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Original Article

Clinical Significance of Hyperechogenic Bowel in Second-Trimester Ultrasound Scan

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ABSTRACT

Background: This study aimed to report the incidence of bowel obstruction, chromosomal abnormality, congenital infection, fetal growth restriction (FGR), and otheranomalies in fetuses with hyperechogenic bowel (HEB) diagnosed during the second-trimester fetal ultrasound scan.

Methods: In total, 350 fetuses with a diagnosis of HEB in our maternal-fetal medicine referral center were evaluated with a detailed fetal ultrasound examination by an experienced perinatologist. If no associated anomalies were observed, women were counseled about the risk of potential fetal disorders and offered appropriate testing, including detailed fetal sonography, karyotype, maternal cytomegalovirus (CMV), and toxoplasmosis serology,as well as serial fetal biometry and bowel diameter follow up.

Results: Altogether there were 18(5.1%) fetuses with associated problems, including major anomalies, chromosomal abnormalities, and CMV infection. Moreover, 32(9.1%) fetuses developed FGR during follow-up.

Conclusion: An overall rate of adverse conditions of 14.2% with prenatally detected HEB serves to inform obstetricians and emphasizes the importance of careful screening fetal ultrasound studies and timely referral for an additional assessment about associated findings.It should be noted that isolated HEB has good outcomes.

Keywords: Echogenic bowel, Fetus, Pregnancy, Prenatal diagnosis

Introduction

The echogenicity of the fetal bowel is assessed during the routineantenatal ultrasound examination in weeks 18-22 to detect hyperechogenic bowel (HEB). This sonographic finding has been described as a normal variant due to hypoperistalsis or decreased fluid content of meconium. It is also known as a marker for several fetal disorders, such as cystic fibrosis, aneuploidy, toxoplasmosis, and cytomegalovirus (1-5). Moreover, studies have shown that the HEB is associated with fetal growth restriction (FGR) (2). It has also been reported that when the fetus ingests bloody fluid, the bowel can appear echogenic since blood is very echogenic (6). The HEB is probably a sign of bowel abnormalities, such as bowel obstruction (8).In addition, an association of HEB was observed with lactose intolerance and celiac disease (15).

Despite all these findings, if HEB reported as an isolated finding, the prognosis is usually good (7).Given that the prevalence of HEB is estimatedat 4.2 per 1000 singleton pregnancies (16), these findings highlight the need for investigating the underlying etiology carefully leading to the development of a precise management protocol of fetal echogenic bowel.

This study aimed to evaluate the clinical significance of HEB in our population and assess the need for additional investigations in isolated HEB cases.

Methods

Since all pregnant women should have to do ultrasonography between 18-22 weeks of

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gestation in Iran, a case series study was conductedon all singleton pregnancies with a diagnosis of HEBatMaternal-Fetal Medicine Center of Mahdiyeh Teaching Hospital or the private office of Dr Solmaz Piri, Tehran, Iran. These patients were ultrasound-scanned using a GE healthcare Austria (voluson E8) machine with a transducer of 3-5 MHz by one of the two academics educated perinatologists. Our criteria for the diagnosis of HEB was echogenicity similar to or greater than that of adjacent bone, whereas the ultrasound gain was set to the lowest point at which bone appeared white (1).

The demographic characteristics of the patients covering such information as age, gravidity, gestational age, history of smoking or medication by the mother, history of medical illness in mother, history of bleeding during pregnancy, and telephone number were recorded in this study. In these patients, if the bowel seemed dilated, the diameter of the small intestine and colon were measured simultaneously in order to diagnose bowel obstruction. The location of the placenta (to ensure that retroplacental bleeding is checked) and amniotic fluid index were recorded in this study.

In all fetuses, a detailed fetal ultrasound scan wasperformed, and if the simultaneous structural disorder of the fetus was present, other soft markers or further evidence in favor of fetal infection were recorded in this study.All mothers were asked if they had recently had vaginal bleeding (6). The maternal serologies including IgG, IgM, and avidity testing were orderedfor recent cytomegalovirus (CMV) or toxoplasmosis infection (3).If there was serologic evidence of recent maternal infection, fetal infection (CMV, toxoplasmosis) were further evaluated by a polymerase chain reaction (PCR) of DNA in amniotic fluid or amniocytes (9,10).If a karyotype was not already available, further assessment including amniocentesis for definitive fetal chromosomal studies or cell-free DNA screening of maternal blood was suggested (4,5).

