

# Hyperechogenic fetal bowel: an ultrasonographic marker for adverse fetal and neonatal outcome?

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## Summary

**“Soft markers” are considered variants of normal and should be considered distinct from fetal anatomic malformations. Hyperechogenicity of the fetal bowel, is one of the few soft markers that can also associated with a variety of other pathologic conditions. In this review we will focalise our attention on the significance of an increased echogenicity of fetal bowel and on management of fetuses with this condition.**

*Key Words: prenatal screening, ultrasonography, fetal softs markers, hyperechogenic fetal bowel.*

## Introduction

The use and understanding of ultrasound of the so-called “soft markers” and their screening relative risks is an important option in the care of pregnant women (1-3). Currently, the presence of a “significant” ultrasound marker adds risk to the likelihood of fetal pathology, but the absence of soft markers, except in controlled situations, should not be used to reduce fetal risk (4-6).

Individual soft markers will vary in the degree of association with fetal aneuploidy. Detection of multiple soft markers will increase the significance of the finding, compared with seeing the same marker isolated (7, 8). “Soft markers” are considered variants of normal but should be considered distinct from fetal anatomic malformations and (or) growth restriction that also increase perinatal and genetic risks (9-12).

Hyperechogenicity of the fetal bowel, is one of the few that can also associated with a variety of other pathologic conditions. Perhaps this is even more important than the association with aneuploidy and therefore should be carefully considered in every fetus in which this marker is detected. Fetal echogenic bowel, first described in 1985 (13), remains poorly understood with no clear definition or guidelines for clinical management. This has important consequences for parents, obstetricians, radiologists, neonatologists and paediatric surgeons.

## Definition

Hyperechogenicity has been defined by most authors as bowel of similar or greater echogenicity than surrounding bone (14-16), but others have relied on comparisons with fetal liver (17, 18) or lung (19).

These subjective assessments are prone to significant inter-observer variation but attempts to introduce objective measures have been difficult (19).

## Incidence

Fetal echogenic bowel is present in 0-6% to 1-4% of all second trimester fetuses (16-18) and is detectable at the time of routine antenatal ultrasound scanning. Fetal small bowel becomes progressively more visible by ultrasound scan during the second trimester as relatively ‘bright’ meconium accumulates within its lumen from about 16 weeks’ gestation.

It is readily distinguishable from the more florid features of meconium peritonitis such as fetal ascites, intra-abdominal calcification, and intestinal dilatation (13, 20-22).

Hyperechogenicity as an isolated finding before 20 weeks’ gestation is usually transient, disappearing on serial scans during the next few weeks (13, 14, 22-24). Resolution is associated with normal bowel function in most infants (14, 18, 22). Persistently hyperechogenic small bowel in the third trimester is more likely to reflect underlying pathology even though a normal outcome is still possible (22, 23). The few reports of isolated hyperechogenic colonic meconium arising in the third trimester have not been associated with underlying pathology (25).

## Ultrasound and Grading System for Echogenic Bowel

A grading system based on comparison of the echogenicity of fetal bowel and surrounding bone relative to the ultrasound machine gain setting minimizes observer variability and should be used.

Grading scale proposed by Slotnick et al. (26):

Grade 0 = Normal

Grade 1 = Increased echogenicity, but less echogenic than bone

Grade 2 = Echogenicity equal to bone

Grade 3 = Echogenicity greater than bone

Whenever echogenic bowel is suspected, the gain setting should be lowered to enable this comparison and to ensure that bowel hyperechogenicity is real (26). This should help to minimize a false-positive diagnosis of hyperechogenicity.

### Pathogenic mechanism

The development of hyperechogenic bowel may be attributable to hypoperistalsis and/or decreased fluid content of the meconium (27). This could explain its occurrence in fetuses with karyotype abnormalities where no gross bowel pathology has been identified (28) and in mechanical proximal bowel obstruction or Cystic Fibrosis (CF). Resolution of hyperechogenicity in the normal fetus parallels the increase in swallowed amniotic fluid in later pregnancy. The link between hyperechogenic fetal bowel and placental dysfunction is complex but it has been suggested that chronic intrauterine gut ischaemia is responsible for both the hyperechogenicity and impaired neonatal function (17, 29).

