



# Evaluation of The Frequency and Types of Structural Heart Disease in Fetuses of Pregnant Women According to Risk Groups by Fetal Echocardiography

## Gebelerin Risk Gruplarına Göre Fetüslerindeki Yapısal Kalp Hastalığı Sıklığı ve Tiplerinin Fetal Ekokardiyografi Tetkiki ile Değerlendirilmesi

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### Abstract

**Aim:** The aim of this study is to evaluate the frequency of congenital heart diseases (CHD) encountered in low-risk and high-risk pregnant women by fetal echocardiographic (FE) examination.

**Material and Method:** The records of 855 pregnant women with a gestational week greater than 16 who applied to the pediatric cardiology outpatient clinic of our hospital between July 2019-October 2021 and underwent FE were analyzed retrospectively.

**Results:** CHD was detected in 109 (12.7%) of 855 pregnant women who were referred to our center and underwent FE examination. Frequency of CHD was given according to risk groups. The rate of CHD in patients in the high-risk group was 15.2%, while it was 9% in patients in the low-risk group ( $p=0.008$ ). Significant CHD was 6.2% in the high-risk group versus 2.7% in the low-risk group ( $p=0.016$ ). The most common structural cardiac anomaly in FE examination was ventricular septal defect (38.5% in 42 fetuses), and the second most common cardiac anomaly was atrioventricular septal defect (18.3% in 20 fetuses).

**Conclusion:** We found a higher rate of CHD in pregnant women in the high-risk group than in the low-risk group and especially significant CHD was more common in pregnant women in the high-risk group. Therefore, we strongly recommend performing FE examination, especially in high-risk pregnant women.

**Keywords:** Fetal echocardiography, congenital heart defect, fetuses

### Öz

**Amaç:** Bu çalışmanın amacı düşük riskli ve yüksek riskli gebelerde karşılaşılan konjenital kalp hastalıkları (KKH) sıklığının fetal ekokardiyografi (FE) tetkiki ile araştırılmasıdır.

**Gereç ve Yöntem:** Temmuz 2019-Ekim 2021 tarihleri arasında hastanemiz çocuk kardiyoloji polikliniğine başvuran ve FE uygulanan gestasyonel haftası 16 dan büyük 855 gebenin kayıtları geriye dönük olarak incelendi.

**Bulgular:** Çalışma yaptığımız merkezimize yönlendirilerek FE incelemesi yapılan 855 gebenin 109'unda (%12,7) KKH saptandı. KKH sıklığı risk gruplarına göre verildi. Başvuru nedenlerine göre yüksek riskli grupta yer alan hastalarda DKH'nın oranı %15,2 iken düşük riskli gruptaki hastalarda %9 olarak tespit edildi ( $p=0,008$ ). Önemli DKH yüksek riskli grupta %6,2 iken düşük riskli grupta %2,7 idi ( $p=0,016$ ). Fetal ekokardiyografi incelemesinde en sık rastlanan kardiyak anomali ventriküler septal defekt (42 fetusta %38,5) ve ikinci sıklıkta tespit ettiğimiz kardiyak anomali ise atrioventriküler septal defekt idi (20 fetusta %18,3).

**Sonuç:** Yüksek risk grubundaki gebelerde düşük risk grubundakilere göre daha yüksek oranda KKH saptandı ve özellikle önemli düzeydeki KKH yüksek risk grubundaki gebelerde daha sık oranda mevcuttu. Bu nedenle özellikle yüksek riskli gebelerde FE incelemesi yapılmasını şiddetle tavsiye ediyoruz.

**Anahtar Kelimeler:** Fetal ekokardiyografi, konjenital kalp defekti, fetüs



## INTRODUCTION

Examination of the fetal heart and cardiovascular system has improved significantly in the last 25-30 years as a result of technological development in imaging systems.<sup>[1]</sup> Thanks to fetal echocardiography (FE), congenital heart diseases (CHD) can be detected in the prenatal period and possible mortality and morbidity can be prevented by giving birth in an appropriate medical center where it can be intervened. In addition fetal arrhythmias can be diagnosed in FE and medical treatment can be performed in the antenatal period.

