RESEARCH ARTICLE / ARAŞTIRMA MAKALESİ

DOI: 10.4274/atfm.galenos.2023.05924
Ankara Üniversitesi Tıp Fakültesi Mecmuası 2023;76(1):45-49

MEDICAL SCIENCES / DAHİLİ TIP BİLİMLERİ

Left Subdiaphragmatic Echogenic Focus in the Fetus and Its Effect on Prognosis

Fetüste Sol Subdiyafragmatik Ekojen Odak ve Prognoza Etkisi

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Abstract

Objectives: The aim of this study was to determine the effect of fetal left subdiaphragmatic echogenic foci (LSEF) on prognosis and to research its clinical significance.

Materials and Methods: In this retrospective study, obstetric ultrasound was performed for 20142 pregnant women, at 16-40 gestational weeks. The fetuses who were diagnosed with LSEF incidentally were included in the study. The number and size of echogenic foci, associated anomalies and serological test results were recorded. The fetuses with LSEF were followed by ultrasound every 4 weeks until delivery, and postnatal ultrasound on the second month of life was performed for the cases who didn't exhibite resolution.

Results: During the study period, 285 fetuses were found to have 315 LSEFs with a prevalence of 1.4%. Twelve (4.2%) of the fetuses had minor anomalies (7 intracardiac echogenic foci, 4 minimal pyelectasis, 1 hyperechogenic bowel) and one of them (0.3%) had aneuploidy+major anomaly (1 atrioventricular septal defect+Trisomy 21). Intrauterine 274 fetuses (n=286 LSEF) were able to be followed, 242 LSEF (84.6%) disappeared antenatally, 18 LSEF (6.2%) showed regression. In the second month of neonatal period, 6 LSEF (2%) persisted including the case with aneuploidy.

Conclusion: LCEF had no clinically significant effect on the prognosis of the cases without aneuploidy, and postnatal follow up was not recommended for these cases.

Key Words: Echogenicity, Fetus, Isolated, Calcification, Subdiaphragmatic

Öz

Amaç: Bu çalışma, fetüste sol subdiyafragmatik ekojen odakların (SSEO) prognoza etkisi ve klinik öneminin araştırılması amacı ile planlanmıştır.

Gereç ve Yöntem: Bu retrospektif çalışmada, 16-40 gebelik haftaları arasındaki 20142 gebeye obstetrik ultrason incelemesi yapılmış olup sol subdiyafragmatik alanda tesadüfen ekojen odak saptanan fetüsler çalışmaya dahil edildi. Ekojen odakların sayısı, boyutu, eşlik eden anomaliler ve serolojik testlerin sonuçları kaydedildi. Doğuma kadar 4 hafta aralıklarla ultrason takibi yapılmış olup rezolüsyon göstermeyen olgular için postnatal 2. ayda ultrason kontrolü yapıldı.

Bulgular: Çalışmaya dahil olan 285 fetüste 315 SSEO saptanmış olup SSEO prevelansı %1,4 bulunmuştur. Olguların 12'sinde (%4,2) eşlik eden minör anomaliler (7 intrakardiyak ekojen odak, 4 hafif pelviektazi, 1 ekojen barsak) ve birinde (%0,3) anöploidi+majör anomali (1 atrioventriküler septal defekt+Trizomi 21) izlendi. Antenatal takip edilebilen 274 fetüste saptanan 286 SSEO'nun 242'si (%84,6) intrauterin dönemde kayboldu, 18'i (%6,2) spontan küçülme gösterdi. Neonatal 2. ayda, anöploidi olgusu dahil 6 SSEO (%2) sebat etti.

Sonuç: Kromozomal anomali olmayan olgularda, SSEO prognozda klinik olarak anlamlı bir değişikliğe yol açmamaktadır. Bu olgularda postnatal takibe gerek yoktur.

