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Original Article

Is Multiple Pregnancy Really a Risk Factor? The Results of Fetal Echocardiography in a Tertiary Care Center

Çoğul Gebelik Gerçekten Bir Risk Faktörü mü? Üçüncü Basamak Merkezde Fetal Ekokardiyografi Sonuçları

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ABSTRACT

Objective: The aim of this study was to analyze the frequency and results of congenital heart defects (CHD) in multipl pregnancies by fetal echocardiography. Among these, to evaluate critical congenital heart diseases such as hypoplastic left heart syndrome, interrupted aorta, and pulmonary atresia etc that require care in a tertiary center.

Method: This retrospective cohort study was conducted in pregnant women who admitted for fetal echocardiography. The data of the pregnancy were obtained retrospectively from the hospital records. A total of 9,440 pregnant women were enrolled in this study between January 2016 and September 2019. Two hundred and forty-one of them were multiple pregnancies (232 twins, 7 triplets and 2 quadruplets).

Results: Congenital heart disease rate was 4.31% in singleton pregnancies and 8.7% in multiple pregnancies. The prevalence of CHD was significantly higher in multipl pregnancies (p=0.05). There was no statistically significant difference between the two groups with respect to rate of critical congenital heart disease (p=0.32).

Conclusion: Multiple pregnancies had increased congenital heart defect risk compared with singleton. Therefore, it is important to refer for fetal echocardiography when necessary. Fetal echocardiography is routinely recommended in high-risk pregnancies such as monocarionic twin pregnancies. However, in pregnant women without risk factors for CHD is also seen. Postnatal follow-up of congenital heart disease is important, and early diagnosis of these diseases with fetal echocardiography is important.

Keywords: Congenital heart defect, fetal echocardiography, multipl pregnancy

ÖZ

Amaç: Bu çalışmanın amacı, çoğul gebeliklerde doğumsal kalp hastalığı (DKH) sıklığını fetal ekokardiyografi ile değerlendirmek ve sonuçlarını incelemektir. Bunlar arasında hipoplastik sol kalp sendromu, kesintili aort ve pulmoner atrezi vb. gibi üçüncü basamak bir merkezde bakım gerektiren kritik DKH'yi değerlendirmektir.

Yöntem: Bu retrospektif kohort çalışması, fetal ekokardiyografi için başvuran gebelerde gerçekleştirildi. Gebelerin verileri geriye dönük olarak hastane kayıtlarından elde edildi. Ocak 2016 ile Eylül 2019 arasında toplam 9.440 gebe çalışmaya alındı. Bunların 241'i çoğul gebelikti (232 ikiz, 7 üçüz ve 2 dördüz).

Bulgular: Doğuştan kalp hastalığı oranı tekil gebelerde %4,31 ve çoğul gebelerde %8,7 idi. Çoğul gebeliklerde doğuştan kalp hastalığı prevalansı anlamlı olarak daha yüksekti (p=0,05). Kritik doğuştan kalp hastalığı oranı açısından iki grup arasında istatistiksel olarak anlamlı fark yoktu (p=0,32).

Sonuç: Çoğul gebelikler, tekil gebeliklere göre daha yüksek DKH riskine sahipti. Bu nedenle gerektiğinde fetal ekokardiyografiye başvurmak önemlidir. Monokariyonik ikiz gebelikler gibi yüksek riskli gebeliklerde rutin olarak fetal ekokardiyografi önerilmektedir. Ancak doğuştan kalp hastalıkları risk faktörü olmayan gebelerde de görülmektedir. Doğuştan kalp hastalığının doğum sonrası takibi önemlidir ve bu hastalıkların fetal ekokardiyografi ile erken teşhisi önemlidir.

Anahtar kelimeler: Doğumsal kalp hastalığı, fetal ekokardiyografi, çoğul gebelik

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INTRODUCTION

Congenital heart defects are the most common birth defects and the most important cause of anomaly-related mortality during infancy [1-3]. Recent developments in fetal echocardiography has made feasible and highly accurate prenatal diagnosis of congenital heart disease possible in appropriate settings [4,5].

