was ranked first, followed by unbalanced AVSD. Although no generalization can be made because the sample was small, the distribution of the results in the eastern Mediterranean region was like this. HLHS and unbalanced complete AVSD were common cyanotic CHDs, and they were referred to pediatric cardiology because the 4-chamber image was not obtained in the first scan. In cyanotic CHDs such as tetralogy of Fallot and BAT, positive results were obtained by examining 3-vessel imaging in addition to five-chamber (left and right ventricular outflow-tract views) imaging. Therefore, as stated in other studies, looking at all 3 positions in the first scan will increase the scanning efficiency.[9]

Performing fetal echocardiography in high-risk pregnancies has been recommended in many studies.[10] Even low-risk pregnancies may have accompanying cardiac anomalies. Therefore, fetal echocardiography screening seems important. In our study, 77.5 % of the pregnant women with major cardiac anomalies were low-risk pregnancies.[11] Even if there is no significant difference between high- and low-risk midwifery, a larger number of studies are needed.

In a study examining fetal autopsy results and comparing them with fetal echocardiography results, pathologies related to pulmonary veins and other vascular structures were rarely missed.[12] There was no patient missed in this way in our study. We think that it is especially important to evaluate the opening of the pulmonary veins, coronary sinus, superior vena cava, and the inferior vena cava (IVC).

When the mortality results were evaluated, losses were observed in three fetuses accompanied by cardiomyopathy and syndromic diseases. Fetal interventions like aortic or pulmonary balloon valvuloplasty, and/or atrial needle septoplasty can be performed in some patients. These fetal interventions could have also high mortality, and success rates depend on the patient, congenital heart pathology, and timing of the process. Significant heart failure in fetus could increase the mortality rates of these procedures.[13] In our country, interventions have started in some centers. In our study, although intervention was considered for two patients with critical aortic stenosis, no intervention was performed because the risk of mortality would be high due to significant heart failure. It is thought that as experience in fetal intervention increases, the number of procedures will increase.[14]

It is not necessary to start PGE1 infusion in every patient with cyanotic CHD in the postnatal period. However, it is necessary to be prepared for any situation, keeping in mind that postnatal physiology may change. The patient with Ebstein anomaly had to start PGE1 infusion due to functional pulmonary atresia in the postnatal period.

When looking at the prognosis of cyanotic CHD; In cases of critical aortic stenosis and/or aortic coarctation, especially affecting the left heart chamber, there have been patients who died due to pre-operative heart failure, cardiogenic shock or sepsis, and heart failure after the operation. In cases where the left heart chambers are affected, myocardial involvement may be more pronounced and the prognosis may be worse. Other studies have also reported that the prognosis is poor in patients with lower z scores, especially in cases where the size of left heart structures such as the mitral valve, aortic annulus, and left ventricle decreases.[15] Similarly, in this study, the prognosis was poor in patients with prominent hypoplasia. Although there is mostly no significant heart failure in the intrauterine period in right ventricular pathologies such as pulmonary valve critical stenosis, these patients are generally treated gradually in the postnatal period, going through two stages, starting with Blalock-Taussig (BT) shunt or patent ductus arteriosus (PDA) stent. In other studies, these patients generally did not require any intervention during the intrauterine period.[16,17] The mortality rate in this study represents both intrauterine and postnatal postoperative results, so the high ratio could be related to this.

Although chromosome analysis is not recommended for every cyanotic congenital heart disease, it seems logical to perform chromosome analysis in patients with additional risk factors and additional anomalies.[18] In our study, the possibility of syndrome and chromosomal anomalies seems to be increased in certain cyanotic CHDs such as AVSD and conotruncal anomalies.

Study Limitations

The fact that it is a retrospective study in a single center and the relatively small number of samples can be considered among the limitations of the study. Nevertheless, it is important because it shows data about cyanotic CHDs in patients who underwent fetal echocardiography in a certain region. Although the rate of cyanotic CHD was high in this study conducted in the Eastern Mediterranean region, this may be because not all patients were sent to the cardiology clinic.

CONCLUSION

With fetal echocardiography, major cardiac anomalies and cyanotic CHDs can be diagnosed and follow-up treatment plans can be made in the intrauterine and postnatal periods safely. These patients with major cardiac anomalies should be offered delivery primarily in pediatric CVS centers, as they may not be stabilized for transport. The risk of mortality is higher in both the intrauterine and postnatal periods of patients in whom the left heart structures are affected and/or there are genetic syndromes. The course of disorders

affecting the right heart structures, especially the pulmonary valve, may be better in the prenatal and postnatal periods. Chromosomal analysis and additional anomaly screening should be recommended in these patients with cyanotic CHD.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of Mersin University Clinical Researches Ethics Committee (Date: 01.11.2023, Decision No: 748).

Informed Consent: All patients signed the free and informed consent form.

Referee Evaluation Process: Externally peer-reviewed.

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