Anahtar Kelimeler: Ekojenite, Fetüs, İzole, Kalsifikasyon, Subdiyafragmatik

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Received/Geliş Tarihi: 27.02.2023 **Accepted/Kabul Tarihi:** 24.04.2023

Introduction

Echogenic foci (EF) detected in the abdomen of the fetus may appear as sonographic markers indicating infectious pathologies or anomalies. These EF are not specific and it may not always be easy to diagnose accompanying pathologies. Differential diagnoses include meconium peritonitis, hyperechoic bowel, toxoplasma, rubella, cytomegalovirus, herpes simplex (TORCH) infections, neoplasms, and portal vein thromboembolisms. The location and distribution of EF in the abdomen should be carefully evaluated (1). Small calcifications commonly found in the abdomen and pelvis are mostly evaluated in favor of meconium peritonitis, and calcifications in the liver are evaluated in favor of infection, tumor, or vascular pathology (2,3). Determining the number, location, and distribution of EF in the abdomen gives very important clues for making diagnoses and predicting the prognosis of many diseases.

EF observed in the right upper quadrant of the abdomen suggest calcifications in the liver but left subdiaphragmatic EF (LSEF) have not been sufficiently clarified in the literature. This study aimed to investigate the prognosis and clinical significance of LSEF detected in antenatal ultrasound.

Materials and Methods

This retrospective cohort study was conducted at a secondary referral center specialized in maternal health care between January 2015 and November 2021. Participants were selected from a cohort of 20,142 pregnant women who were referred for an obstetric ultrasound examination between 16-40 weeks of gestation. Electronic health records and the electronically stored radiologic images were retrospectively analyzed. Fetuses with an incidental finding of having an EF in the subdiaphragmatic area of the left upper quadrant of the abdomen were included in the analysis. All sonographic examinations were performed by an experienced radiologist on obstetric ultrasound using a high-resolution ultrasound device with a convex 6-1.9-MHz probe (Toshiba Aplio 500, Japan). The same machine was used throughout the study.

EF was defined as hyperechoic image which is 1-6 mm in length with no obvious acoustic shadowing (Figure 1). The fetuses who had LSEF in at least two imaging planes were included in the study, whereas fetuses who had LSEF in a single imaging plane and multiple pregnancies were excluded from the study. In the case of identification of LSEF, the location, number, and size of the EF in the longest plane were stated in the written report and digital images were electronically recorded along with other abnormal findings of fetuses. First trimester screening tests and serologic tests were performed for all fetuses, and amniocentesis was performed in the case of indication. Informed consent was obtained from all pregnant women to participate in the study. The research was conducted ethically in accordance with the guidelines for human studies and World Medical Association Declaration of Helsinki. The study was approved by the local research ethics committee of İstinye University Clinical Research Ethics Committee (3/2022.F-52)

Fetuses with LCEF were followed every 4 weeks until birth through sonographic examinations. Postnatal sonography was performed in the 2nd month of life for all cases with LSEF. The clinical data about the babies with LSEF were retrieved from the electronic health records of the pediatric clinic of the study center.

Statistical Analysis

The SPSS 22.0 statistical package was used for statistical analysis. The Shapiro-Wilk test was used to test the normality of data distribution. Descriptive statistics were expressed as mean, standard deviation, number, and frequency.