The incidence of congenital heart diseases (CHD) has been reported to be 6-12 per 1000 live births.<sup>[2,3]</sup> It is known that the incidence of CHD increases due to various maternal, hereditary and fetal reasons. Pregnancies can be divided into high-risk and low-risk in terms of CHD risk, according to the application indications for FE. Accordingly, those with an indication for absolute FE (estimated CHD risk >2%) are classified as high risk and those with an estimated CHD rate <2% are classified as low risk (**Table 1**).<sup>[1]</sup>

**Table 1.** Common Indications for Referral for Fetal Echocardiogram<sup>[1]</sup>

Indications with higher risk profile (estimated >2% absolute risk)
Maternal pregestational diabetes mellitus
Diabetes mellitus diagnosed in the first trimester
Maternal phenylketonuria (uncontrolled)
Maternal autoantibodies (SSA/SSB+)
Maternal medications
ACE inhibitors, Retinoic acid, NSAIDs in third trimester
Maternal first trimester rubella infection
Maternal infection with suspicion of fetal myocarditis
Assisted reproduction technology
CHD in first degree relative of fetus (maternal, paternal or sibling with CHD)
First or second degree relative with disorder with Mendelian inheritance with CHD association
Fetal cardiac abnormality suspected on obstetrical ultrasound
Fetal extracardiac abnormality suspected on obstetrical ultrasound
Fetal karyotype abnormality
Fetal tachycardia or bradycardia, or frequent or persistent irregular heart rhythm
Fetal increased NT >95% ( $\geq 3$ mm)
Monochorionic twinning
Fetal hydrops or effusions
Indications with lower risk profile (estimated >1% but <2% absolute risk)
Maternal medications
Anticonvulsants, Lithium, Vitamin A, SSRIs (only paroxetine), NSAIDs in first/second trimester
CHD in second degree relative of fetus
Fetal abnormality of the umbilical cord or placenta
Fetal intra-abdominal venous anomaly
Not indicated ( $\leq 1\%$ risk)
Maternal gestational diabetes mellitus with HbA1c <6%
Maternal medications
SSRIs (other than paroxetine), Vitamin K agonists (Coumadin), although fetal survey is recommended
Maternal infection other than rubella with seroconversion only
Isolated CHD in a relative other than first or second degree
ACE, angiotensin-converting enzyme; CHD, congenital heart disease; HbA1c, hemoglobin A1c; NSAID, nonsteroidal anti-inflammatory drug; NT, nuchal translucency; SSRI, selective serotonin reuptake inhibitor.

In our study, we aimed to investigation of the frequency of congenital heart diseases (CHD) encountered in low-risk and high-risk pregnant women by fetal echocardiography (FE) examination.

## MATERIAL METHOD

Ethics committee approval was obtained from Ministry of Health and the local Ethics Committee (Decision No: 2021-10/13). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

The records of 855 pregnant women with a gestational week greater than 16 who applied to the pediatric cardiology outpatient clinic of our hospital between July 2019 and October 2021 and underwent FE were analyzed retrospectively. Pregnant women were referred by the obstetricians and radiology specialists in our hospital and surrounding hospitals for FE examination for various reasons, such as suspicion of CHD in obstetric ultrasonography or inability to clearly see the fetal heart. Echocardiography measurements of the patients were performed by the same pediatric cardiologist using Vivid S60N (GE Gingmed Ultrasound AS Strandpromenaden 45, 3191 Horten, NORWAY) device and 1.5-6 MHz C 1-6 D Convex probe. 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. In accordance with the segmental approach; systemic and pulmonary venous connections; atrium and ventricular morphology (including the ratio of both atrium and ventricular cavities, wall thicknesses of the ventricles, anatomy of the atrial and ventricular septum); atrioventricular and semilunar valve morphology and size; The origin, size and positional relationships of the aorta and pulmonary artery; and the aortic and ductal arches were examined. AV valves, aortic and pulmonary valves, ductal and aortic arch velocities were recorded by pulsed Doppler examination. Cardiac rhythm was examined using two-dimensional, M-mode and pulsed Doppler methods. All echocardiographic examinations were performed according to the 2014 American Heart Association guidelines.<sup>[1]</sup>

Pregnant women with a CHD risk above 2% in the AHA guideline were in the high-risk group, while pregnant women with a CHD risk below 2% were classified as low-risk (**Table 1**).<sup>[1]</sup>

Structural cardiac anomalies detected in FE were divided into three groups according to the classification created by Wren et al and Hunter et al. (**Table 2**).<sup>[2,4]</sup>

In our study, the results of pregnant women in whom we detected fetal arrhythmia or who had covid 19 infection were also included.

