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ORIGINAL ARTICLE

The Relationship Between Fetal Cardiac Echogenic Foci Detected in Fetal Echocardiography and Congenital Heart Diseases: A Cross-sectional Study

Fetal Ekokardiyografide Saptanan Fetal Kardiyak Ekojenik Odakların Konjenital Kalp Hastalıkları İle İlişkisi: Kesitsel Bir Çalışma

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ABSTRACT

Aim: To determine the prevalence of intracardiac echogenic focus and investigate the possible association of congenital heart diseases in risky pregnancies.
Methods: A total of 380 pregnant women in the 17th to 36th weeks of gestation were included in our study. The patients were classified as low-risk and high-risk groups according to various referral reasons such as any drug usage, presence of chromosomal or fetal anomalies, number and characteristics of previous pregnancies, congenital or acquired heart diseases in the family, and presence of family history.
Results: Based on the selective criteria 134 (35.26%) pregnant women were classified as the low-risk group while 246 (64.74%) pregnant were classified as the high-risk group. Maternal diabetes (13.16%) was the most common reason for referral in the high-risk group. However, in low-risk pregnancies, the lack of a good image of the fetal heart by ultrasound was the major reason for referral (21.05%). Intracardiac echogenic foci were detected in a total of 77 (20.26%) cases, 68 (50.75%) of whom were in the low-risk group and nine (3.66%) cases were in the high-risk group. Left ventricular echogenic foci were detected in 59 (44.03%) fetuses in low-risk pregnancies and four (1.63%) fetuses in high-risk pregnancies (p=0.001). Additionally, only one fetus in a low-risk pregnancy and one fetus in a high-risk pregnancy had echogenic foci in one of the ventricles with congenital heart diseases.
Conclusion: In conclusion, we found the prevalence of intracardiac echogenic foci in low-risk pregnancies as 50.75%, higher than in high-risk pregnancies. This can be attributed to ethnicity, tertiary hospital referrals, a relatively low number of patients, and other associated factors. Additionally, in our study, no correlation was found between congenital heart diseases and intracardiac echogenic foci in both low- and high-risk pregnancies.

Keywords: Congenital heart diseases, intracardiac echogenic focus, risky pregnancies

ÖZ

Amaç: Çalışmamızın amacı intrakardiyak ekojenik odak prevalansını belirlemek ve riskli gebeliklerde konjenital kalp hastalıklarıyla olası ilişkisini araştırmaktır.
Yöntem: Çalışmamıza 17-36. gebelik haftasında olan toplam 380 gebe dahil edildi. Hastalar herhangi bir ilaç kullanımı, kromozomal veya fetal anomalilerin varlığı, önceki gebeliklerin sayısı ve özellikleri, ailede konjenital veya edinilmiş kalp hastalıkları ve aile öyküsünün varlığı gibi çeşitli sevk nedenlerine göre düşük riskli ve yüksek riskli gruplar olarak sınıflandırıldı.
Bulgular: Seçici kriterlere göre 134 (%35,26) gebe düşük riskli grup olarak sınıflandırılırken, 246 (%64,74) gebe yüksek riskli grup olarak sınıflandırıldı. Yüksek risk grubunda en sık sevk nedeni maternal diyabet (%13,16) idi. Ancak düşük riskli gebeliklerde, ultrasonografi ile fetal kalbin iyi görüntülenmemesi sevk için en önemli nedendi (%21,05). Toplam 77 (%20,26) gebede intrakardiyak ekojenik odaklar tespit edildi, bunlardan 68 (%50,75) tanesi düşük risk grubunda ve 9 (%3,66) tanesi de yüksek risk grubundaydı. Düşük riskli gebeliklerde 59 (%44,03) fetüste ve yüksek riskli gebeliklerde 4 (%1,63) fetüste sol ventrikülde ekojenik odaklar tespit edildi (p=0,001). Ek olarak, konjenital kalp hastalığı tespit edilen düşük ve yüksek risk grubundaki birer fetüste sol ventrikülde yerleşimli ekojenik odaklar tespit edildi. Sonuç: Sonuç olarak, düşük riskli gebeliklerde intrakardiyak ekojenik odakların prevalansını %50,75 olarak bulduk ki bu yüksek riskli gebeliklere göre daha yüksekti. Bu durum; etnik kökene, üçüncü basamak hastane sevklerine, nispeten düşük hasta sayısına ve diğer ilişkili faktörlere bağlanabilir. Ek olarak, çalışmamızda, hem düşük hem de yüksek riskli gebeliklerde konjenital kalp hastalıkları ile intrakardiyak ekojenik odaklar arasında bir ilişki tespit edilmedi.

