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Original Article

Assessment of risk factors for congenital heart disease through prenatal fetal echocardiography and the correlation with postnatal diagnoses

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ABSTRACT

Background: Congenital Heart Disease (CHD) constitutes a significant cause of morbidity and mortality in newborns. Identifying CHD prenatally and understanding associated risk factors can aid in early diagnosis, intervention, and postnatal management. This study aims to assess risk factors for CHD using prenatal fetal echocardiography (FE) and investigate their correlation with postnatal diagnoses.

Patients and Methods: In this study, we included 993 pregnant women presenting to the pediatric cardiology outpatient clinic between December 2018 and December 2020, considered at risk for CHD. We retrospectively evaluated the cases' postnatal echocardiography data with detected CHD during fetal echocardiography.

Results: The average age of the patients was 29.8±5.7, and the mean gestational week was 23.61±3.9. Among the pregnant women, 253 (25.47%) were primiparous, 740 (74.53%) were multiparous, 103 cases (9.32%) involved multiple pregnancies, and 259 (26.08%) had chronic diseases. The most common reason for fetal echocardiography referral was the suspicion of CHD in fetuses with dysmorphic findings detected during obstetric ultrasonography. Among the cases, 329 (33.1%) were classified as low-risk, while 664 (66.9%) as high-risk. Among all patients, the most commonly observed prenatal CHD were Ventricular Septal Defects (VSD) (8.2%), Hydrops Fetalis (6.1%), and large Atrial Septal Defects (ASD) (3.9%). The overall prevalence of CHD was 31.6%. The accuracy of postnatal echocardiography in confirming the diagnoses made with fetal echocardiography was 94%.

Conclusion: Prenatal diagnosis of congenital heart diseases is crucial for planning prenatal and postnatal management and providing families with the option of pregnancy termination in severe anomalies. Fetal echocardiography has shown significant potential for early diagnosis of CHD, even in low-risk fetuses, and its inclusion in routine prenatal screenings by increasing the number of experienced specialists and centers could play a crucial role in reducing CHD-related mortality and morbidity rates.

Keywords: Fetal echocardiography, congenital heart diseases, prenatal diagnosis, high risk pregnancy

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INTRODUCTION

Congenital Heart Diseases (CHDs) constitute a significant portion of congenital anomalies worldwide and are a leading cause of neonatal mortality and morbidity.[1] CHD is observed in approximately 0.8% of live births. A large portion of congenital heart diseases occur due to polygenic multifactorial causes. CHD accounts for a considerable proportion of mortality among children with congenital malformations.[2,3]

Fetal echocardiography (FE) is a reliable and non-invasive method used to diagnose and evaluate structural heart diseases in the prenatal period.[4] Fetal echocardiography, particularly in high-risk pregnancies, enables early detection of structural heart diseases and determines appropriate treatment approaches. The early diagnosis of structural heart disease during pregnancy can significantly impact the baby's quality of life and health outcomes.[5,6] The increasing experience in fetal echocardiography is vital for making accurate diagnoses in the early stages, providing families with the option of terminating the pregnancy in case of severe anomalies, and optimizing the timing of surgical interventions and treatments in the postnatal period.[7] Using fetal echocardiography helps families and healthcare professionals make informed decisions during the prenatal and postnatal periods.[8]

In this study, we aim to investigate the indications for the referral of pregnant women to our clinic for fetal echocardiography, early diagnosis of structural heart abnormalities with prenatal and postnatal fetal echocardiography, and the examination of risk factors. Additionally, we aim to evaluate the accuracy and correlation of fetal echocardiography results during the prenatal and postnatal periods.

PATIENTS AND METHODS

This study included 993 pregnant women referred from the Department of Obstetrics and Gynecology to the Department of Pediatric Cardiology Dokuz Eylül University Hospital between December 2018 and December 2020, considered at risk for CHD. We collected the pregnant women's demographic information, pregnancy history, parity, multiple pregnancies, consanguineous marriage status, maternal chronic diseases (diabetes mellitus, phenylketonuria, Lupus and Sjögren's syndrome, hypothyroidism, vitamin D deficiency), medication use, smoking, alcohol, and substance use, as well as the results of prenatal screening tests (2nd and 3rd-trimester screenings), and karyotype results if amniocentesis performed. We retrospectively evaluated the postnatal echocardiography data of cases with detected CHD during fetal echocardiography.