**Table 2.** Current classification system in pediatric cardiology for structural heart diseases.<sup>[2,4]</sup>

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
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)
Minor (no intervention- four chambers and four valves)	includes mainly small ventricular septal defect, less severe aortic stenosis, and pulmonary stenosis

### Statistical Analysis

Statistical analysis of the study was performed using the Statistical Package for the Social Sciences (SPSS) for Windows version 20.0 package program. The expression n (%) was used for categorical variables, and for continuous variables, the mean±SD (standard deviation) values were used if they were compatible with the normal distribution. If they do not, the median (lower-upper limit) was used. Descriptive analysis was used in the analysis of the distribution and frequency of the data, and Chi-Square test was used in comparing two independent groups in frequency data. Mann-Whitney U test was used to compare two independent groups that were not normally distributed. Statistical significance was inferred at  $p < 0.05$ .

### RESULTS

The mean age of the pregnant women was  $29.1 \pm 4.8$  years and the mean week of gestation was  $25.2 \pm 5.7$  weeks. FE examination was performed 1090 times in 855 pregnant women who applied to our outpatient clinic (620 pregnant women once and 235 pregnant women twice). While 137 of the pregnant women applied to our polyclinic voluntarily, 718 pregnant women were consulted by obstetricians and radiology specialists (**Table 3**).

**Table 3.** Demographic findings of pregnant women

Age (Year) Mean±SD	29.1±4.8
Pregnancy week (Week) Mean±SD	25.2±5.7
Number of pregnant women who applied voluntarily (n/N; %)	137/855; 16%
Number of pregnant women consulted by obstetricians and radiology specialists (n/N; %)	718/855; 84%
Number of high-risk pregnancies (n/N; %)	520/855; 61%
Number of low-risk pregnancies (n/N; %)	335/855; 39%

Fetal echocardiography examination was repeated in 235 pregnant women with unclear images (due to maternal obesity or fetal position mismatch), complex and significant heart disease or arrhythmia.

Four patients with hypoplastic left heart syndrome (HLHS) and one tricuspid atresia underwent medical abortion; Except for the aborted fetuses, the findings in other infants with CHD detected in FE were confirmed by

postnatal transthoracic echocardiography. In the postnatal transthoracic echocardiography examination of three fetuses with small ventricular septal defect (VSD) in FE examination, it was observed that VSD disappeared. All other CHD detected in FE examination were also present in postnatal transthoracic echocardiography examination. Postnatal transthoracic echocardiography was performed in many babies who did not have CHD in FE examination, and CHD was not detected in any of them.

According to FE indications,<sup>[1]</sup> in high-risk pregnant women; Pregestational diabetes (4.1%) was the most common maternal indication, CHD in parents and siblings (13.9%) was the most common hereditary reason, and fetal cardiac anomaly suspected in obstetric ultrasonography (24%) was the most common fetal reason. In the low-risk group, advanced maternal age (15.4%) and inability to clearly evaluate the fetal heart in obstetric ultrasonography (11.5%) were the most common reasons for admission. In the high-risk group, the highest rate of CHD was detected in 9 (50%) of 18 fetuses with fetal karyotype anomaly (7 of 10 fetuses with Down syndrome [5 AVSD, 1 VSD, 1 tetralogy of Fallot], two of four fetuses with DiGeorge syndrome [2 truncus arteriosus]) and in 47 (22.9%) of 205 fetuses with suspected fetal cardiac anomaly in obstetric ultrasonography. In the low-risk group, CHD was detected in 5 (12.8%) of 39 fetuses with anomaly in the umbilical cord or placenta, and in one (12.5%) of 8 pregnant women who used anticonvulsants, SSRI and NSAID in the first trimester (**Table 4**).