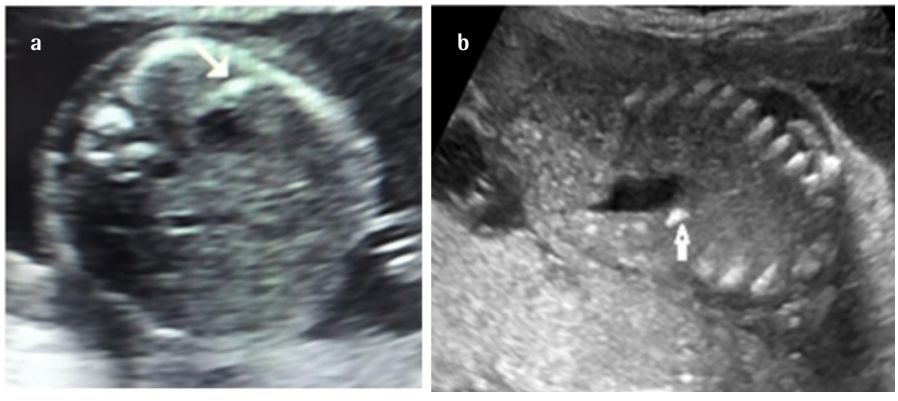

Figure 1: Left subdiaphragmatic echogenic focus (white arrow) in a 24-weeks fetus. **a.** Axial section, **b.** Sagittal section

Results

Routine obstetric ultrasound examinations revealed that 285 fetuses (1.4%) had LSEF (315 EF) out of 20,142 fetuses. The mean ± standard deviation gestational age of fetuses at the time of diagnosis was 18.5±2 weeks of gestation and ranged between 11 to 25 weeks. Maternal and fetal demographic characteristics and concomitant anomalies are presented in the Table 1.

During the study, 261 (91.5%) of 285 fetuses had a single EF, 19 (6.6%) had two EF, and 5 (1.7%) had three or more EF (Figure 2).

The diameters of the EF ranged from 2 to 6 mm (mean, 2.7±0.9 mm). LSEF were oval, rod, or round in shape, and posterior acoustic shadowing was not observed in any. Concomitant minor anomalies were observed in 12 (4.2%) fetuses (intracardiac EF n=7, mild pelviectasis n=4, echogenic bowel n=1), and one (0.3%) had a major anomaly [atrioventricular septal defect (AVSD)]. Amniocentesis of the fetus with AVSD revealed the presence of trisomy 21. Five of the fetuses with intracardiac EF had single EF, two of them had 2 EF in the left subdiaphragmatic area. The fetuses with mild pelviectasis, echogenic bowel and AVSD had single EF.

Antenatal follow-up could not be performed for 11 (3.8%) pregnant women included in the study because of not attending the ultrasound controls. Two hundred eighty-six LSEF were detected in the remaining 274 fetuses; 242 (84.6%) disappeared in the intrauterine period during antenatal follow-up and 18 (6.2%) showed spontaneous regression. Twenty-one (7.3%) that did not show intrauterine resolution could be evaluated in the postnatal period, and only six (2%) persisted in the neonatal 2nd month (Figure 3). In persistent fetuses, calcification foci were observed in the subcapsular area of the left liver lobe or the area adjacent to the spleen in the postnatal ultrasound examination. One of the persistent fetuses had trisomy 21 and no accompanying anomalies were detected in the others. The fetuses with minor anomalies were also followed up in the postnatal period and none of them had any abnormal finding. In serologic tests, eight pregnant women had immunoglobulin (Ig) G positivity in terms of TORCH infections, but postpartum infection was not observed in any of them.

Table 1: Maternal and fetal demographic characteristics and concomitant anomalies

Maternal-Fetal demographic characteristics	**Value (minumum-maximum)**	
Maternal age		27±3 (20-39)
Gestational age at diagnosis		18.5±2 (17-25) **N (%)**
Fetus gender	Male Female	151 (52.2%) 134 (47.0%)
Concomitant minor anomalies	IEF*	7 (2.4%)
	Pelviectasis	4 (1.4%)
	Echogenic bowel	1 (0.3%)
Concomitant major anomalies/aneuplody	AVSD**/Trisomy 21	1 (0.3%)