Inclusion criteria

We included pregnant women with a gestational age of 18 weeks or more who agreed to participate and divided them into two groups according to their risk factors.

High-risk group

The maternal factors were diabetes, medication use, advanced maternal age (>40 years), presence of CHD, TORCH infection, and presence of collagen vascular disease.

The fetal factors were polyhydramnios/oligohydramnios, increased nuchal translucency, fetal anomalies, arrhythmia, immune/non-immune hydrops, and chromosomal anomalies presence.

The hereditary factors were the previous history of fetal anomalies in previous pregnancies or the family history of CHD.

Low-risk group

The low-risk group comprised pregnant women who voluntarily sought medical attention, had suspicions of CHD, or had inadequate fetal ultrasound evaluation in the second trimester. Exclusion criteria

We excluded pregnant women with a gestational age below 18 weeks, cases requiring termination of pregnancy before delivery, and those who refused to participate.

Ethics

The study received ethical approval from the Dokuz Eylül University Non-Interventional Clinical Research Ethics Committee (approval date 08/05/2019, number 2019/12-19).

Fetal echocardiography

A team of pediatric cardiology specialists experienced in this field performed the fetal echocardiography examinations, conducting the fetal cardiac evaluations using a high-resolution ultrasound system (Philips Affiniti 50c System, Philips, Netherlands, C; 5-1 MHz transducer). They employed standard techniques to determine the fetal position and cardiac axis and to obtain Doppler and M-mode measurements. The team assessed structural anomalies using 2D echocardiographic images while evaluating rhythm problems using M-mode and Doppler techniques.[5]

Statistical analysis

We performed the statistical analyses using SPSS Statistics V 26.0 (IBM Corp., Armonk, New York, USA). Our team examined the distribution and frequencies of the data and analyzed continuous or categorical variables to determine statistically significant differences between groups. We presented the parametric test results as mean and ± standard deviation and used percentages to categorize pregnant women and risk factors. Our team used the Chi-square test to compare parametric values between groups while using the Student's T-test for non-parametric data. A p-value of <0.05 was considered statistically significant for indicating differences.

RESULTS

We included 993 pregnant women in the study, with a mean age of 29.8±5.7 years and an average gestational age of 23.61±3.9 weeks. Among the participants, 253 (25.47%) were primiparous, 740 (74.53%) were multiparous, 103 (9.32%) had multiple pregnancies, 259 (26.08%) had chronic diseases, and 128 (12.9%) reported consanguineous marriages. The demographic characteristics of the pregnant women are present in Table 1. The most common reasons for fetal echocardiography referrals were the evaluation of suspected CHD in fetuses with dysmorphic findings during obstetric ultrasonography (16.46%), seeking a second opinion from another center (15%), and multiple pregnancies (9.32%) (Table 2). We classified 329 (33.1%) of the cases into the low-risk group and 664 (66.9%) into the high-risk group. The most commonly detected prenatal CHD anomalies were Ventricular Septal Defects (VSDs) (8.2%), Hydrops Fetalis (6.1%), and large Atrial Septal Defects (ASDs) (3.9%). In the postnatal group, the anomaly rates we observed were VSD (7.3%), isolated Hydrops Fetalis (5.9%), and large ASD (4.5%).