CHD was detected in 109 (12.7%) of 855 pregnant women who underwent FE. The rate of CHD in patients in the high-risk group was 15.2%, while it was 9% in patients in the low-risk group (0.008). Significant CHD was 6.2% in the high-risk group versus 2.7% in the low-risk group (0.016). There was no statistical difference between the two groups in terms of the incidence of complex and minor CHD (**Table 5**).

The most common structural cardiac anomaly in FE examination was VSD (42 of 109 fetuses with CHD; 38.5%), the second most common cardiac anomaly was AVSD (20 of 109 fetuses with CHD; 18.3%). Complex cardiac anomalies were found in 43 (30.5%) of 109 fetuses with CHD, significant cardiac anomalies in 41 fetuses (37.6%) and minor cardiac anomalies in 25 fetuses (22.9%) (**Table 6**).

**Table 4.** Distribution of structural cardiac heart disease ratios in high-risk and low-risk pregnancies<sup>(1)</sup>

High-risk group	n	CHD n (%)
<b>Maternal indications</b>		
Maternal pregestational diabetes mellitus	35	2 (5.7)
Diabetes mellitus diagnosed in the first trimester	3	0 (0)
Maternal phenylketonuria (uncontrolled)	2	0 (0)
Maternal autoantibodies (SS-A ve SS-B)	2	0 (0)
ACE inhibitors-Retinoic acid and NSAIDs in third trimester	18	1 (5.6)
Maternal first trimester rubella infection	1	0 (0)
Maternal infection with suspicion of fetal myocarditis	12	0 (0)
Assisted reproduction technology	14	0 (0)
<b>Familial indications</b>		
CHD in first degree relative of fetus (maternal, paternal or sibling with CHD)	119	10 (8.4)
First or second degree relative with disorder with Mendelian inheritance with CHD association	4	0 (0)
<b>Fetal indications</b>		
Fetal cardiac abnormality suspected on obstetrical ultrasound	205	47 (22.9)
Fetal extracardiac abnormality suspected on obstetrical ultrasound	35	6 (17.1)
Fetal tachycardia or bradycardia, or frequent or persistent irregular heart rhythm	20	1 (5)
Fetal karyotype abnormality	18	9 (50)
Fetal increased NT >95% (≥3 mm)	6	2 (33)
Monochorionic twinning	2	0 (0)
Fetal hydrops or effusions	24	2 (8.3)
<b>Total (High-risk group)</b>	<b>520</b>	<b>79 (15.2)</b>
<b>Low-risk group</b>		
Maternal use of anticonvulsants, SSRIs (only paroksetin) and NSAIs in the first trimester	8	1 (12.5)
CHD in second degree relative of fetus	27	2 (7.1)
Fetal abnormality of the umbilical cord or placenta	39	5 (12.8)
Maternal infection other than rubella with seroconversion only	15	1 (6.7)
Failure to clearly evaluate the fetal heart in obstetric ultrasonography	98	8 (8.2)
Maternal age > 35 years	132	12 (9.1)
Multiple pregnancies other than monochorionic twinning	16	1 (6.3)
<b>Total (Low-risk group)</b>	<b>335</b>	<b>30 (9)</b>
<b>Total (High-risk and low-risk group)</b>	<b>855</b>	<b>109 (12.7)</b>

CHD, congenital heart disease; SS-A, anti-Sjögren's syndrome-related antigen A; SS-B, anti-Sjögren's syndrome type B; ACE, angiotensin-converting enzyme; NSAID, nonsteroidal anti-inflammatory drug.

**Table 5.** Distribution of structural cardiac heart disease types in high-risk and low-risk pregnancies.

	High-risk n/n (%)	Low-risk n/n (%)	Total n/n (%)	p
Complex	31/520 (6)	12/335 (3.6)	43/855 (5)	0.091
Significant	32/520 (6.2)	9/335 (2.7)	41/855 (5)	0.016
Minor	16/520 (3)	9/335 (2.7)	25/855 (2.9)	0.625
Total CHD	79/520 (15.2)	30/335 (9)	109/855 (12.7)	0.008

CHD, congenital heart disease.