Anahtar Kelimeler: Riskli gebelikler, intrakardiyak ekojenik odak, konjenital kalp hastalığı

Introduction

Schechter et al. first described fetal intracardiac echogenic focus (ICEF) in 1987 (1). ICEF is a condition frequently encountered during routine fetal echocardiography (ECG) and can sometimes be a reason for referral for fetal ECG. ICEF is a small structure seen in the fetal heart with either an isolated or multiple echogenic foci that are as bright as bone (2). Also, during the routine fetal ECG, ICEF is found within the papillary muscles of the ventricles on a four-chamber view. Although its etiology is unknown, it is thought to occur due to a normal variant or increased mineralization in the development of the papillary muscle or chordae within the ventricle (2). Also, the study of Levy and Mintz suggested that ICEF may be incomplete fenestration of the chordae tendineae or papillary muscle (3). Additionally, Brown et al. identified

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fetuses with an echogenic focus with histologically clarified mineralization present in the papillary muscle in 1994 (4). In this way, many studies reported that ICEF is a benign variant with no clinical significance (5,6). Some of the studies conducted on this subject have reported that ICEF is a variation of normal development, while others have drawn attention to its relationship with chromosomal abnormalities and congenital heart diseases (7-10).

The reported incidence of ICEF varies between 0.5 and 20% with an overall frequency of 5.6% (11,12). On the other hand, the prevalence of ICEF also varies among races, ethnicities, and populations (7). Also, the incidence would depend on the reason for the ultrasound (US) referral. In patients at high risk for perinatal problems studies suggested a possible association of ICEF with fetal aneuploidy (7-10). Further studies showed that ICEF might be a benign finding in low-risk populations (13,14).

Many studies showed that ICEF is frequently found in the left ventricle neither than in the right ventricle with rare cases being bilateral (5,15)., Also, Wax and Philput, reported that the biventricular location of ICEF is associated with fetal aneuploidy in a high-risk population, not cardiac structural defects in 1998 (16). Also, Bronshtein and colleagues suggested that ICEF located in the right ventricle may be a signal of poor prognosis (17).

To shed light on this issue, in our study, ICEF and congenital heart diseases detected in high- and low-risk pregnant women undergoing fetal ECG in our hospital were investigated. The purpose of this study was to determine the prevalence of ICEF and to investigate the possible association of congenital heart diseases in low and high-risk pregnancies.

Materials And Methods

Study population

The study with a retrospective design was approved by the Medical Research Ethics Committee of the Medical School of Karamanoğlu Mehmetbey University (Date: 26.09.2024, decision no: 10-2024/01, and reg. no: E-11095095-050.04-216359). The study was performed under the 1961 Declaration of Helsinki and its later amendments. Written informed consent was obtained from all patients for the use of data from medical records.

This study is a retrospective research performed between January 2023 and September 2024. A total of 380 pregnant women between the 17th to 36th weeks of gestation were included in our study. The patients consisted of pregnant women referred by obstetricians due to various reasons classified as high-risk and low-risk groups (18). The study population was analyzed in detail for pregnancy history, reasons for referral to our clinic, any drug usage, presence of chromosomal or fetal anomalies, number and characteristics of previous pregnancies, congenital or acquired heart diseases in the family, and presence of family history. Also, all pregnant women were grouped as either high-risk or low-risk pregnancies according to these parameters. Also, echocardiographic confirmation was done in the babies after birth for congenital heart diseases.

Fetal echocardiography (ECG)

Fetal heart examinations were performed using a Philips Affiniti 50 (Philips Healthcare, Andover, Netherlands) ECG device with 2.5-5 MHz transducers by the same echocardiographic scanner. All fetal echocardiographic examinations were performed using standard techniques determining the fetal position and heart axis and providing Doppler and M-mode measurements (19,20). In all the cases, four-chamber views, outflow-tract views, three-vessel views, and aortic and ductal arch views were done. Fetal heart rate was noted and any arrhythmia was confirmed with M-mode imaging, color Doppler, and pulse-wave Doppler were used whenever necessary. All the images were recorded.

