

# Fetal Intracardiac Echogenic Focus in Pregnants Underwent Amniocentesis

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## Abstract

**Objective:** It was aimed to define the frequency of intracardiac echogenic focuses in the fetuses with normal karyotype and with Down syndrome in our study population.

**Methods:** The intracardiac echogenic focuses obtained from second line USG are tested in the fetuses whom made amniocentesis and karyotyping because of the reasons like old maternal age, increased risks with in scanning tests, structural anomalies in the USG and family history.

**Results:** The 1,350 fetuses whom made karyotype analysis; 1,293 of the fetuses obtained with normal karyotype. Thirty-two of the fetuses diagnosed with Down syndrome, 10 of fetuses with trisomy 18, 6 of them with trisomy 13, 5 of them with Turner syndrome and 4 of fetuses are obtained with other aneuploidies. The frequency of fetal intracardiac echogenic focuses was found 2.4% with in normal fetuses, 12.5% fetuses with in Down syndrome, 0% of fetuses with trisomy 18, 16.6% of fetuses with trisomy 13, 0% of fetuses with Turner syndrome and 4 fetuses having other karyotypes. The frequency of echogenic focuses was found higher significantly in fetuses with Down syndrome than the fetuses who have normal karyotype ( $p<0.05$ ).

**Conclusion:** Although the frequency of fetal intracardiac echogenic focuses are seen to be higher in fetuses with Down syndrome by comparison with the fetuses which have normal karyotype, more studies must be performed to accept it as a marker.

**Keywords:** Fetal intracardiac echogenic focus, Down syndrome, karyotype analysis.

## Amniosentez yapılan gebelerde fetal intrakardiyak ekojenik odak

**Amaç:** Normal karyotipli ve Down sendromlu fetüslerde saptanan intrakardiyak ekojenik odakların görülme sıklığını araştırmak.

**Yöntem:** İleri maternal yaş, tarama testlerinde risk artışı, ultrasonografide yapısal anomaliler, aile öyküsü gibi nedenler ile amniosentez ve karyotipleme yapılan fetüslerde 2. düzey ultrasonografide saptanan intrakardiyak ekojenik odaklar değerlendirildi.

**Bulgular:** Karyotip analizi yapılan 1,350 fetüsün 1,293'ü normal, 32'si Down sendromu, 10'u trizomi 18, 6'sı trizomi 13, 5'i Turner sendromu, 4'ü de değişik anöploidili tanısı aldı. Fetal intrakardiyak ekojenik odak normal karyotipli fetüslerde %2.4, Down sendromlu-larda %12.5, trizomi 18'de %0, trizomi 13'de %16.6, Turner sendromu ve 4 değişik anöploidili fetüste %0 oranında saptandı. Down sendromlu olgulardaki görülme oranı normal karyotipli fetüslerden anlamlı olarak yüksek bulundu ( $p<0.05$ ).

**Sonuç:** Fetal intrakardiyak ekojenik odak Down sendromlu olgularda normal karyotipli olgulara göre daha sık izlense de bir belirteç olarak kabul edilmesi için daha fazla çalışma yapılmalıdır.

**Anahtar Sözcükler:** Fetal intrakardiyak ekojenik odak, Down sendromu, karyotip analizi.

## Introduction

Frequency of chromosomal aberrations in newborn children is approximately 1 in 165.<sup>[1]</sup> Chromosomal aberrations increase as the mother's age increases. However, because only pregnant

women over 35 are checked with screening tests, 80% of the fetal aneuploidies may be overlooked.<sup>[1,2]</sup> The evaluation of obstetric ultrasound findings in aneuploid diagnosis is used to detect risky pregnancies. The most common findings

known as aneuploidy markers are echogenic intracardiac focus, echogenic bowel, shortness of long bones and renal pyelectasis. The detection of these soft markers increases the risk of trisomy.<sup>[21]</sup>

In this study, echogenic intracardiac focuses that were detected in normal fetuses and those with Down syndrome after carrying out amniocentesis and karyotyping for different reasons, have been examined and discussed.

