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Original Article

Prevalence of echogenic intracardiac focus and its association with fetal aneuploidy and adverse perinatal outcomes in Turkish pregnancies

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Abstract

Aim: The association between echogenic intracardiac focus (EIF) and fetal aneuploidy is well established, with a recognized ethnic variation. This study aimed to investigate the prevalence of EIF in Turkish pregnancies and examine its association with fetal aneuploidy and adverse pregnancy outcomes.

Material and Methods: We conducted a retrospective cohort study of second-trimester obstetric ultrasonography (16–24 weeks) at a university hospital for over 4 years. During the evaluation, all pregnancies with and without EIF were divided into three groups; Group 1: control group (randomly selected patients without EIF, n = 100); Group 2: isolated EIF group, (EIF is the sole finding, n = 45) and Group 3: non-isolated EIF group, (EIF with accompanying other ultrasound findings for fetal aneuploidy and/or presence of congenital anomalies, n = 21). The pregnancy outcomes of patients with isolated and non-isolated EIF and control group were compared.

Results: Overall, 2590 obstetric sonograms were examined, with an EIF prevalence of 2.55%. The presence of other ultrasonography findings and/or congenital anomalies accompanying EIF was associated with an increased risk of fetal aneuploidy, and 2 of 21 (9.5%) pregnancies in the non-isolated EIF group had fetal aneuploidy. In addition, non-isolated EIF was associated with perinatal mortality, preterm delivery, and polyhydramnios when compared to controls and isolated EIF pregnancies. There was no difference in the pregnancy outcomes between control and patients with isolated EIF.

Conclusion: EIF is a rare occurrence in Turkish pregnancies and as a sole finding, it is not associated with fetal aneuploidy or other adverse pregnancy outcomes. However, the presence of ultrasonography findings and/or congenital anomalies accompanying EIF was associated with an increased rate of fetal aneuploidy and adverse pregnancy outcomes.

Keywords: Echogenic intracardiac focus; fetal aneuploidy; pregnancy

INTRODUCTION

Echogenic intracardiac focus (EIF) occurs due to incomplete fenestrations or increased mineralization of the papillary muscle and/or chordae tendineae in the cardio ventricles (1,2). During the ultrasonographic examination of the fetal heart, EIF is visualized as a small bright area (similar echogenicity to that of bone) located in the left or right ventricle from a four-chamber view.

EIF was first described by Schechter et al. in 1987 (3). In the second-trimester ultrasound examination, EIF was observed between 0.5% and 20% of all pregnancies (4,5). During the past two decades, second-trimester ultrasonography findings, such as loss of nasal bone, increased nuchal fold, pyelectasis, hyperechoic bowel, femoral/humeral shortening, and EIF were evaluated as a variation of the normal fetal anatomy. Although the sensitivity and specificity were low, the detection of these findings in the ultrasonographic examination was associated with an increased risk of fetal aneuploidy (5-10). Of these findings, EIF was also associated with congenital heart diseases (11,12). However, some studies in the literature have shown no association between the presence of EIF and fetal aneuploidy, congenital heart diseases, or adverse pregnancy outcomes (13,14). These conflicting results may be associated with several factors, including image quality of ultrasound, definition of EIF, technical and ethnic/racial factors, and presence of accompanying ultrasound findings for fetal aneuploidy or congenital anomalies (13,15–18).

Therefore, we aimed to investigate the prevalence of EIF in Turkish pregnancies and its association with fetal aneuploidy and adverse perinatal outcomes.

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MATERIAL and METHODS

In this retrospective cohort study, we screened the medical records of 2,590 pregnant women who underwent ultrasonography examination between 16 and 24 weeks of gestation from January 2016 to February 2020 at Balikesir University, Faculty of Medicine, Department of Gynecology and Obstetrics. The study protocol was in accordance with the Helsinki Committee requirements. Ethical approval was obtained from the institutional Ethical Committee of Balikesir University, School of Medicine (Date: 29.04.2020 no: 2020/65). Data was obtained from patient electronic medical records (discharge summaries, laboratory records and medical charts). EIF was identified in 66 of 2590 pregnancies. During the evaluation, all pregnancies with and without EIF were divided into following three groups according to the presence of EIF and accompanying ultrasound findings for fetal aneuploidy, such as lose of nasal bone, pyelectasis, hyperechoic bowel, femoral/ humeral shortening, and single umbilical artery, and/or congenital anomalies. A power analysis was performed by using the data regarding with the frequency of congenital abnormality reported in the previous publications (19) and necessary sample size in control group was found as 100 when the desired significance level was set at .05 (alpha) and power was set at 0.8 (1-Beta). Therefore, it was calculated that 100 control patients were required for 21 patients in the non-isolated EIF group in order to test whether there was a statistically significant difference in the frequency of congenital anomaly between non-isolated EIF and the control group. Thus, 100 of the remaining 2524 patients without EIF was selected for control group. Group 1: control group (randomly selected patients without EIF, n = 100); Group 2: isolated EIF group, (EIF is the sole finding, n = 45) and Group 3: non-isolated EIF group, (EIF with accompanying other ultrasound findings for fetal aneuploidy and/or presence of congenital anomalies, n = 21). The groups were compared for maternal, perinatal, and genetic outcomes.