Statistical analysis

All statistical analyses were performed using the Statistical Package for Social Sciences (SPSS), version 16.0 software program(Chicago, IL, USA). Data in parametric tests were given as mean and ± standard deviation. Data were presented as percentage values. The chi-square test was used to compare parametric values between groups, and the student t-test was used for non-parametric data. A p-value of <0.05 was considered statistically significant.

Results

A total of 380 pregnant women were included in the study. The low-risk and high-risk pregnancy groups constituted under the criteria during referrals are seen in Table 1. In this way, 134 (35.26%) pregnant women were classified as the low-risk group while 246 (64.74%) pregnant were classified as the high-risk group. Maternal diabetes mellitus (13.16%), dysrhythmia

(5.26%), and a history of a previous child or fetus with extracardiac abnormality (8.42%) were the most common reasons for referral in the high-risk group. However, in low-risk pregnancies, the lack of a good image of the fetal heart by US was the major reason for referral (21.05%).

Table 1. Distribution of pregnant women by low-risk and high-risk factors

Risk Groups and Factors	n=380	%
1. Low-risk Group		
Lack of good image of the fetal heart by US	80	21.05
Suspicion of CHD during 2nd trimester by US	41	10.78
Self-referral	13	3.43
Total	134	35.26
2. High-Risk Group		
2. a. Maternal Factors		
Gestational DM	50	13.16
In vitro fertilization	18	4.75
Multiple pregnancies	14	3.68
Maternal use of medicine	11	2.89
Advanced maternal age	13	3.43
Maternal CHD	7	1.84
Maternal rheumatologic diseases	5	1.32
Maternal TORCH infections	1	0.26
2. b. Fetal Factors		
Dysrhythmia	20	5.26
Polyhydramniosis, oligohydramniosis	13	3.43
Fetal extracardiac anomaly	12	3.16
Chromosomal anomaly	2	0.52
Increased nuchal translucency	3	0.79
2. c. Hereditary Factors		
Previous child or fetus with CHD	21	5.52
Previous child or fetus with extracardiac anomaly	32	8.42
Familial CHD (excluding parents and siblings)	24	6.31
Total	**246**	**64.74**

CHD: Congenital heart diseases, DM: Diabetes mellitus, TORCH: Toxoplasma, O (others), rubella, cytomegalovirus, herpes simplex virus, US: Ultrasound

The demographic data are summarized in Table 2. The comparison of the pregnant women included in the study according to their risk status revealed p=0.06. In the risk groups, the mean ages were 27.19±1.28 and 27.91±3.79 years, respectively and no statistically significant difference was found between the groups (p>0.05). The mean gestational week was 23.52±1.99 and 23.13±2.71 weeks in the study population, respectively. Similarly, no statistical difference was detected for this parameter between the groups (p>0.05). The percentages of primiparas in low- and high-risk groups were 64.93 and 58.94%, respectively. Additionally, two and four pregnancies were multiple in the low-risk and high-risk groups, respectively.

Table 2. The demographic data of the study population.

	Low-risk Group (n=134)	High-risk Group (n=246)	p
Age (years)	27.19±1.28 (19-44)	27.91±3.79 (21-44)	**>0.05**
Gestational week (weeks)	23.52±1.99 (17-36 weeks)	23.13±2.71 (17-36 weeks)	>0.05
Primipara (n/%)	87/64.93	145/58.94	>0.05
Multipara (n/%)	45/33.58	97/39.43	>0.05
Multiple pregnancy (n/%)	2/1.49	4/1.63	>0.05

ICEF was detected in a total of 77 (20.26%) cases, 68 (50.75%) cases were in the low-risk group and nine (3.66%) cases were in the high-risk group (Table 3). Left ventricular echogenic foci were detected in 59 (44.03%) fetuses in low-risk pregnancies and four (1.63%) fetuses in high-risk pregnancies, respectively and the statistical significance was achieved (p=0.001). Also, right ventricular echogenic foci were detected in seven (5.22%) fetuses in low-risk pregnancies and one (0.41%) fetus in high-risk pregnancies, respectively (p=0.03). It was observed that ICEF were single in 71 cases and multiple in six cases. In addition, ICEF was located in both ventricles in one (0.75%) and two (0.81%) cases in the risk groups, respectively (p=0.08). Also, multiple echogenic foci in one of the ventricles were detected in one (0.75%) case in the low-risk group and 2 (0.81%) cases in the high-risk group, respectively (p=0.07).