Every 4-week follow-up sonography from week 28 (11)was recommended to re-evaluate fetal growth and the fetal bowel (in terms of symptoms of bowel obstruction) since the fetuses were at an increased risk of FGR. In the follow-up sonography after 28 weeks, if the small intestine had a diameter greater than 7 mm or the colon had a diameter greater than 18 mm, or peristalsis was seen in the colon (12), obstruction would have been suspected; accordingly, they were evaluated after birth. Our definition of FGR was according to the Delphi procedure in 2016 (3), and the Hadlock chart was used (14).All patients were followed-up till after birth to recognizedisorders related to HEB that was diagnosed at any time during pregnancy. Eventually, fetuses or neonates with adverse outcomes were compared with normal ones in terms of accompanying sonographic findings.

Statistical Analysis

The data obtained from this case series study were analyzed in SPSS software (version 21) through descriptive statistics (i.e., frequency and mean).

Ethical Considerations

The study protocol was approved by the Ethics Committee of Shahid Beheshti University of Medical Sciences, Tehran, Iran (IR.SBMU.RETECH.REC.1398.692). Moreover, written consent was obtained from all patients participating in the studyin order not to undermine the patient's rights.

Results

This study evaluated 350 fetuses with HEB,all of them were singleton pregnancies. The mean maternal age was 34 years old (age range: 19-47 years), and the majority of them were under 35 years of age. Among these mothers, 163 (46.6%) cases were primigravida, and all the pregnancies were between 18-22 weeks of gestation (mean: 20 weeks). The details of preexisting medical records revealed that 24 (6.9%), 18 (5.1%), and 53 (15.1%) mothers had pregestational diabetes, chronic hypertension, and hypothyroidism, respectively. Moreover, 1 (0.3%) case had the nephrotic syndrome, and another case (0.3%) had inflammatory bowel disease. In addition, 8 (2.3%), 2 (0.6%), and 2 (0.6%) mothers suffered from epilepsy, systemic lupus erythematosus, and asthma, respectively.

It is worth mentioning that almost all mothers were non-smokers, except for5 (1.4%) cases.In addition, all of them received multivitamins (prenatal supplements), and the most prevalent drugs they took other than multivitamins included aspirin, enoxaparin, levothyroxine, metformin, insulin, methyldopa, and vaginal progesterone. Notably, none of these medications were parasympatholytic or parasympathomimetic to be able to affect the bowel movements of the fetus (Table1).

Placental location was recorded in all cases, and 4 (1.2%) cases had placenta previa. Moreover,

Table 1. Summary characteristics of women with ultrasound findings of fetal echogenic bowel

ITEM	Included case, n (%) 350
Maternal age ≥ 35 years old	153 (43.7%)
Primigravida	163 (46.6%)
Multigravida	187 (53.4%)
Smoker	5 (1.4%)
Medication usage*	144 (41.1%)
Preexisting medical condition	101 (28.8%)

* Other than the routine supplements of pregnancy

the positions of the placenta were anterior (n=150, 42.8%), posterior (n=154, 44.0%), lateral (n=16, 4.5%), and fundal (n=2, 0.6%). In one of the patients, the subchorionic hematoma was found. It should be noted that 45 (12.8%) mothers had a history of vaginal bleeding overthe last 2 weeks of sonography.

Out of all patients, anhydramnios, oligohydramnios, and polyhydramnios were identified in 9 (2.6%), 36 (10.3%), and 3 (0.9%) mothers. The remained cases (n=302,86.2%) had normal amniotic fluid index.

Furthermore, 60 (17.1%) patients underwent chorion villus sampling or amniocentesis before the diagnosis of HEB due to indications, such as the first or second positive trimester screening test. In total, 6 (1.7%) mothers were subjected to amniocentesis after the diagnosis of HEB. The others declined to do invasive testing; therefore, cell-free DNA testing was requested for them.

Simultaneously with the HEB, ventriculomegaly was identified in20 (5.7%) fetuses. Moreover, other soft markers included short nasal bone (n=24, 6.9%), hydronephrosis (n=9, 2.6%), short humerus (n=19, 5.4%), short femur (n=21, 6.0%), single umbilical artery (n=1, 0.3%), and increased nuchal fold (n=12, 3.4%)(Table2).

After completing allevaluations, the complications in fetuses included multiple anomalies (n=2,0.6%), central nervous system anomaly (i.e., dandy-walker syndrome) (n=1,0.3%), cardiac disease (n=2, 0.6%) (tetralogy of fallot [n=1] and transposition of great arteries [n=1]), omphalocele (n=1,0.3%), jejunal atresia (n=1,0.3%), hydropsfetalis (n=1,0.3%), chromosomal disorder (n=3, 0.9%) (trisomy 21[n=2] and trisomy 22[n=1]), fetal CMV infection that was confirmed by amniotic fluid PCR (n=1, 0.3%). It should be mentioned that 32 (9.1%) fetuses developed FGR, and ichthyosis was diagnosed after birth in2 (0.6%) newborns.

In total, 8 (2.3%) newbornsdied within28 days of birthdue to prematurity (n=2), sepsis (n=1), cardiac anomaly (n=1), hydropsfetalis (n=1), and labor asphyxia (n=1); however, the cause of death of the other two newborns was unclear.