Intracardiac echogenic focus was present in 158 (18.5%) of 855 pregnant women who underwent FE examination, and the majority (80.4% in 127 pregnant women) comprised the echogenic focus within the left ventricle. While intracardiac focus was detected in 101 (19.4%) of 520 high-risk pregnant women, intracardiac echogenic focus was found in 57 (17%) of 335 low-risk pregnant women ( $p=0.387$ ). CHD was detected in 21 (13.3%) of 158 fetuses with intracardiac echogenicity, and 88 (12.6%) of 607 fetuses without intracardiac echogenicity were found ( $p=0.826$ ). CHD was found in 15 (14.9%) of 101 fetuses in the high-risk group with intracardiac echogenicity, and in 6 (10.5%) of 57 fetuses in the low-risk group with intracardiac echogenicity ( $p=0.442$ ).

We did not detect CHD in any of the 12 pregnant women who had covid 19 infection. Two had mild sinus tachycardia. There was no any cardiac problem in the postpartum controls.

**Table 6.** Distribution of structural heart diseases detected as a result of fetal echocardiography

CHD	n	%
<b>Complex</b>		
AVSD	20	18.3
HLHS	7	6.5
Truncus arteriosus	6	5.5
Tricuspid atresia	5	4.6
DORV + TGA	2	1.8
Ebstein abnormality	1	0.9
DILV	1	0.9
TAPVR	1	0.9
Total (Complex)	43	39.5
<b>Significant</b>		
Large VSD (requiring operation)	20	18.3
TGA	6	5.5
Critical PS	5	4.6
Tetralogy of Fallot	5	4.6
Coarctation of aorta	3	2.8
Critical AS	1	0.9
DORV	1	0.9
Total (Significant)	41	37.6
<b>Minor</b>		
Small VSD	22	20.2
Less severe PS	2	1.8
Less severe AS	1	0.9
Total (Minor)	25	22.9
<b>Total CHD (Complex + Significant + Minor)</b>	<b>109</b>	<b>100</b>

CHD, congenital heart disease; AVSD, atrioventricular septal defect; HLHS, hypoplastic left heart syndrome; DORV, double outlet right ventricle; TGA, transposition of great arteries; DILV, double inlet left ventricle; TAPVR, total anomalous pulmonary venous connection; VSD, ventricular septal defect; PS, pulmonary stenosis; AS, aortic stenosis.



Cardiac arrhythmia was detected in 20 fetuses. Fetal supraventricular tachycardia (SVT) was found in 12 fetuses, premature atrial and ventricular beats were found in 4 fetuses, and sinus tachycardia and sinus bradycardia were found in two fetuses each.

## DISCUSSION

Most of the newborns with CHD can be detected with a high accuracy in the prenatal period by FE.<sup>[5,6]</sup> Therefore, it is very important which pregnant women need FE examination. Tegnander et al.<sup>[3]</sup> found CHD with a rate of 14.6% in the prenatal and postnatal period in their study consisting of 29460 fetuses. In various studies on FE in the literature, fetal CHD is present at different rates such as 4.9%, 11.1%, 2.7% and 1.9%.<sup>[6-9]</sup> In studies conducted in our country, it was reported that CHD was found at rates such as 13.1%, 5.6%, 9.4%, 13.3% and 7% as a result of fetal echocardiography.<sup>[10-14]</sup> In our study, we found the rate of CHD as 12.7% in 855 fetuses. Since the rates of consanguineous marriages differ between countries, the incidence of genetically inherited heart diseases may vary. Indications can be chosen differently when referring pregnant women to FE. Finally, the knowledge and skills of obstetricians and radiology specialists who send patients for FE examination as a result of obstetric ultrasonography examination may be different. For all these reasons, we think that the rates of CHD detected in FE may have been reported differently.