## Methods

It has been evaluated the cases which had invasive tests with the indications of advanced maternal age, increasing risk in screening tests, childbirth that has chromosomal aberrations before, family history and ultrasonographic indications such as structural anomalies and cases that were performed amniocentesis in the last 1.5 years in our hospital. Before the amniocentesis, level 2 ultrasound scan was performed to all pregnant women in their 16th to 20th week of pregnancy by the specialist physicians of our hospital. Echogenic intracardiac focuses and other pathologies that were detected by ultrasonographic examination were added into the computer records. The cases, whose karyotyping analysis was fully obtained after carrying out amniosynthesis, were taken into the scope of the study. The frequency rate of the fetal echogenic intracardiac focuses which are detected in fetuses with mainly Down syndrome and other chromosomal aberrations are compared with the fetuses with normal karyotype. The cases that karyotype analysis is not reached was excluded.

Chi-Square test was used in statistical evaluations.

## Results

Normal chromosome structure was detected in 1,293 cases out of 1,350 after karyotyping analysis in our working group. Trisomy 21 was diagnosed in 32 cases (2.4 %). Echogenic intracardiac focus was detected in 39 out of 1,293 cases with normal karyotype by ultrasonographic scan. Echogenic intracardiac focus was detected in 4 % of the 32 cases with Down syndrome (12.5%). When the echogenic focus rates in fetuses with normal karyotype and Down syndrome are compared, a statistically significant difference was reported ( $p < 0.05$ ). Trisomy 18 was diagnosed in 10 cases. Echogenic intracardiac focus was not monitored in these cases. Trisomy 13 was diagnosed in 6 cases. Echogenic intracardiac focus was monitored in one of these cases (16.6%). Echogenic focus was not monitored in 5 Turner syndrome, 1 Klinefelter syndrome and 3 aneuploidy cases (Table 1).

Chromosomal aberration rate in total 44 fetuses, whose echogenic focuses are monitored, are calculated as 11.4 % (5 fetuses).

## Discussion

In general, echogenic intracardiac focus is monitored in 2-5% of the fetuses.<sup>[3-5]</sup> Focus is usually monitored in the left ventricular, but it may occur in the right ventricular or in both. The focuses may be solitary or more and 95% of them vanish in the third trimester.<sup>[6]</sup>

**Table 1.** Karyotype and echogenic intracardiac focus results of 1,350 cases .

Karyotype analysis	n	Echogenic intracardiac focus	
		n	%
Normal karyotype	1,293	39	2.4
Down syndrome	32	4	12.5
Trisomy 18	10	0	0
Trisomy 13	6	1	16.6
Turner syndrome	5	0	0
Klinefelter syndrome	1	0	0
Pseudomosaicism of Y chromosome	1	0	0
47Xi idic	1	0	0
46X(14) 46XY(56)	1	0	0

While some authors claim that echogenic focus is the marker of Down syndrome,<sup>[3,7,8]</sup> the others haven't found a relationship between the focus and Down syndrome.<sup>[4,7,9]</sup>

Brown et al. showed that the finding of an echogenic intracardiac focus at ultrasonography correlates with mineralization within a papillary muscle of the fetal heart.<sup>[10]</sup> Bromley et al. in 1995 reported a 4.9% incidence of EIF (echogenic intracardiac focus) among 1,334 fetuses studied. They also found that extremely high rate of 18% of fetuses with trisomy 21 had an EIF and that sonographic identification of an EIF had a fourfold increase risk of trisomy 21.<sup>[3]</sup> Petriskovsky et al. reported a 3.6% incidence of EIF in 1,139 patients, all of whom had a normal karyotype. The authors reported that they didn't detect any correlation between echogenic focus and adverse perinatal outcome.<sup>[6,11]</sup> EIF rate in our study was 2.4% among 1,293 fetuses with a normal karyotype at a similar rate in these studies.