Table2. Simultaneous soft markers

Soft marker	Included cases n (%)
Ventriculomegaly	20 (5.7%)
Short nasal bone	24 (6.9%)
Hydronephrosis	9 (2.6%)
Short humerus	19 (5.4%)
Short femur	21 (6.0%)
Single umbilical artery	1 (0.3%)
Increased nuchal fold	12 (3.4%)

Intrauterine death developed in8 (2.3%) fetuses, and 23 (6.6%) mothers terminated the pregnancy due to other simultaneous anomalies, CMV infection, genetic disorders, or anhydramnios.

The only newborn with jejunal atresia underwent surgery after birth, and the other 310 (88.5%) mothersowned healthy live birth. Table 3 summarizes concomitant findings in fetuses with trisomy and CMV infection. It reveals that the HEB is not an isolated finding in none of these clinical conditions.

Table3. Accompanying findings in fetuses with *the* genetic disorder, infection, and bowel disorder

Diagnosis	Accompanying sonographic findings
Trisomy 21	Increased nuchal fold
Trisomy 21	ventriculomegaly
Trisomy 22	Increased nuchal fold, short femur, short humerus
CMV* infection	ventriculomegaly
Jejunal atresia	polyhydramnios

* Cytomegalovirus

Discussion

This study aimed to understand the significance of HEB in fetuses during the second trimester. The result of our study showed that despite therelationshipof HEB with chromosomal abnormalities, bowel obstruction, and congenital infection, it is not an isolated sonographic finding in the mentioned cases. Moreover, all fetuses with adverse outcomes,except for FGR had accompanying findings on sonography, including soft markers, amniotic fluid index abnormality, or structural anomaly.

In our population, 32 (9.1%) fetuses with isolated HEB developed FGR, and others obtained a good outcome.

Other studies showed a relationship between blood ingestionby the fetus and HEB (6). In total, 45 patients had a history of vaginal bleeding, and one case of subchorionic hematoma was identified in the present study. Moreover, 60 patients had a history of invasive prenatal testing before the echogenic bowel was seen on ultrasound, which is

probably due to blood ingestion; however, it is not confirmed.

In our study, 3 (0.9%) fetuses had chromosomal abnormalities without any major structural disorder on ultrasonography although they had soft markers other than HEB simultaneously. This rate is lower thanthat reported ina study byD'Amico A et al. in 2020. They reported that the incidence of chromosomal abnormalities was 3.3% in fetuses with HEB (4). The prevalence of chromosomal abnormalities has a wide range in different studies, and it varies from 3.6% to 16% in other studies (1, 5). Patients with other structural anomaly or anhydramnios on sonography refused to participate in a karyotype study before or after termination. Therefore, the lower incidence rate in our study population may be attributed to the lack of access to all genetic results.

There was one (0.3%) confirmedcase of congenital infection with ventriculomegaly in our study. This result is consistent with the findings of a study conducted by Al-Kouatly HB et al. (1). The rate of congenital infection was also low in other studies (2, 3).

Bowel abnormalities were reportedby up to 3% in a study performed in Nova Scotia (10). However, in our study, there was one case of omphalocele and one case of jejunal atresia with polyhydramnios, which was in line with the results of a study performed by Laird A et al. (8).

It seems that if there are bowel abnormalities, it will be associated with the findings, such as polyhydramnios or bowel dilatation on sonography.

Several studies indicated different rates of FGR development.It was estimated at 9.1% and 14% in the present study and the study conducted by Findley R et al., respectively (2); however, it was obtained at 34% in another study (3). These differences are possibly due to variations in FGR definitions and different nomograms that have been used for FGR detection.

Among the limitation of this study, one can name a lack of assessment of fetuses in terms of cystic fibrosis due to the high expense of genetic tests for this disease in Iran. Moreover, the screening of these genes is very time-consuming in our laboratories; accordingly, the parents lose time for legal abortion and almost all of our patients refuse to carry it out. The other limitation was the lack of performing other diagnostic tests in patients who had another finding with poor outcome in sonography since these parents preferred to terminate the pregnancy without additional evaluations.

Given that the correct guidance of couples in case of isolated HEB is very importantto avoid creating too much anxiety and at the same time prevent underestimation, further studies are suggested to investigate the isolated cases of HEB with prospective design and financial sponsor to reduce parental costs.

Conclusion

Despite the rate of adverse clinical conditions with HEB which are observed in the second-trimester sonography (14.2%) which shows its importance, it should be emphasized that isolated HEB in ultrasound wasnot associated with any undesirable consequences other than FGR. Therefore, this study highlights the significance of precise detailed fetal sonography while there is HEB.

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Conflicts of interest

The authors declare that they have no conflict of interest regarding the publication of the study.

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