Table 3. Distribution of fetal cardiac echogenic foci detected in fetal echocardiography by pregnancy risk groups.

Fetal cardiac echogenic focus location	**Low-risk (n=134)**	**High-risk (n=246)**	*p*
Left ventricle	59 (44.03%)	4 (1.63%)	0.001
Right ventricle	7 (5.22%)	1 (0.41%)	0.03
Both ventricles	1 (0.75%)	2 (0.81%)	0.08
Multiple in one ventricle	1 (0.75%)	2 (0.81%)	0.07

In the low-risk group, ventricular septal defect was detected in four cases (2.98%) (Table 4). However, a ventricular septal defect was detected in two cases (0.81%), double outlet right ventricle in two cases (0.81%), hypoplastic left heart syndrome in three cases (1.22%), tricuspid atresia in two cases (0.81%), pulmonary atresia/hypoplasia in three cases (1.22%), tricuspid atresia and TGA in one case (0.41%), aortic coarctation/aortic arch hypoplasia in one case (0.41%), corrected TGA in one case (0.41%) and truncus arteriosus in one case (0.41%) were detected in the high-risk group (Table 4). Additionally, one fetus in a low-risk pregnancy and one fetus in a high-risk pregnancy had echogenic foci in one of the ventricles with congenital heart diseases.

Table 4. Distribution of congenital heart diseases by low-high risk groups.

Congenital Heart Disease	**Low-risk Group (n=134)**	**High-risk Group (n=246)**
Ventricular septal defects	4 (2.98%)	2 (0.81%)
Double outlet right ventricle	-	2 (0.81%)
Hypoplastic left heart syndrome	-	3 (1.22%)
Tricuspid atresia	-	2 (0.81%)
Pulmonary atresia/hypoplasia		3(1.22%)
Tricuspid atresia and TGA	-	1 (0.41%)
Aortic coarctation/aortic arch hypoplasia	-	1 (0.41%)
Corrected TGA	-	1 (0.41%)
Truncus arteriosus	-	1 (0.41%)
Total	**4 (2.98%)**	**16 (6.51%)**

TGA; Transposition of great arteries

Rhythm disturbances were also detected in our study. In this way, premature atrial extrasystoles were detected in three fetuses in the low-risk group while premature ventricular beats were detected in five pregnant women in the high-risk groups.

Discussion

ICEF are small structures typically located within the ventricles in the papillary muscle or chordae region. They have an echogenicity comparable to fetal bone. Also, ICEF usually moves synchronously with the mitral or tricuspid valve and they are not attached to the ventricular wall (1–4). Reducing the flow gain to ensure that the ribs do not disappear before their echogenicity is an important test to minimize false-positive results, as the papillary muscles can often be seen as echogenic dots (21). Although unclear, the etiology is likely a normal variant of papillary muscle development or increased mineralization of the papillary muscle or chordae within the ventricle (2). Some authors consider it to be a marker of disease in the fetus (5,6) while others believe it is a normal variant and a benign finding (2,3). In general, factors like technique, experience, and equipment influence the detection rate of ICEF. The prevalence of ICEF was reported between 0.5–20% of pregnancies in the literature (3,11,13). On the other hand, in the study by Shipp et al., the incidence of ICEF was as high as 30.4% in Asian mothers (22). This variation in the reported literature can be attributed to the operator's experience, the sophistication of the equipment, gestational age at the time of examination, maternal body habitus and the study population examined (3,11,13). The overall prevalence of ICEF in our study was 20.26% and it is comparable to that of other studies. The relatively higher prevalence of our result can be associated with ethnicity and different living spaces. Another reason why the prevalence of ICEF is higher in our study is that selected pregnant women are referred to our tertiary hospital. On the other hand, the prevalence of ICEF is significantly different between low- and high-risk pregnancies in the literature. The studies showed a prevalence of 0.5%-6.9% in low-risk pregnancies (8,13,14) while a prevalence of 2.7%-19.4% in high-risk pregnancies (2,8,10,13,14). During the same year, Simpson et al. published a prevalence of 6.9% for ICEF among a low-risk cohort out of the United Kingdom, while Merati et al. reported a prevalence of 3.2% in a low-risk Italian population (13,23). In our study, we found this prevalence as 50.75% in the low-risk group and 3.66% in the high-risk group, respectively. The high prevalence in the low-risk group in our study can be explained by the referral of selected pregnant women to our clinic, ethnicity, different living areas, and the low number of patients.