EIF has been defined as echogenic structures, similar to the bone, observed from different angles (four-chamber and long-axis views), measuring between 1 and 5 mm in diameter. When an EIF was identified at 16–24 weeks of gestation, pregnant women were invited for follow-ups with serial scans after 24 weeks of gestation to investigate congenital heart diseases. Fetal doppler echocardiography was used to exclude cardiac malformations.

Ultrasonographic examinations of all participants were performed by two experienced obstetrician and gynecologist, using a transabdominal 3-5 MHz convex probe with GE Voluson 730 expert ultrasonography device. The fetal heart was viewed in both longitudinal and transverse sections. All women with EIF also evaluated during the postnatal period by a pediatrician or pediatric cardiologist.

Demographic data, physical examination, ultrasound findings, and laboratory results of pregnant women were recorded during the pregnancy and early neonatal period. The presence of other ultrasonography findings for fetal aneuploidy was evaluated as previously described (12). Preterm delivery has been defined as any birth before 37 weeks of gestation. Intrauterine growth restriction (IUGR) has been defined as less than normal fetal growth, characterized by an estimated fetal weight less then the 10th percentile for a given gestational age. Low birth weight has been defined as a birth weight of less than 2500 grams. Amniotic fluid index (AFI) was measured in centimeters in each of the four maternal abdominal quadrants. AFI <5 was considered as oligohydramnios and >20 was considered polyhydramnios. The preeclampsia was diagnosed using current guideline of ACOG (American College of Obstetricians and Gynecologists) (20). The diagnosis of GDM was made when two of the four values on the oral glucose tolerance test were abnormal according to the Carpenter and Coustan criteria (21). Fetal chromosomal abnormalities were established by reviewing amniocentesis reports or declerations pediatricians interviewed.

Statistical analysis

MedCalc Statistical Software version 19.2.1 (MedCalc Software Ltd, Ostend, Belgium; https://www.medcalc.org; 2020) was used for the statistical analysis. The distribution of all variables in both the EIF and control was studied by describing the mean ± standard deviation (SD) or median (min-max), where applicable. Whether the distributions of continuous variables normal or not was determined by Kolmogorov–Smirnov test. Also, the Levene test or F test was used for the evaluation of the variances. The Chi-square test was used to compare categorical datas. While the mean differences between more than two independent groups were analyzed by one-way ANOVA, the Kruskal–Wallis test was applied for comparisons of the median values. When the p values from one-way ANOVA or Kruskal–Wallis test statistics was statistically significant the Scheffé test or posthoc analysis nonparametric multiple comparison test was used to determine which group differed from which others. A p-value of < 0.05 was considered statistically significant.

RESULTS

In this study, ultrasonographic screening was performed in 2590 pregnancies between 16 and 24 weeks of gestations, and EIF was identified in 66 of them. According to these observations, the prevalence of EIF was 2.55%.

The demographic features of all pregnant women (100 pregnant women in the control group, mean age 27.4 years; 45 pregnant women in the isolated EIF group, mean age 27.8 years; and 21 pregnant women in the non-isolated EIF group, mean age 28.6 were compared. The average age of the pregnant women were similar between the groups (p = 0.6920). The characteristics of participants are summarized in Table 1 and Table 2

We observed 6 (9.1%) congenital anomalies and 17 (25.8 %) accompanied ultrasonographic findings for fetal aneuploidy in patients with EIF (Table 3 and Table 4).