Bromley et al. reported a 4.8% incidence of aneuploidy in 290 fetuses that had an EIF.<sup>[12]</sup> Chromosomal aberration rate in our study was 11.4% among 44 fetuses with EIF.

A meta-analysis conducted in 2001 by Smith-Bindman and friends determined that, (a total of 56 studies describing 1,930 fetuses with Down syndrome and 130,365 unaffected fetuses were included) when ultrasonographic markers were observed with structural malformations to detect Down syndrome, sensitivity for each one was 16% and when structural malformations were not observed, this rate was only 1%. Of the 5 studies in the meta-analysis that specifically looked at EIF, there were a total of 5,948 patients, 7.3% of whom had EIF. Authors suggested that in existence of intracardiac echogenic focus, if amniocentesis is offered in order to final exact diagnose of Down syndrome fetus, it is come up with that 2 in low risk group patient and 1 in high risk group of patient is going to be lost connection with amniocentesis complications.<sup>[13]</sup> In our study, there were a total of 32 Down syndrome cases, 12.5 % of whom had EIF, which was significantly higher than fetuses with a normal karyotype (2.4%). In trisomy 13 cases, this rate was extremely high rate of 16.6 % , but this marker was not observed in 10 cases with Trisomy 18. Roberts et al. reported a

16% incidence of EIF among Down syndrome cases and 2% incidence of EIF in the normal population.<sup>[5]</sup> Similarly, Bromley et al. detected a 18% incidence of EIF among Down syndrome cases and a 5% incidence of EIF among normal fetuses.<sup>[3]</sup>

Winter et al. evaluated 3,303 fetuses with an ultrasonographic scan and karyotype analysis and determined that EIF was found in 4.6% of normal fetuses and 30% of fetuses with trisomy 21. The authors concluded that, an isolated echogenic intracardiac focus was associated with a 4.8 fold increase in relative risk for trisomy 21.<sup>[14]</sup>

Nyberg et al. evaluated the ultrasound findings in 186 fetuses with Down syndrome and 8,728 controls and they reported that EIF was the most common marker found among affected fetuses after exclusion of major anomalies (7.1%).<sup>[15]</sup> Rebarber et al. reported a 14.8% incidence of intracardiac fetus among 148 Japanese patients, whose maternal age was 30.7 on the average, but they didn't find any abnormal karyotypes.<sup>[16]</sup> These data are contradicted with idea of Bromley and Winter which says intracardiac focus trisomy 21 increases. This contradiction bring question mind; can we reach different result in ultrasonographic analysis in different societies or not.

Coco et al. evaluated 12,672 patients and detected 479 cases of echogenic focus; 90.4% of which were isolated. Eleven patients had fetuses with Down syndrome (0.09%), but only 3 of these had an echogenic focus. Up to statistical analysis; although the fetuses with an echogenic intracardiac focus have an increased risk of aneuploidy, amniocentesis need not be offered to patients who are otherwise at low risk and have an isolated echogenic intracardiac focus.<sup>[17]</sup> In another study that evaluated 62,111 patients and found 2,223 echogenic intracardiac focus, Down syndrome was detected in 218 fetuses (0.4%). It is emphasized that the detection of isolated echogenic focus doesn't increase the risk of trisomy 21 for patients whose maternal age is younger than 35 years old.<sup>[18]</sup> In a study where intracardiac echogenic focus and multiple echogenic focus are compared in terms of aneuploid risk, 6 (8.5%) patients with Down syndrome is found in 71 fetuses with multiple echogenic focus and 1 (0.6%) patient with Down syndrome is found in 171 fetuses with single echogenic focus.<sup>[19]</sup>

## Conclusion

Echogenic intracardiac focus is monitored in Down syndrome cases more than normal karyotype cases, however more research should be done in order to detect EIF as the marker of Down syndrome.

