Original Article

Intracardiac echogenic focus: Its importance during routine prenatal ultrasound screening in a black African population

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Abstract

Background: Intracardiac echogenic focus (ICEF) is defined as a small bright structure within the fetal heart with similar or greater echogenicity to the surrounding bone. The cause of ICEF is unknown, although it is generally believed to be a normal variant. However, several authors have reported a possible association between an ICEF and chromosomal abnormalities, while some others have found an association with structural cardiac anomalies. There are presently no data on this subject in sub-Saharan Africa about the possible correlation with other anomalies.

Materials and Methods: This was a prospective, cross-sectional, hospital-based study in a native West African population that spanned 5 years and 5 months. All the pregnant women who presented for routine prenatal ultrasound screening for fetal anomaly between 18 and 22 weeks' gestation age during the study period were included in the study. The prevalence and pattern of ICEF and correlations with cardiac anomalies were determined.

Results: In this study, 1.986 fetuses were evaluated for ICEF. The prevalence of ICEF was 2.2%, and more commonly (38.6%) seen in fetuses of mothers aged 30–34 years. Twenty-five percent (25%) occurred in fetuses of mothers that are older than 35 years. Most cases (65.7%) occurred in mothers that had no risk factors for the cardiac anomaly. Majority of the ICEF were solitary and within the left ventricle (95.5% and 93.2%, respectively). About 2.3% of the ICEF were biventricular. Among those that had further echocardiographic evaluation, 15% had major structural cardiac defects.

Conclusion: A left ventricular ICEF may not indicate a normal variant in all cases. We propose the addition of detailed fetal echocardiography to rule out structural cardiac anomalies.

Keywords: Intracardiac echogenic focus, prenatal screening, structural cardiac anomalies

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INTRODUCTION

Intracardiac echogenic focus (ICEF), defined as a small bright structure within the fetal heart with similar or greater echogenicity to the surrounding bone, was first described by Schechter *et al.* in 1987.[1] Of late, ICEF has received increasing attention as one of the most recent sonography soft marker that has been described in the literature[2] but yet to be fully understood. The incidence ranged between 0.5% and 32.4% in the previous studies.[3-7] The cause of ICEF is unknown, although it is generally believed to be a normal variant. Some authors believed it may be the result of a small area of mineralization within the cardiac papillary

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muscles or failure of the chordae tendineae to fenestrate during cardiogenesis.[3,6,7] However, the only consistent finding in those evaluated histologically is mineralization within the papillary muscle.[3,7]

ICEF may be single or multiple, and they are commonly seen within the left ventricle, although in a few instances, they may be seen in other chambers, especially the right ventricle.[1,3,6,8,9]

Although there is no consensus as to whether the echogenic focus is a normal variant or a marker of fetal abnormality,[8-11] various works have reported that there may be no correlation between ICEF and cardiac pathologic anomalies,[9-11] it is widely agreed that it is a soft marker for some chromosomal anomalies specifically trisomies 13 and 21.[12-14] Other common soft markers reported in literature include makers for aneuploidy, which include echogenic bowel, choroid plexus cyst, shortened long bones (femur and humerus), and renal pelvicaliectasis.[13] At present, studies have shown that right-sided ICEFs were more frequently associated with fetal cardiac anomalies than were left-sided or bilateral ICEFs.[15,16] Whereas other researchers reported that right-sided or bilateral ICEFs had an approximately twice greater risk of aneuploidy compared to the left-sided foci.[8]

Most of the time, ICEF is seen during a routine prenatal ultrasound performed around weeks 18–22 of the pregnancy. The detection of ICEFs may be affected by factors such as the resolution of the ultrasound machine, sonographer's experience, and the fetal position.[9] Initial data on ICEFs were derived from the Western populations,[1-6] and it was only in recent years that similar studies started to emerge from the rest of the world. Little is known about the prevalence of ICEF in a number of regions like sub-Saharan Africa, where prenatal screening for fetal anomalies has only been introduced in the past 10 years.