There are quite different publications regarding the incidence of CHD in high and low risk pregnant women who underwent FE. Hallioğlu et al.<sup>[10]</sup> reported a rate of 13.3% (complex CHD 5.1%, significant CHD 2.3% and minor CHD 5.9%) in the high-risk group and 16.3% (complex CHD 6.1%, significant CHD 2.8%, and minor CHD 7.4%) in the low-risk group. Özbarlas et al.<sup>[11]</sup> reported a rate of 7.8% (complex CHD 4.1%, significant CHD 2.3%, and minor CHD 1.4%) in the high-risk group and 2.7% (complex CHD 0.6%, significant CHD 0.8%, and minor CHD 1.3%) in the low-risk group. In most of the generally reported publications, the most common CHD detected in FE was reported as VSD and AVSD.<sup>[7,10,11,13,15,16]</sup> In our study, we also had a statistically significantly higher rate of CHD in the high-risk group (15.2%) than in the low-risk group (9%). Likewise, we found that the rate of complex CHD (6%) and significant CHD (6.2%) in the high-risk group were statistically significantly higher than the rate of complex CHD (3.6%) and significant CHD (2.7%) in the low-risk group. The most common CHD detected was VSD with a rate of 38.5% and AVSD with a rate of 18.3%.

If fetal chromosome testing reveals a genetic mutation, deletion, trisomy or aneuploidy, the risk of congenital anomalies is generally high and FE should be performed in addition to detailed obstetric ultrasonography examination. Likewise, increased nuchal thickness also increases the risk, especially in terms of Down syndrome.<sup>[17]</sup> In our study, half of 18 fetuses with fetal karyotype anomaly had CHD. Of the fetuses with karyotype anomaly, 10 had Down syndrome and

four had DiGeorge syndrome. CHD was detected in 7 of 10 fetuses with Down syndrome (5 AVSD, 1 VSD, 1 tetralogy of Fallot). Truncus arteriosus was detected in half of four fetuses with DiGeorge syndrome. CHD was detected in 2 of 6 patients whose nuchal translucency was above the 95% percentile (both were AVSD and prenatal diagnosis could not be made because the family did not allow amniocentesis, but they were found to have Down syndrome after birth).

In the presence of extracardiac anomaly in obstetric ultrasonography examination, CHD has been reported with a rate of 20-45% depending on the type of malformation and the gestational week at which FE examination was performed.<sup>[18,19]</sup> In our study, we found CHD in 6 (17.1%) of 35 patients with extracardiac anomalies (two each, central nervous system, gastrointestinal system and musculoskeletal system anomalies). Interestingly, five of the six patients had complex CHD and one had significant CHD. This shows us that in the presence of extracardiac malformation, accompanying cardiac anomalies can be severe; and in this respect, it is necessary to be more careful in terms of CHD in pregnancies with extracardiac anomaly and FE echocardiography should be performed.

There are different reports in the literature regarding CHD rates detected as a result of FE performed due to suspected cardiac anomaly in obstetric ultrasonography (48.7%, 27.7%, 32%, 16% and 68%).<sup>[8,10,11,20,21]</sup> In our study, we detected 22.9% CHD in 45 out of 205 fetuses, who were suspected of fetal cardiac anomaly in the obstetric ultrasonography examination and performed FE examination. Intracardiac focus was present in 189 (70%) of the remaining fetuses and therefore they were consulted. We can attribute the great difference in this regard to the fact that the knowledge and skills of the obstetricians and radiologists who perform the obstetric ultrasonography examination and the pediatric cardiologists who perform the FE examination may differ. In addition, another reason may be the different levels of accessibility of centers that can perform FE.

CHD was detected in 8 (8.2%) of 98 fetuses who were consulted to our outpatient clinic because the fetal heart could not be seen clearly in obstetric ultrasonography. One of them was complex and important cardiac anomalies such as tricuspid atresia and the other tetralogy of Fallot. Therefore, if the fetal heart cannot be seen clearly on obstetric ultrasonography, consultation from a fetal echocardiography specialist should be sought. By providing continuous training to all obstetricians and radiology specialists who perform obstetric ultrasonography examination, on how to evaluate the fetal heart, it will be possible to diagnose babies with CHD more frequently in the prenatal period.

CHD in the mother, father or siblings may increase the likelihood of CHD in the next pregnancy. CHD is seen at 2-3% in the baby to be born when the father has CHD, 2-6% when the siblings have CHD.<sup>[22]</sup> The risk of recurrence of nonsyndromic, nonchromosomal CHD is >2 times as high if the mother is affected versus the father or a sibling.<sup>[22,23]</sup> In our study, we

found CHD in four (5.7%) of 70 fetuses with siblings with CHD, in one (5.3%) of 19 fetuses with fathers with CHD, and in five (16.6%) of 30 fetuses with CHD in their mothers.