Multiple births account for 1-2% of all pregnancies, and its incidence has been increasing gradually, possibly as a consequence of increased usage of assisted reproductive technologies [6]. The rate of congenital malformations was reported to be higher in twin pregnancies compared with single pregnancies [7-10]. Congenital heart defects are the most common congenital anomalies with an incidence rate of one in 8:1000 live births [2]. The incidence of congenital heart defects in multiple births was reported as one in 20:1000 live births [5]. Several studies reported 4 to 9-fold increased risk of heart malformations in monozygotic twin pregnancies [10-13].

This study aims to evaluate the prevalence of congenital heart defects in singleton versus multiple pregnancies. We also aimed to evaluate the type of congenital heart disease and the neonatal outcome in our cohort of patients.

MATERIALS and METHODS

The study was a retrospective analysis of pregnant patients referred to the pediatric cardiology unit of our hospital, from January 2016 to September 2019 for fetal echocardiography. The study was approved by the University of Health Sciences Turkey, İzmir Tepecik Training and Research Hospital Clinical Research Ethics Committee (approval number: 11/15, date: 14.09.2020. All participants had provided their written informed consent during the aforementioned time interval. For all cases, the following parameters were retrieved, and recorded from our database: the ages of the patients, gestational week, number of fetuses, chorionicity, fetal echocardiogram and postpartum echocardiography results. Infants of mothers with missing information were excluded. Cases who were diagnosed after the deadline of the study as patent foramen ovale and patent ductus arteriosus were not included. Data on chorionicity was based on the prenatal ultrasonographic diagnoses. Our primary outcome in this study was the total number of patients with congenital heart disease which were seen on fetal echocardiograms of multiple pregnancies. Secondary outcomes as the number of critical congenital heart disease in singleton and multiple pregnancies were also evaluated. The group of critical congenital heart diseases included hypoplastic left heart syndrome, common arterial trunk, coarctation of the aorta, interrupted aortic arch, pulmonary atresia with intact septum, tetralogy of Fallot, total anomalous pulmonary venous return, d-transposition of great arteries, tricuspid atresia, double outlet right ventricle, Ebstein's anomaly and single ventricle.

Fetal Echocardiography

Fetal echocardiographies were routinely performed on patients who applied to perinatology outpatient clinics. All of the fetal echocardiography examinations were performed by four experienced pediatric cardiologists in our center. Fetal echocardiographies were performed in all cases between 18 to 37 gestational weeks. Fetal heart scans were performed with the patients in supine position, and tilted 15º to the left. The study patients had a detailed transabdominal fetal echocardiography with a full assessment of cardiovascular structural anatomy and function according to the guidelines of the American Institute of Ultrasound in Medicine [14].

The following echocardiography machines were used.

Philips Affiniti 50 (Philips Healthcare, Andover, Netherlands) equipped with C5-1 MHz transabdominal curvilinear transducers or;

Philips Epiq C7 (Philips Medical Systems, Bothell, WA, USA; 2014) equipped with C5 MHz transabdominal curvilinear transducers.

A detailed and complete echocardiographic examination was performed in every case, including biometric measurements along with a thorough and sequential scanning and identification of each view including 4-chamber view, 3-vessel view, trachea and 3-vessel view, outflow tract view, and aortic and ductal arches view. All ultrasonographers strictly followed the standard guidelines for scanning and diagnosis of heart malformations.

Statistical Analysis

All statistical analyses were performed using SPSS 21.0 (SPSS Inc., Chicago, IL); $p<0.05$ was considered statistically significant. Continuous data were expressed as mean value ± standard deviation. Numbers and percentages of congenital heart lesions in singleton and

multiple pregnancy groups were calculated. Comparison between the two groups were performed using chi-square test.

RESULTS

Fetal echocardiography was performed in 9,440 cases including 241 multiple and 9,199 singleton pregnancies. The group of multiple pregnancies consisted of twin (96.3%), triplet (2.9%), and quadruplet (0.8%) pregnancies. The mean maternal age of the patients was 30.5±5.8 years (16-47 years), and the mean gestational age at the time of referral was 22.3±3.8 weeks. A total number of 418 cases with congenital heart defects including 397 singletons (4.31%). and 21 twins (8.7%) had been delivered during the study period: The prevalence of congenital heart defects was significantly higher in twin pregnancies (p=0.005). There was no statistically significant difference between the two groups with respect to rate of critical congenital heart disease (p=0.32). The most common cardiac lesion identified in both groups was ventricular septal defect. Cardiac lesions which were identified in singleton and twin pregnancies are summarized in Table 1, 2. The relation between chorionicity and the presence of congenital heart defects is shown in Table 3.