*Intracardiac echogenic foci, **Atrioventricular septal defect

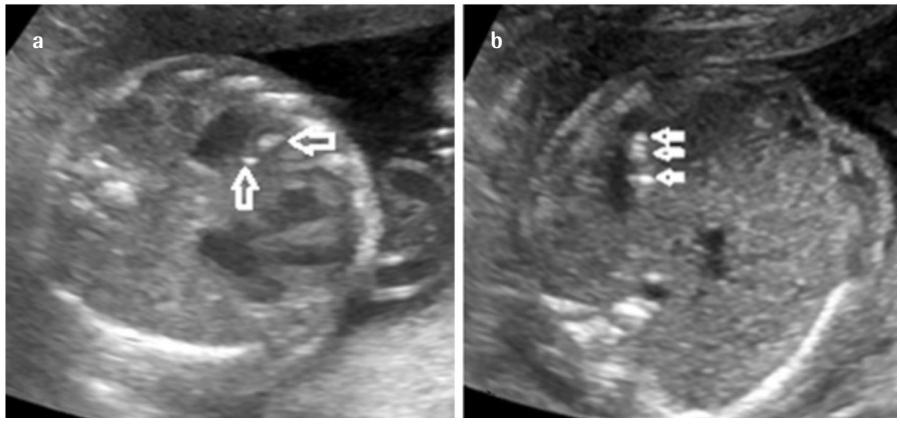

Figure 2: Axial section of the fetal abdomen. **a.** Two left subdiaphragmatic echogenic foci (white arrows) are seen in a 22-weeks pregnant. **b.** More than two echogenic foci (white arrows) are detected adjacent to the stomach in a 23-weeks pregnant

Discussion

In this study, the prevalence of LSEF detected during the antenatal period was found as 14 per 1000 pregnancies (1.4%, n=285/20,142). Approximately 85% of those disappeared in the intrauterine period, and 6% showed spontaneous regression. The rate of accompanying minor anomalies was 4.2%, and the rate of chromosomal anomalies was 0.3%. Chromosomal anomalies were found in one of six persistent cases. No relationship was observed between TORCH infections and LSEF. This study is the largest study on this subject in the literature.

Echogenicity observed in fetal tissues, called calcification, is used for echoes that are the same as adjacent bone echogenicity (4). In previous studies in the literature, the incidence of intrauterine hepatic calcifications was found to vary between 0.05% and 0.38% (5,6). In this study, the prevalence of LSEF was found as 1.4%, much higher than in previous studies. Isolated calcifications detected in the intrauterine period generally have a good prognosis (5,7). However, the outcome worsens when accompanied by other anomalies. Previous studies found a relationship between intra-abdominal calcifications and chromosomal abnormalities (7,8), intrauterine infections (7,9,10), and circulatory disorders (11). Sahlin et al. (12) emphasized that the probability of chromosomal anomalies in fetuses with intrauterine calcification and accompanying malformation was more than two times that of fetuses with only malformations. In our study, the rate of chromosomal anomalies was found as 3 per 1000 pregnant women, and the frequency of chromosomal anomalies increased compared with the normal population. However, studies with a larger number of cases are needed to determine the prevalence of chromosomal anomalies in fetuses with LSEF.