Advanced maternal age ( $\geq 35$  years) is accepted in the low-risk group for CHD.<sup>[3]</sup> Best et al.<sup>[24]</sup> reported the rate of CHD in advanced age pregnancies as 0.99% and Özbarlas et al. (0%).<sup>[11]</sup> as a result of FE. Pierpoint et al.<sup>[25]</sup> found in their studies that chromosomal disorders was increased in pregnancies at advanced ages and the probability of CHD was high in pregnancies with chromosomal disorders. In our study, 12 (9.1%) of the fetuses of 132 pregnant women over 35 years of age had CHD. Seven of these patients had Down syndrome. These data show us that the risk of chromosomal disorders such as Down syndrome, increases in advanced age pregnancies, and therefore, caution should be taken in terms of CHD.

Today, Covid 19 infection is seen as a pandemic all over the world. It is very severe in pregnant women and can cause problems in the cardiovascular system as in many systems. Myocarditis is also a complication seen in Covid 19 infection.<sup>[26]</sup> There are a few published cases of COVID-19 occurring during pregnancy and due the possibility of mother-fetal vertical transmission. In our study, we performed FE examination to 12 pregnant women with Covid 19 infection; two of them had mild sinus tachycardia and none of them had decreased systolic functions, insufficiency of atrioventricular and semilunar valves, pericardial fluid and CHD. All of the pregnancies resulted in live births and there was no problem that required hospitalization afterwards.

In our study, we found a similar rate of intracardiac echogenic focus in high-risk and low-risk groups; we found no difference in the frequency of CHD between those with and without an intracardiac echogenic focus. In addition, we did not detect any difference in the frequency of CHD in high-risk or low-risk groups with an intracardiac focus.

Fetal arrhythmia may develop due to ischemia, inflammation, electrolyte disturbances, stress, structural cardiac anomalies and gene mutations, and these patients present as fetal tachycardia, bradycardia or arrhythmia in obstetric examination.<sup>[27]</sup> Fetal arrhythmias are found in 2% of normal pregnancies and can be detected up to 16.6% in high-risk pregnancies.<sup>[28,29]</sup> Antiarrhythmic drugs such as digoxin, sotalol, and flecainide are administered alone or in combination to pregnant women with fetal supraventricular tachycardia.<sup>[30]</sup> In our study, fetal arrhythmia was present in 20 (2.3%) of 855 pregnant women with a mean gestational week of 36 (min 33- max 39). While 12 (2.3%) of 520 high-risk pregnant had fetal arrhythmia, 8 of (2.4%) of 335 low-risk pregnant had fetal arrhythmia. We gave medical treatment to 12 pregnant women who were found to have fetal SVT. Eight pregnant women were given digoxin and one pregnant woman sotalol. Three pregnant women whose tachycardia did not improve with single treatment were given digoxin + sotalol treatment. Ten of the patients recovered during the antenatal period and two continued to receive postnatal treatment.

## CONCLUSION

We performed FE examination on pregnant women who were consulted with various indications. As a result we found a higher rate of CHD in pregnant women in the high-risk group than in the low-risk group and especially significant CHD was more common in pregnant women in the high-risk group. Therefore, we strongly recommend performing FE examination, especially in high-risk pregnant women.

The most important limitation of our study was that autopsy could not be performed due to the fact that families did not allow medical abortion due to their socio-cultural structure. In addition, the number of our cases was insufficient for epidemiological data. Therefore, multicenter studies with higher numbers of cases will enable the prediction of high and low risk pregnancies in terms of CHD.

## ETHICAL DECLARATIONS

**Ethics Committee Approval:** Ethics committee approval was obtained from Ministry of Health and the local Ethics Committee (Decision No: 2021-10/13).

**Informed Consent:** Because the study was designed retrospectively, no written informed consent form was obtained from patients.

**Referee Evaluation Process:** Externally peer-reviewed.

**Conflict of Interest Statement:** The authors have no conflicts of interest to declare.

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**Author Contributions:** All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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