Trisomy 21 was detected in two cases with twin pregnancies and intrauterine death developed in 10 fetuses. Of the twins with prenatally identified congenital heart defects, 13 patients were born in our center. Prenatal diagnosis of twins using fetal echocardiography was all the same except in one case who had hypoplastic left heart syndrome which was originally had received

Table 1. Cardiac lesions identified in single pregnacy

CHD	**VSD**	**AVSD**	**CoA**	**HLHS**	**UH**	**DORV**	**TOF**	**ASD**	**VSD-PA**
n (%)	101 (1.1)	56 (0.6)	35 (0.4)	33 (0.4)	26 (0.3)	25 (0.3)	23 (0.2)	17 (0.2)	16 (0.2)
CHD	**PS**	**AS**	**TGA**	**TA**	**TAPVD**	**EA**	**EC**	**APV**	**Normal/Total**
n (%)	15 (0.2)	11 (0.1)	10 (0.1)	10 (0.1)	8 (0.1)	6 (0.1)	4 (<0.1)	1 (<0.1)	8,802 (95.7)/9,199 (100)

CHD: Congenital heart disease, VSD: Ventricular septal defect, AVSD: Atrioventricular septal defect, CoA: Coarctation of aorta, HLHS: Hypoplastic left heart syndrome, UH: Univentricular heart, DORV: Double outlet right ventricle, TOF: Tetralogy of Fallot, ASD: Atrial septal defect, VSD-PA: Pulmonary atresia with ventricular septal defect, PS: Pulmonary stenosis, AS: Aortic stenosis, TGA: Transposition of great arteries, EA: Ebstein's anomaly, TA: Truncus arteriosus, TAPVD: Total anomalous pulmonary venous return, APV: Aortopulmonary window, EC: Ectopia cordis

Table 2. Cardiac lesions identified in multipl pregnancy

CHD	**DCDA (n, %)**	**MCDA (n, %)**	**MCMA (n, %)**	**Twins (any chorionicity)**	**Triplet, quadriplet (n, %)**	**Total (n, %)**
VSD	5 (3.9)	1 (1.4)	2 (22.7)	-	1 (12.5)	9 (3.7)
HLHS	1 (0.8)	1 (1.4)	1 (11.1)	-	-	3 (1.2)
DORV	1 (0.8)	1 (1.4)	-	-	-	2 (0.8)
TOF	1 (0.8)	1 (1.4)	-	-	-	2 (0.8)
AVSD	2 (1.6)	-	-	-	-	2 (0.8)
PS	-	1 (1.4)	-	-	-	1 (0.4)
UH	-	1 (1.4)	-	-	-	1 (0.4)
AS	-	1 (1.4)	-	-	-	1 (0.4)
Normal	118 (92.2)	62 (89.9)	6 (66.7)	27	7 (87.5)	220 (91.4)
Total	128 (100)	69 (100)	9 (100)	27	8 (100)	241 (100)

CHD: Congenital heart disease, DCDA: Dichorionic, diamniotic, MCDA: Monochorionic/diamniotic, MCMA: Monochorionic-monoamniotic, VSD: Ventricular septal defect, HLHS: Hypoplastic left heart syndrome, DORV: Double outlet right ventricle, TOF: Tetralogy of fallot, AVSD: Atrioventricular septal defect, PS: Pulmonary stenosis, UH: Univentricular heart, AS: Aortic stenosis

Table 3. CCHD distribution in the groups

	CCHD (n)	**CHD (n)**	**p**	**Total CHD (n)**	**Total patient**
Single pregnacy	193 (2.09)	204 (2.21)	0.32	397 (4.31)	9199
Multipl pregnancies	8 (3.31)	13 (5.3)	0.32	21 (8.71)	241

CCHD: Critical congenital heart disease, CHD: Congenital heart disease

the diagnosis of single ventricle. Of these cases, one with unbalanced atrioventricular septal defect died due to sepsis, two cases with hypoplastic left heart syndrome exited after stage 1 repair.