The aims of this study are to determine the prevalence of ICEF among fetuses presenting for prenatal ultrasound screening and to determine the association of ICEF with other structural abnormalities.

MATERIALS AND METHODS

This was a prospective, cross-sectional, hospital-based study which spanned 5 years and 5 months. The study was conducted at the Ultrasound Unit of the antenatal clinic of a South-Western Nigerian tertiary hospital between September 2012 and February 2018. All the pregnant women who presented for routine prenatal ultrasound screening for fetal anomaly between 18 and 22 weeks' gestation age during the study period were included in the study. The age range of the mothers was between 18 and 51 years.

Examination of the fetal heart was initially done as part of the routine prenatal ultrasound screening for fetal anomaly between 18 and 22 weeks of gestation by an experienced radiologist trained in prenatal ultrasonography. A pediatric cardiologist certified in fetal echocardiography also examined the fetal hearts. The guidelines for examination of the fetal heart by the International Society of Ultrasound in Obstetrics and Gynecology, as well as the European Guidelines for fetal echocardiography, were used, respectively, by the radiologist and the pediatric cardiologist to assess the fetal heart. The four chambers of the heart were examined by the radiologist for the presence of a bright echogenic focus, which is commonly seen within the left ventricle [Figures 1 and 2]. The number and location of the echogenic focus were documented. The fetuses with ICEF were then referred for fetal echocardiography by the fetal cardiologist. Less than half of the fetuses with ICEF had fetal echocardiography done because this was introduced midway into the study. The presence or absence of other cardiac abnormalities was then documented. The ages of the mothers, as well as other risk factors, were documented.

Statistical analysis was performed using the SPSS IBM version 20 spreadsheet (IBM version 20.0. Armonk, NY, USA: IBM Corp.). Informed consent was obtained from the patients before the procedures were carried out.

RESULTS

Forty-four (44) fetuses with echogenic foci within the heart were detected among the one thousand nine hundred and eighty-six (1986) fetuses that were examined during the study period giving a prevalence of 2.2%. Most (17, 38.6%) of the mothers of the fetuses with ICEF were in the 30–34 age group [Figure 3]. Twenty-nine (65.9%) of the mothers had no known risk factors, 11 (25%) were >35 years of age while twin cyesis, maternal sickle cell anemia disease, retroviral infection, and previous baby with congenital heart disease were the indication in four of the mothers, respectively [Table 1]. Forty-two (95.5%) had only one focus, whereas the remaining 2 (4.5%) had two foci [Table 2]. Forty-one (93.2%) had the focus within the left ventricle, 2 (4.5%) had it in the right ventricle, whereas only one fetus (2.3%) had a focus each within the right and left ventricles, respectively [Table 3 and Figure 4].

Twenty (20) out of the 44 fetuses had detailed fetal echocardiography by the fetal cardiologist after detection which were confirmed. Five (25%) of the fetuses had

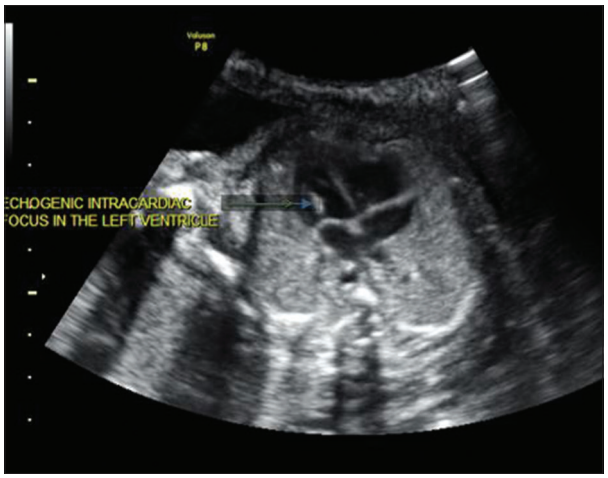

Figure 1: Ultrasound of the chest showing an echogenic focus (labeled) within the left ventricle of a fetus at 20 weeks of gestation