Intracardiac echogenic focus can be found in one or both ventricles, and they may be a single or multiple foci (23,24). The most frequent finding

is a single focus in the left ventricle (2,13,16). Similarly, in our study, single focus in the LV was mostly detected in both risk groups 44.03% in the low-risk and 1.63% in the high-risk group. Also, a single focus in the right ventricle was more often observed in the low-risk pregnancy group (5.22%) than in the high-risk pregnancy group (0.41%). Some researchers have suggested that right-sided or bilateral ICEF carries a higher risk of chromosomal abnormalities than left-sided ones (10,12,25). Also, some studies suggested that multiple ICEFs are associated with poor prognosis and should be analyzed in detail (17). However, most of these studies were based on small sample sizes and limited to fetal chromosomal abnormalities. Also, in our study, no similar correlation was found between right-sided or bilateral ICEF and congenital heart defects.

Barsoom et al. reported a very low (1.5%) sensitivity and 87.5% specificity for screening an isolated ICEF for congenital heart disease in a low-risk population (26). On the other hand, some studies showed that isolated echogenic focus is a risk factor for congenital heart disease in a low-risk population. Similarly, Shakoor et al. reported the prevalence of cardiac defects as 4.2% in fetuses with ICEF in their study (27). Additionally, Goncalves et al. reported a prevalence of 1.6% after excluding cases with chromosomal abnormalities, which is twice the prevalence in the overall study population (0.8%). (28). In addition, the study by Chiu et al. suggested that ICEF neither increased nor decreased the risk of cardiac structural defects, but fetuses with echogenic foci in the right ventricle showed a higher risk for cardiac structural defects (29). On the other hand, Didly et al. performed neonatal ECG on fetuses with the antenatal finding of ICEF and compared with the fetuses without such findings and they concluded that both antenatal and postnatal evaluation by fetal ECG is not indicated (30). Also, similar findings are observed by others (3,7,8,13,23-27). Similarly, our study supported these findings that we have found no correlation between the locations of ICEF and congenital heart diseases in low- and high-risk pregnancies.

Our study has some limitations. First, our hospital is a tertiary hospital, and patients with a suspected fetal cardiac anomaly are referred from all over the areas of our city, so the incidence of ICEF may be higher than that of the general population. Second, the number of pregnancies in each group was relatively low. Third, the identification of ICEF may be influenced by a variety of factors such as gestational age, fetal ECG image quality, and fetal position.

In conclusion, we reported a 20.26% prevalence of ICEF in our study population. Also, the prevalence of ICEF was 50.75% in low-risk pregnancies relatively higher than that of studies. However, this can be attributed to ethnicity, tertiary hospital referrals, a relatively low number of patients, and other associated factors. So, routine genetic analysis should not be required in low- and high-risk pregnancies with ICEF. Additionally, in our study, no correlation was found between congenital heart diseases and ICEF in both low-risk and high-risk pregnancies. In this way, larger controlled studies are needed to confirm the findings of this study.

Ethical Declarations

Ethics Committee Approval

The study was obtained from our University Medical Research Ethics Committee (Date: 26.09.2024, Decision No: 10-2024/01, Number: E-11095095-050.04-216359).

Informed Consent

Signed written informed consent was taken from all participants.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support. Author Contributions: Conception And Design: HA; Data Collection And/Or Processing: HA, GS, and FŞ; Supervision; HA and GS; Literature Review; HA and FŞ; Analysis and/or Interpretation: HA and GS: Writing; HA; Critical Review; GS and FŞ.

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