DISCUSSION

In this retrospective-cohort study, the prevalence of congenital heart defects was significantly higher in multiple pregnancies when compared to singleton pregnancies. The rate of congenital heart defects was 8.7% in multiple and 4.31% in singleton pregnancies. Herskind et al. [15] studied 25-year data of 41,525 twin pregnancies in Denmark. In their study the prevalence of congenital heart defects was 1.4% in twin, and 0.87% in 74,773 singleton pregnancies, and the authors concluded that twin pregnancies increased the rate of congenital heart defects. In our study, the prevalence of congenital heart defects in twin pregnancies was higher than those reported in prior population- based studies. A possible explanation for this difference might be that our population consisted of patients who were referred to a tertiary care center- who had fetal echocardiography indications.

Best and Rankin [6] studied the prevalence of congenital heart defects in twin and singleton pregnancies in North England between 1998-2010, and found that congenital heart defects were significantly more prevalent in twin pregnancies with a rate of 1.3%, and congenital heart defects were more common in monochorionic twins compared to dichorionic twins. In our study, the prevalence rates of congenital heart defects were 11.7% in monochorionic and 10.1% in dichorionic twins. In a meta-analysis, Bahtiyar et al. [12] found that the prevalence of congenital heart defects in monochorionic/diamniotic gestations was nearly nine-fold higher and 40 patients with congenital heart defects were found in 830 twin pregnancies. The current study confirms that monochorionic/diamniotic twin pregnancies were associated with congenital heart defects which further supports the idea that fetal echocardiography should be necessary for all monochorionic/diamniotic twin pregnancies. Li et al. [16] showed that in 2 pairs of the twins, the two fetuses had the same kind of CHD. They also noted that of 12 patients, 4 were in high and 8 in low-risk categories. None of the twins in our study had the same heart disease.

There is no definite explanation why the prevalence of congenital heart defects is higher in multiple pregnancies. There are, however, possible explanations regarding genetic and hemodynamic aspects [17-19]. One theory suggests that the unequal division of cells in monozygotic twins as a possible explanation. Another possible explanation for this is that genetic basis of several cardiac anomalies may cause discordant manifestations in different patients. Hillebrand et al. [20] reported a case of twins with 22q11 deletion, one of them had congenital heart defects and other one aortic interruption, ventricular septal defect and atrial septal defect. Several studies have shown that multiple pregnancies significantly worsen the performance of ultrasound in pregnancy. In the study of Paladini et al. [21], diagnostic performance of fetal echocardiography in experienced center was good with a sensitivity of 88.8% and specificity of 99.8 percent.

Study Limitations

The current study has several limitations. We only studied fetal echocardiography records of our tertiary care center. Further work is required to establish the prevalence of multiple pregnancies and congenital heart defects in population-based studies. Another weakness of this study, is that we did not have information on whether the patient had used assisted reproductive technologies.

CONCLUSION

The main goal of the current study was to determine the prevalence of congenital heart defects in multiple pregnancies. This study has revealed that the risk of congenital heart defects increases in multiple pregnancies compared with singleton pregnancies. Our small sample size was also a limitation of this study.

Ethics

Ethics Committee Approval: The study was approved by the University of Health Sciences Turkey, İzmir Tepecik Training and Research Hospital Clinical Research Ethics Committee (approval number: 11/15, date: 14.09.2020).

Informed Consent: Since our study had a retrospective design, informed consent was not obtained from the patients.

Peer-review: Externally and internally peer-reviewed.

Author Contributions

Surgical and Medical Practices: T.D., A.R.B., H.G.P., A.Ş., N.N., C.K., Concept: T.D., B.G., C.K., Design: T.D., B.G., A.R.B., H.G.P., A.Ş., Data Collection and/or

Processing: T.D., A.R.B., H.G.P., A.Ş., C.K., Analysis and/or Interpretation: H.G.P., C.K., Literature Search: B.G., N.N., Writing: T.D., B.G., A.Ş.

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