## References

1. Drugan A, Johnson MP, Evans MI. Ultrasound screening for fetal chromosome anomalies. *Am J Med Genet* 2000;90:98-107.
2. Hook EB. Chromosome abnormalities in older women by maternal age-evaluation of regression derived rates in chorionic villus biops specimens. *Am J Med Genet* 1990;35:184-7.
3. Bromley B, Lieberman E, Laboda L, Benaceraff BR. Echogenic intracardiac focus: a sonographic sign for fetal Down syndrome. *Obstet Gynecol* 1995;86:998-1001.
4. Merati R, Lovotti M, Norchi S, et al. Prevalence of fetal left ventricular hyperechogenic foci in a low risk population. *Br J Obstet Gynecol* 1996;103:1102-4.
5. Roberts DJ, Genest D. Cardiac histologic pathology characteristic of trisomies 13 and 21. *Hum Pathol* 1992;23:1130-40.
6. Petrikovski BM, Challenger M, Wyse LJ. Natural history of echogenic foci within ventricles of the fetal heart. *Ultrasound Obstet Gynecol* 1995;5:92-4.
7. Simpson JM, Cook AC, Sharland GK. The significance of echogenic foci in the fetal heart: a prespective study of 228 cases. *Ultrasound Obstet Gynecol* 1996;8:225-8.
8. Sepulveda W, Cullen S, Nicolaidis P, et al. Echogenic foci in the fetal heart: a marker of chromosomal abnormality. *Br J Obstet Gynecol* 1995;102:490-2.
9. How HY, Villafane J, Parihus RR, Spinnato JA 2nd. Small hyperechoic foci of the fetal cardiac ventricle: a benign sonographic finding? *Ultrasound Obstet Gynecol* 1994;4:205-7.
10. Brawn DL, Roberts DJ, Miller WA. Left ventricular echogenic focus in the fetal heart: Pathologic correlation. *J Ultrasound Med* 1994;13:613-6.
11. Petrikovsky B, Challenger M, Gross B. Unusual appearances of echogenic foci within the fetal heart: are they benign? *Ultrasound Obstet Gynecol* 1996;8:229-31.
12. Bromley B, Lieberman E, Benaceraff BR. The incorporation of maternal age into the sonographic scanning index for the detection at 14-20 weeks of fetuses with Down's syndrome. *Ultrasound Obstet Gynecol* 1997; 10:321-4.
13. Smith-Bindman R, Hosmer W, Feldstein VA, Deeks JJ, Goldbery JD. Second trimester ultrasound to detect fetuses with Down syndrome: a meta-analysis. *JAMA* 2001;285:1044-55.
14. Winter TC, Anderson AM, Cheng EY, Komarniski CA, Souter VL, Uhnich SB, Nyberg DA. Echogenic intracardiac focus in second trimester fetuses with trisomy 21: usefulness as a US marker. *Radiology* 2000;216:450-6.
15. Nyberg DA, Souter VL, El Bastawissi A, Young S, Luthhardt F, Luthy DA. Isolated sonographic markers for detection of fetal Down syndrome in the second trimester of pregnancy. *Ultrasound Med* 2001;20: 1053-63.
16. Rebarber A, Levey KA, Funai E, Monda S, Paidas M. An ethnic predilection for fetal echogenic intracardiac focus identified during targeted midtrimester ultrasound examination: a retrospective review. *BMC Pregnancy Childbirth* 2004;4:12-6.
17. Coco C, Jeanty P, Jeanty C. An isolated echogenic heart focus is not an indication for amniocentesis in 12672 unselected patients. *J Ultrasound Med* 2004;23:489-96.
18. Shanks AL, Odibo AO, Gray DL. Echogenic intracardiac foci: associated with increased risk for fetal trisomy 21 or not? *J Ultrasound Med* 2009;28:1639-43.
19. Towner D, Gerscovich EO, Chiong BB, Morris LR, McGahan JP. Comparison of single versus multiple echogenic foci in the fetal heart regarding risk of aneuploidy. *J Ultrasound Med* 2010;29:1061-7.