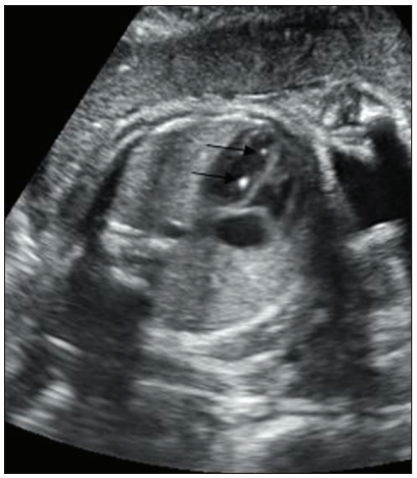

Figure 2: Ultrasound of the chest two echogenic foci (arrows) of different sizes within the left ventricle of a fetus at 22 weeks of gestation

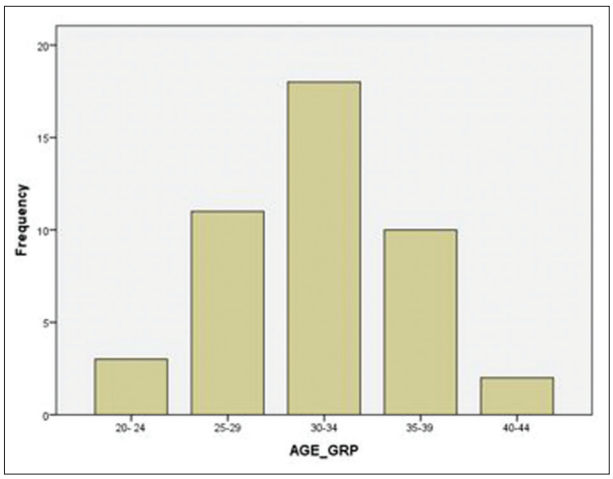

Figure 3: A bar chart showing the distribution of age groups among the mothers of the fetuses with intracardiac echogenic foci

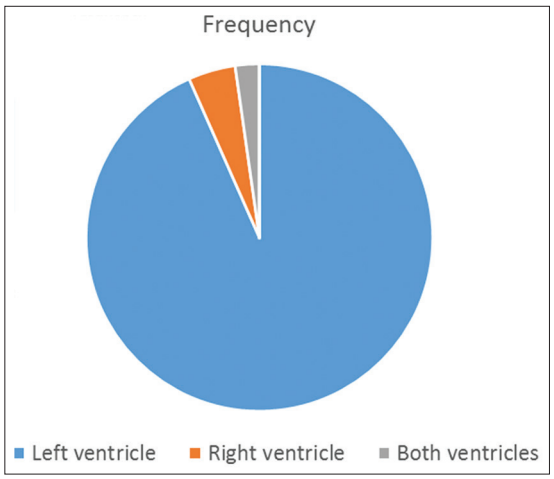

Figure 4: A Pie chart showing the distribution of intracardiac echogenic foci within the ventricles

structural cardiac anomalies, which were tricuspid regurgitations, ventricular septal defect (VSD), accelerated flow in the aorta, and hypoplastic left heart on fetal echocardiography [Table 4]. Three (60%) of these were classified as major anomalies, whereas the remaining 2 (40%) were minor anomalies [Table 4]. One out of the two fetuses with VSD had other soft markers, which were choroid plexus cysts and echogenic bowel; she had karyotyping done postdelivery, which confirmed Edwards' syndrome. No other structural abnormalities were detected in all the other fetuses during the prenatal screening for fetal anomalies.