Table 1. Demographic characteristics of pregnancies with EIF

	Control (n = 100)	isolated EIF (n = 45)	Non-isolated EIF (n = 21)	P value
Maternal age (year), mean±SD	27.4±5.4	27.8±5.8	28.6±6.3	0.6920*
Gravidity, n (%)				
1	30 (30.0)	14 (31.1)	6 (28.6)	0.0850$
2	45 (45.0)	21 (46.7)	6 (28.6)	
≥3	25 (25.0)	10 (22.2)	9 (42.9)	
Parity, n (%)				
≤1	62 (62.0)	27 (60.0)	9 (42.9)	0.1992$
>1	38 (38.0)	18 (40.0)	12 (57.1)	
Gestational age at delivery (week), mean±SD	39.0±1.1	38.5 ±1.2	38.0 ±2.9	0.4211#
Fetal weight (gr), mean±SD	3238.2±411.5	3191.8 ±434.7	3119.3±720.1	0.5127#
Fetal Height (cm)	51.2	50.9	50.1	0.4569#
Fetal gender, n (%)				
Female	48 (48.0)	20 (44.4)	9 (42.9)	0.8369$
Male	52 (52.0)	25 (55.6)	12 (57.1)	
Number of gestation, n (%)				
Single pregnancies	92 (92.0)	42 (93.3)	9 (42.9)	0.4075$
Twin pregnancies	8 (8.0)	3 (6.7)	12 (57.1)	
Type of Delivery, n (%)				
Vaginal Delivery	68 (68.0)	27 (60.0)	12 (57.1)	0.7799$
Cesarean section	32 (32.0)	18 (40.0)	9 (42.9)	
Presence of fetal aneuploidy, n (%)	0 (0)	0 (0)	2 (9.5)	0.0009$
Presence of Congenital Anomalies, n (%)	3 (3.0)	0 (0)	6 (28.6)	< 0.0001$
High Risk in screening test results, n (%)	8 (8.0)	4 (8.9)	3 (14.3)	0.6584$
The rate of amniocentesis, n (%)	5 (5.0)	4 (8.9)	9 (42.9)	< 0.0001$
Presence of other ultrasonography findings, n (%)	9 (9.0)	0 (0)	17 (81.0)	< 0.0001$

*ANOVA, #Kruskal Wallis, $Chi-Squared test

Table 2. Perinatal outcome of pregnant women with EIF

	Control (n = 100)	isolated EIF (n = 45)	Non-isolated EIF (n = 21)	P value
Perinatal mortality rate n (%)				
Live birth	100 (100)	45 (100.0)	19 (90.5)	**0.0009$**
Stillbirth/early neonatal death	0	0 (0)	2 (9.5)	
Preterm Delivery, n (%)	**7 (7.0)**	**3 (6.7)**	**5 (23.8)**	**0.0410$**
IUGR, n (%)	3 (3.0)	2 (4.4)	1 (4.8)	0.8708$
Oligohidramniosis, n (%)	5 (5.0)	2 (4.4)	3 (14.3)	0.7145$
Polihidramniosis, n (%)	**3 (3.0)**	**1 (2.2)**	**3 (14.3)**	**0.0478$**
Gestational Diabetes Mellitus, n (%)	6 (6.0)	3 (6.7)	3 (14.3)	0.4054$
Preeclampsia, n (%)	3 (3.0)	1 (2.2)	2 (9.5)	0.8708$
Intensive care unit admission, n (%)	9 (9.0)	4 (8.9)	4 (19.0)	0.3626$
Delivery type, n (%)				
Spontan delivery	68 (68.0)	27 (60.0)	12 (57.1)	0.7799$
Cesarean section	32 (32.0)	18 (40.0)	9 (42.9)	
1. min. Apgar Score	9 (9.0)	9 (6-9)	9(4-9)	0.4851#
5. min. Apgar Score	9 (9.0)	9(7-10)	9(3-10)	0.2782#

#Kruskal Wallis, $Chi-Squared test, IUGR: intrauterin growth restriction

In the non-isolated EIF group, we observed 2 (9.5%) fetal aneuploidy, 1 patient with EIF and aortic coarctation, amniocentesis was performed, and Turner Syndrome was diagnosed at 22 weeks of gestation. The other patients had EIF and nasal bone loss, amniocentesis was performed, and Down syndrome was diagnosed at 21 weeks of gestation. The fetal aneuploidy rate was significanly higher in the non-isolated EIF patients compared to the controls and isolate EIF pregnancies (p = 0.0009).