Table 1. Demographic characteristics of pregnant women

Age, year (*mean ± SD, min-max*)	29.8±5.7 (17-51)
Gestational week (*mean ± SD, min-max*)	23.61±3.9 (18-39)
Primipar, n (%)	253 (%25.47)
Multipar, n (%)	740 (%74.53)
Multiple pregnancy, n (%)	103 (%12.8)
High risk pregnancy, n (%)	664 (%66.9)
Low risk pregnancy, n (%)	329 (%33.1)
Maternal chronic disease, n (%)	259 (%26.08)
Consanguineous marriage, n (%)	128 (%12.9)

Table 2. The indications for pregnant women's referrals for fetal echocardiography

Reason for referral	n	(%)
Dysmorphic features in the fetus	163	16.4
Secondary consultation	149	15.0
Multiple pregnancy	127	12.8
Maternal chronic disease	75	7.6
Inadequate evaluation on obstetric USG	73	7.4
Hyperechoic focus in fetal heart	66	6.6
Increased risk in screening	60	6.1
History of CHD in a previous pregnancy	48	4.8
Maternal History of CHD	45	4.6
Advanced maternal age	29	2.9
Maternal medication use	26	2.6
Hydrops fetalis	23	2.3
Rhythm disorder in baby	17	1.7
Genetic pathology in previous pregnancy	4	0.4
Other reasons	87	8.8

The prevalence of CHD detected with fetal echocardiography was 27.12% in the high-risk group and 4.92% in the low-risk group. Among all cases, normal findings were observed in 68.4% of patients, while the overall prevalence of CHD was 31.6%. We performed postnatal echocardiography in 53.8% of the cases, and while 66.6% of them had no abnormal results, 172 patients received a diagnosis of CHD. Our outpatient clinic's accuracy in diagnosing CHD with fetal echocardiography was 94%. We presented the CHD cases detected by prenatal and postnatal echocardiography in Table 3.

Three patients diagnosed with Atrioventricular Septal Defect (AVSD) had Down syndrome. A patient with pulmonary stenosis was diagnosed with Williams syndrome, and another with a large ASD was diagnosed with Holt-Oram syndrome during the postnatal period. Four of the 17 fetuses referred for suspected rhythm disorders in the high-risk group were diagnosed with supraventricular tachycardia and three with complete atrioventricular block. In the low-risk group, we observed four fetuses with atrial premature contractions. A fetus with an atrioventricular block was diagnosed with Sjögren's syndrome when anti-Ro and anti-La autoantibodies tested positive in the mother. Another mother in the low-risk group was diagnosed with Systemic Lupus Erythematosus.

Table 3. Congenital heart diseases detected in prenatal and postnatal echocardiography

	Prenatal (n:993) (n/%)	Postnatal (n:534) (n/%)
Congenital heart diseases	313/31.6	172/33.4
Ventricular septal defect	82/8.2	39/7.3
Hydrops fetalis	61/6.1	32/5.9
Large atrial septal defect	39/3.9	24/4.5
Pulmonary stenosis	36/3.6	19/3.5
Hyperechoic focus	34/3.4	16/2.9
Tetralogy of Fallot	15/1.5	8/1.49
Atrioventricular septal defect	9/0.90	7/1.31
Great artery transposition	7/0.70	6/1.12
Coarctation of the aorta	5/0.50	4/0.74
Aortic stenosis	4/0.40	5/0.93
Tricuspid atresia	4/0.40	3/0.56
Pulmonary atresia	4/0.40	3/0.56
Double outlet right ventricle	3/0.30	3/0.56
Truncus arteriosus	2/0.20	2/0.37
Hypoplastic left heart syndrome	2/0.20	2/0.37
Other	6/0.60	5/0.92