DISCUSSION

ICEF is one of the most controversial sonographic features that has been described in the literature.[1-3] Some authors think that it represents a marker for disease in the fetus, whereas others think that it is a normal variant. ICEFs are very frequent findings during routine fetal ultrasound examination with a prevalence that ranges between 0.45% and 32.4%.[3-7] The prevalence in this study is 2.2%, which is similar to the findings of Mirza *et al*.[4] among the Middle Eastern population with a prevalence of 2.8%. Coco *et al*.[17] in a study in the USA found a prevalence of 3.8%. However, higher prevalence was recorded in the studies by Rebarber *et al*.[5] and Levy and Mintz[6] in the USA as well as Bhagwat[13] in India who had the prevalence of 14.8%, 22%, and 17.2%, respectively. Shipp *et al*.,[7] however, found a much higher prevalence of 32.4% among the Asian population. Levy and Mintz,[6] in their study, suggested that because of the high prevalence, ICEF is likely to be of a benign etiology, whereas Mirza *et al*.[4] and Rebarber *et al*.[5] suggested that there is a possibility of ethnic variation since it appears to be rare in some population and more common in other ones. This study is likely the first in sub-Saharan Africa and it suggests a low incidence in our environment. Further studies in this region are, however, advised.

Table 1: Risk factors of the mothers of the fetuses with intracardiac echogenic focus

Indication	Frequency (%)
No risk factor	29 (65.92)
Maternal age >35 years	11 (25.00)
HBSS	1 (2.27)
Previous baby with CHD	1 (2.27)
Retroviral infection	1 (2.27)
Twin cyesis	1 (2.27)
Total	44 (100.00)

CHD – Congenital heart defects; HBSS – Sickle cell hemoglobinopathy

Table 2: Frequency of the numbers of echogenic foci within the ventricles

Number of foci	Frequency (%)
1	42 (95.5)
2	2 (4.5)
Total	44 (100.0)

Table 3: Distribution of the intracardiac echogenic foci within the ventricles

Location	Frequency (%)
Both ventricles	1 (2.3)
Left ventricle	41 (93.2)
Right ventricles	2 (4.5)
Total	44 (100.0)

Table 4: Frequency and classification of associated structural cardiac anomalies on fetal echocardiography

Associated anomalies with ICEF	Frequency (%)	Category
None	15 (75)	-
VSD	2 (10)	Major
Tricuspid regurgitation	1 (5)	Minor
Hypoplastic left heart	1 (5)	Major
Accelerated aortic flow	1 (5)	Minor
Total	20 (100)	

ICEF – Intracardiac echogenic focus, VSD – Ventricular septal defect

The location of the ICEF may play a role in its etiology and significance. Most of the ICEFs are located within the left ventricle with the incidence varying between 72% and 98%,[1,3,6,8,9] and this was demonstrated in this study with an incidence of 92.3%. Most studies concluded that ICEFs located within the left ventricle, are likely related to the papillary muscle and/or chordae tendinae. Thus, indicating a normal variant, especially when there is no structural anomaly with the heart.

The significance of right ventricular or biventricular ICEF in the fetal heart in contrast to isolated left ventricular finding is not yet clear. Some studies suggested that right-sided ICEF were more frequently associated with fetal cardiac anomalies than were left-sided or bilateral ICEFs.[15,16] While some others suggest that right-sided or bilateral intracardiac echogenic foci had an approximately twice-greater risk of aneuploidy compared to the left-sided foci.[9] This was, however, not supported by our study since the three fetuses with major structural cardiac anomalies had the ICEF within the left ventricle. This indicates that all left ventricular ICEFs may not necessarily be normal variants.