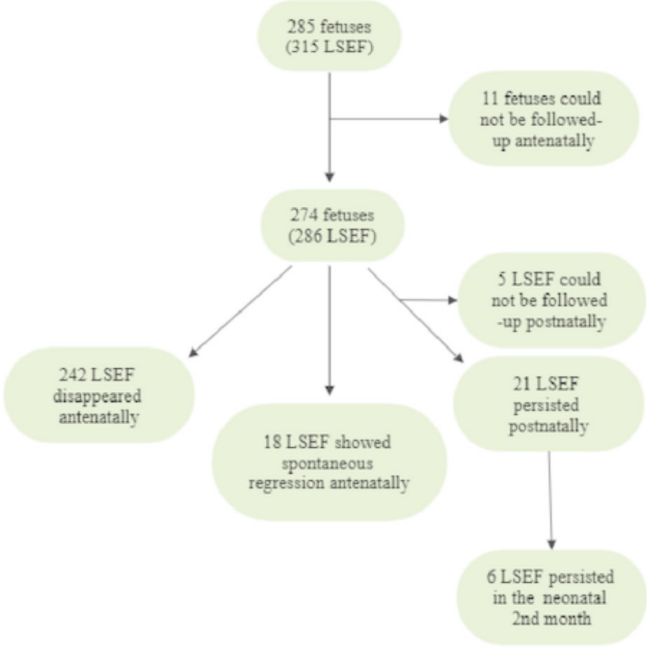

Figure 3: Flow chart of the recruitment and follow-up process

The fetuses with concomitant anomalies had single or two EF and no relationship was found between the number of EF and the concomitant anomalies. Approximately 90% of the LSEF included in the study either disappeared completely during the intrauterine period or reduced in size. Trisomy 21 was found in one of six persistent fetuses in the postnatal period; no chromosomal anomalies were found in any of the fetuses that showed resolution. Although no direct relationship was found between aneuploidy and the persistence of LSEF. LSEF did not lead to a significant change in prognosis in fetuses without accompanying chromosomal anomalies.

Studies in the literature focused more on intrauterine calcifications in the liver, heart, and peritoneum (2,9,12). Heart calcifications have been associated with chromosomal anomalies (12), peritoneal calcifications with meconium peritonitis and intrauterine infections (2), and hepatic calcifications with vascular etiology (13). The etiology of LSEF has not been sufficiently clarified in the literature. In this study, because persistent LSEF were detected in the subcapsular area of the left liver lobe and adjacent to the spleen in postnatal examinations, etiologies related to liver and spleen calcifications could be considered initially. In the literature, calcifications detected in the subcapsular area of the liver have been found to be associated with portal vein thrombosis (1,14). In our fetuses, small thrombi in the portal vein may have played a role in the etiology. It can be predicted that regressed LSEFs in the intrauterine period may be associated with left liver lobe calcifications because liver calcifications tend to regress spontaneously (15).

TORCH infections are one of the other causes of calcifications observed in the abdomen of the fetus and are generally encountered as scattered millimetric echogenicities accompanied by multiple organ anomalies (16). They can be distinguished from LSEF by the scattered location of calcifications and accompanying anomalies. In our study, IgG positivity in terms of TORCH infections was observed in eight pregnant women, and no accompanying infection findings were observed in any of them in the periuterine period. Ji et al. (1) found no significant relationship between LSEF and transplacental infections, as in our study. Another cause of multiple calcifications in the abdomen is meconium peritonitis, which occurs as a result of intestinal obstruction (17). Meconium peritonitis is mostly encountered as calcifications located on the peripheral surfaces of the liver and in the peritoneum. The location of calcifications, accompanying intestinal anomalies, and the presence of ascites are guides in the differential diagnosis of LSEF of more than two in number.

Study Limitations

Among the limitations of the study, first, there was the inability to elucidate the etiopathogenesis of LSEF that showed resolution in the antenatal period. Secondly, the relationship between aneuploidy and the persistence of LSEF could not be evaluated due to the insufficient number of fetuses. Aneuploidy was observed in only one fetus with persistent LSEF in our study. Studies with a larger number of fetuses are needed to evaluate the relationship between chromosomal anomalies and LSEF.

Conclusion

LSEF are encountered more frequently than other calcifications observed in the abdomen with a prevalence of 1.4% and mostly disappear in the intrauterine period. Their etiology has not been fully elucidated and no relation with transplacental infections has been observed. LSEF does not cause a clinically significant change in prognosis of the fetuses without chromosomal anomalies. Postnatal follow-up is not required for the cases without aneuploidy.

Ethics

Ethics Committee Approval: The study was approved by the local research ethics committee of İstinye University Clinical Research Ethics Committee (3/2022.F-52).

Informed Consent: Informed consent was obtained from all pregnant women to participate in the study.

Peer-reviewed: Externally peer-reviewed.

Financial Disclosure: The author declared that they did not receive any financial support during the research and authoring of this article.

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