DISCUSSION

Congenital heart diseases are predominantly multifactorial and rank first as the most common congenital anomaly worldwide.[1] Fetal echocardiography performed by experienced individuals is highly valuable for detecting structural cardiac anomalies. In pregnancies considered at risk for CHD, fetal echocardiography should be part of the prenatal screening between the 18th and 22nd weeks.[5] Although the mean gestational week in our study was 23 weeks, we evaluated most of the cases during the period of optimal imaging. Maternal, fetal, and familial risk factors constitute the three main categories for fetal echocardiography indications.[9] According to the American Heart Association's Fetal Heart Disease Diagnosis and Treatment Guidelines in 2014, a risk of CHD above 2% is considered high-risk, a risk between 1% and 2% low-risk, and a risk of CHD at 1% or below imposes no indication.[10] During routine practice, pregnant women in the high-risk group are usually referred by obstetricians for fetal echocardiography evaluation. However, studies evaluating pregnant women without any risk factors or with low-risk factors have found cardiac anomalies in the range of 2.7% to 4.9%.[5,11,12] In our series, 4.92% of cases were diagnosed with CHD in the low-risk group, consistent with the literature. The most commonly observed cardiac anomaly in both high and low-risk groups in prenatal evaluations is VSD.[7-8,13] In our study, VSD prevalence was 8.2%, similar to the literature. Early diagnosis of patients with a large VSD can benefit surgical planning. Maternal chronic or systemic diseases increase the fetal anomaly risk, leading to a higher prevalence of CHD.[14] The diagnosis of complete AV block in one fetus and Sjögren's syndrome in the mother of another fetus after the diagnosis of complete AV block support this observation. Both fetuses underwent epicardial pacemaker implantation in the postnatal period. In the study by Özbarlas et al., metabolic disorders in the mother, the presence of CHD in previous pregnancies or children, and non-cardiac fetal anomalies were the most common risk factors.[11] In our research, among the risk factors, the presence of chronic diseases in the mother, dysmorphic findings and hyper-echoic foci in the heart, and a history of CHD in the mother or previous pregnancies were the most common. Boughman et al.'s study showed that although different types of CHD vary, families with CHD history have a higher risk for children with CHD than the general population.[15] Among 2102 infants with cardiovascular disease, 13% had reported chromosomal abnormalities. In another study, 28% of cases with detected cardiac anomalies during the intrauterine period had co-existing chromosomal anomalies, which increased in cases with non-cardiac anomalies.[16,17] In our study, three of the cases with karyotype examination had Trisomy 21 (Complete AVSD), two had 22q11 micro-deletion (Di George syndrome; tetralogy of Fallot), and one had a 7q11.23 deletion with Williams syndrome. Some medications used by pregnant women pose a risk for the development of CHD.10 In particular, a pregnant woman using an ACE inhibitor (enalapril) had a fetus with a large secundum ASD and a large PDA with accompanying hydronephrosis. Additionally, approximately 70% of all CHD consists of cardiac anomalies that do not have a syndromic clinic alone, confirming that the etiopathogenesis is multifactorial in a genetic cause absence.[18] In our study, isolated cardiac malformations were found in 7% of patients diagnosed with CHD in the postnatal period. According to data from the European Surveillance of Congenital Anomalies and Twins (EUROCAT) between 2004 and 2010, in 16,791 patients with isolated CHD, 30.3% had isolated CHD.[19] In the study by Best et al., 82.5% out of 5070 patients had isolated CHD, 5.7% had structural abnormalities with accompanying cardiac anomalies, and 11.9% had genetic or chromosomal abnormalities.[20]

CONCLUSION

We conclude that significant cardiac anomalies, while surely may be present in pregnancies deemed high-risk by the perinatology department, can also present in low-risk fetuses that raise suspicion for CHD in the second trimester.

Our study's results are consistent with the literature, demonstrating that fetal echocardiography has significant potential for early diagnosis of CHD, and increasing the number of experienced experts and centers that include fetal echocardiography in routine prenatal screenings will play a substantial role in reducing mortality and morbidity rates related to CHD.

Limitations

The most significant limitation of our study is the limited sample of patients at one center, which may limit the generalizability of these results. Different results are possible in diverse geographical locations or with other patient groups. Multi-center studies with extensive case series and increased availability of postnatal echocardiographic evaluations will play a crucial role in the early detection of accurate diagnoses through fetal echocardiography, leading to reduced mortality and morbidity rates.

Ethical approval

This study has been approved by the Dokuz Eylül University Non-Interventional Clinical Research Ethics Committee (approval date 08/05/2019, number 2019/12-19). Written informed consent was obtained from the participants.

Author contribution

Surgical and Medical Practices: KY, MK, NÜ; Concept: CKZ, OT; Design: KY, CKZ; Data Collection or Processing: OT, HZG, VÇ, YSB; Analysis or Interpretation: HEB, YDA, HB; Literature Search: HEB, YDA, YSB; Writing: KY. All authors reviewed the results and approved the final version of the article.

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Conflict of interest

The authors declare that there is no conflict of interest.

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