Since ICEF is usually detected during the routine prenatal screening for fetal anomalies, the concern is usually to know if it is associated with other structural cardiac anomalies, thereby making it an indication for more detailed fetal echocardiography. In a study by Barsoom *et al*.[10] on isolated ICEF as an indication for more detailed fetal echocardiography, they found only one fetus with associated structural anomalies, and they concluded that "an isolated ICEF as a screening tool for the congenital cardiac disease had very low sensitivity." Simpson *et al*.[18] also concluded that "the finding of an echogenic focus does not merit detailed fetal echocardiography unless there are other concerns regarding the cardiac structure". Petrikovsky *et al*.[9] reported that all the 41 fetuses with an ICEF who underwent fetal cardiac echocardiography had normal cardiac anatomy. Wolman *et al*.[11] did not find any difference in the incidence of congenital cardiac defects in 138 fetuses with an isolated ICEF compared with a control group of 167 fetuses at low risk, all of whom underwent fetal echocardiography. The conclusion from these studies is that when an isolated ICEF is seen, it is most likely a normal variant and that fetal echocardiography is not indicated. Carriço *et al.,*[19] on the contrary, proposed that even though ICEF represents a normal variant of papillary muscle development, their presence should be interpreted as a possible risk for congenital heart defects. However, Guo *et al.,*[15] in a study in China among 2647 fetuses with ICEF, found cardiac anomalies in 101 (3.8%) fetuses. He suggested that ICEF, especially when right-sided, may signal a poor prognosis and deserves a further search for associated pathologies. In the present study, only twenty fetuses with ICEF underwent echocardiography, with 3 (15%) of them having associated major cardiac anomalies. This study points to the fact that ICEFs among the blacks may necessitate a detailed fetal echocardiographic evaluation.

Several authors have reported a possible association between an ICEF and chromosomal abnormalities, with Down syndrome being the most common.[12-14] In the first two sonographic reports of ICEF and aneuploidy, Bromley *et al*.[8] detected ICEF in 62 (4.7%) of 1312 control fetuses compared with 4 (18%) of 22 fetuses with trisomy 21, and Lehman *et al*.[20] reported ICEF in 39% of fetuses with trisomy 13 before 20 weeks. In another study by Winter *et al*.,[21] there was a 4.8-fold increase in relative risk for trisomy 21 in high-risk population with ICEF. All these

studies advised further genetic studies in fetuses with ICEF. Coco *et al.*,[17] in their study, found an increased risk of trisomy 21 in fetuses with ICEF, but they observed that two out of the three fetuses had other findings which included soft markers such as sandal gap deformity, bilateral pyelectasis, and two vessel cords among others and they concluded that the presence of another major or minor sign with ICEF justifies the performance of amniocentesis rather than an isolated ICEF. Although in our study, genetic test was not conducted routinely in the fetuses with ICEF due to the limitations in our environment, one of the fetuses with additional findings which were choroid plexus cysts and echogenic bowel, had genetic testing done postnatally which confirmed trisomy 13.

Soft markers are generally accepted as potential markers of chromosomal abnormalities during the second-trimester ultrasound scans, and they include nuchal thickening, hyperechoic bowel, ICEF, shortened femur or humerus, and renal pyelectasis with ICEF being the most common. These markers are nonspecific, are also present in fetuses without abnormalities, are often transient, and can be readily detected during the second trimester.[12-14] They may, however, be associated with other soft markers or structural abnormalities. The risk of fetal chromosomal abnormalities, especially Down syndrome, is said to increase with an increased number of soft markers or the presence of other soft markers with structural abnormalities, hence the need for genetic testing.[22,23] A fetus with an isolated soft marker may not need genetic testing. Bhagwat[13] in his study had a very high incidence of ICEF (31.2%), but he found no significant associated structural anomalies in the patients, and he concluded that if ICEF is not associated with other structural abnormalities, the need to perform invasive genetic diagnostic tests may not be warranted. This was corroborated by Brown *et al*.[3] and Rebarber *et al*.[5] However, Nyberg and Souter[12] in their study of 186 fetuses with trisomy 21 and 8728 controls, found ICEF as the most common soft marker (7.1%) in the fetuses with trisomy 21 and they said that the presence of a solitary soft marker should not be ignored.

The limitations of this study include the small number of fetuses that had fetal echocardiography as well as the inability to do karyotyping for the fetuses with ICEF.

CONCLUSION

There may be a need to add fetal echocardiography to rule out structural cardiac anomalies in fetuses with ICEF. However, further studies are needed in this environment to be able to have an in-depth knowledge of ICEF and our peculiarities.

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Conflicts of interest

There are no conflicts of interest.

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