Table 3. Accompanying congenital anomalies
Aortic coarctation
Ventricular septal defect
Omphalocele and cleft of lip and palate
Talipes equinovarus
Ileal atresia
Spina bifida occulta

Table 4. Accompanying ultrasonography findings for fetal aneuploidy
Loss of nasal bone
Lateral ventriculomegaly, 3 patients
Echogenic fetal bowel 4 patients
Fetal pyelectasia 3 patients
Short femur length
Increased nuchal folds
Choroid plexus cyst 3 patients
Single umbilical artery

On the other hand, there was no significant differences in increased rate of high risk in screening test results between the groups (p = 0.6584). However, the rate of amniocentesis was significantly higher in non-isolated EIF group than those in isolated EIF and control group (< 0.0001). In addition, perinatal mortality, preterm delivery, and polyhydramnios were significantly higher in the non-isolated EIF group compared to the control and isolate EIF pregnancies (p = 0.0009, p = 0.0410, and p = 0.0478, respectively). Regarding the accompanied cardiac malformation, 2 (3%) patients with EIF had a cardiac malformation, such as aortic coarctation and ventricular septal defect.

However, the presence of IUGR, oligohydramnios, gestational diabetes mellitus (GDM), preeclampsia, intensive care unit admission rate and cesarean delivery was similar between the groups. In addition, the pregnancy outcomes were comperable between patients in the isolated EIF group and in controls.

DISCUSSION

In this study, we evaluated the pregnancy outcomes of women with EIF. The findings of our study indicated that EIF prevalence was 2.55% in the study population and in 68.1% of them, EIF was the sole ultrasonography finding (isolated EIF group) and these results were comperable with previous studies investigating the frequency of EIF in Turkish population (22).

In comparison to the control and isolated EIF pregnancies, pregnant women in the non-isolated EIF group demonstrated significantly higher adverse maternal and perinatal outcomes, including an increased rate of fetal aneuploidy and perinatal mortality. We also observed that the rate of preterm delivery and polyhydramnios was higher in the non-isolated EIF group compared to control and isolated EIF pregnancies.

In the literature, several studies have shown that the presence of EIF has been associated with an increased risk of fetal aneuploidy and congenital heart diseases (11,12,23). Gonçalves et al. demonstrated that the rate of fetal aneuploidy and congenital heart diseases in pregnancies with EIF were 3.7% and 2.7%, respectively (12). Bromley et al. found that fetuses with EIF had an increased risk of down syndrome (23). Furthermore, Chiu et al. demonstrated that the risk of cardiac structure defects was significantly higher in patients with EIF compared to controls. On the contrary recent studies demonstrated that the presence of EIF was not associated with congenital heart diseases or fetal aneuploidy (11). A recent study conducted by Mirza et al. found that EIF was not associated with aneuploidy or other adverse pregnancy outcomes, and the authors concluded that EIF was incidental with no impact on clinical practice (13). These conflicting results between studies may have resulted due to differences in demographic features of the study population, such as race, ethnicity, and the number of study populations as well as the presence or absence of accompanying ultrasound findings for fetal aneuploidy and/or congenital anomalies. In this study, we found that the rate of fetal aneuploidy and congenital heart diseases in pregnancies with EIF was 3.0% and 3.0%, respectively, and the result was comparable with previous studies (12).

On the contrary, compared to patients with isolated EIF, patients with other accompanying ultrasonography findings and/or congenital anomalies were associated with an increased risk of perinatal mortality, polyhydramnios and preterm delivery. In this study, the isolated EIF patients had a preterm delivery rate of 6.7 %, IUGR 4.4%, oligohydramnios 4.4%, GDM 6.7 %, preeclampsia 2.2%, and intensive care unit admission rate 8.9%. These results were comparable with studies that have previously investigated the perinatal outcomes of pregnancies with isolated EIF (24,25). Furthermore, we found no patients with fetal aneuploidy in the isolated EIF group and controls. According to the findings of our study, we believe that the presence of EIF as the sole ultrasonography finding was not associated with fetal aneuploidy and adverse pregnancy outcomes. However, in patients with EIF accompanied with other ultrasonography findings for fetal aneuploidy and/or congenital anomalies, the rate of perinatal mortality was 9.5%, preterm delivery 23.8%, IUGR 9.5%, oligohydramnios

14.2%, polyhydroamnios 14.2%, GDM 14.2%, preeclampsia 9.5% and intensive care unit admission rate 19.0%, and there was a significant difference in the rate of perinatal mortality, preterm delivery, and polyhydroamnios between the groups.

This study has some limitations. First, this was a retrospective study design. Second, the number of patients included in the study was relatively small. Third, data collection and accounting for all potential confounding variables, such as sociodemographic features and smoking habits of the participants, were not possible.

CONCLUSION

EIF as a sole ultrasonography finding in the second-trimester screening is not associated with fetal aneuploidy or adverse perinatal outcomes in Turkish pregnancies. However, if EIF is detected in the second-trimester screening, patients should be carefully evaluated for the presence of accompanying congenital heart diseases, congenital anomalies, and other ultrasound findings for fetal aneuploidy.

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