### Causes of echogenic bowel

These are the causes of echogenic bowel:

- Fetal aneuploidy, especially Trisomy 21 and less frequently trisomy 18 or 13, Turner's syndrome and triploidy.  
The cause of echogenic bowel in aneuploidy is less clear. It is thought to be due to decreased bowel motility with increased water absorption from the meconium. There appears to be decreased microvillar enzymes activity in the amniotic fluid of aneuploid fetuses. The association of echogenic bowel with aneuploidy, particularly trisomy 21, has been demonstrated in several studies (30, 31).
- Small bowel obstruction proximally (especially duodenal atresia) can produce hyperechogenic bowel by reducing the meconium fluid content (31, 34).
- Oligohydramnios. Echogenic bowel is also thought to be due to decreased amniotic fluid content of meconium (31-34).
- Hirschsprung's disease (increased frequency in fetuses with Down syndrome) could produce hyperechogenic bowel due to hypoperistalsis.
- Bowel atresia (35-37). Echogenic bowel is thought to be due to decreased amniotic fluid content of the meconium.
- IUGR. Most fetuses with IUGR do not have echogenic bowel. The suggested mechanism is bowel ischemia due to hemodynamic redistribution and subsequent mesenteric ischemia is therefore questionable. Intrauterine fetal growth restriction has been estimated to complicate 4% to 18% of pregnancies with echogenic bowel, even in the setting of a normal karyotype (38-41). The association of echogenic bowel with IUGR may be caused in part by ischemia from redistribution of blood flow away from the gut (32). The presence of IUGR or elevated maternal serum alpha-fetoprotein in the second trimester in association with echogenic bowel seems to be associated with a particularly poor fetal prognosis. In one series, all six fetuses with both echogenic bowel and elevated maternal serum alpha-fetoprotein were growth restricted: four died in utero, one of two live-born infants died during the neonatal period, and the single survivor developed necrotizing enterocolitis requiring surgery (42). This poor prognosis has been confirmed in other studies (43). Poor perinatal outcome due to uteroplacental insufficiency, especially in cases in which the maternal se-

rum alpha-fetoprotein concentration is elevated (31, 34, 35, 44). As alpha-fetoprotein is a pure fetal product, cases with raised levels are likely to have experienced significant fetomaternal bleeding. This group may represent a subset of fetuses with severe placental damage.

- Intra-amniotic hemorrhage (29, 45). Echogenic bowel is probably due to swallowed blood products resulting in a hypercellular meconium, probably with small clots within the bowel lumen. This is thought to be caused by fetal swallowing of blood, which is very echogenic. One series found that 22% of fetuses with echogenic bowel had evidence of heme pigment in amniotic fluid (46). In another series, 3.1% of amniotic fluid was grossly contaminated with blood (47). Petrikovsky et al. (48) examined 28 fetuses before and 12 hours after intrauterine transfusion, a procedure that commonly introduces blood into the amniotic cavity by post-puncture bleeding. Although none of the fetuses had echogenic bowel before intrauterine transfusion, 25% of these fetuses had evidence of bowel echogenicity within 12 hours of the bleeding episode and 18% still had evidence of echogenicity 2 weeks later (48). In general, pregnancies with evidence of intra-amniotic bleeding but without additional anomalies have a good prognosis (43).
- Cystic fibrosis (CF). Echogenic bowel has been reported to be found on ultrasound in 50% to 78% of fetuses affected with CF (49, 50). The association of echogenic bowel with fetuses affected with CF is thought to be caused by changes in the consistency of meconium in the small intestine as a result of abnormalities in pancreatic enzyme secretion. This can result in detectable sonographic findings, such as diffuse echogenic bowel, focal echogenic bowel with calcifications, a hyperechoic mass, or bowel dilation (38, 41, 50). These findings may appear as early as the second trimester (41, 50), CF has been reported to affect 0.8% to 13.3% of fetuses with echogenic bowel (40, 47, 51-55), markedly higher than the rate of CF expected in a white population in which the carrier frequency is 1 in 25. As with any screening marker, echogenic bowel is most predictive of CF in populations at highest risk for CF. High-risk populations, however, are those that are most likely to be screened routinely for CF. There is some evidence that the detection of echogenic bowel in populations at low-risk for this disease does not increase the risk of CF when compared with the background risk.
- Other less common associations. Cytomegalovirus (CMV), Toxoplasmosis, Parvovirus. The association of congenital infections with echogenic bowel has been reported to be from 0% to 10% (40). The most commonly detected infectious agent is CMV. Simon-Bouy et al. (47) prospectively checked maternal rubella, toxoplasmosis, and CMV serologies (IgG and IgM) in 682 cases of fetal echogenic bowel. When seroconversion was observed, CMV polymerase chain reaction testing was performed in amniotic fluid. Parvovirus B19 polymerase chain reaction was also performed in all cases. A total of 19 viral infections were diagnosed, which represented 2.8% of fetuses: 15 (2.2%) CMV and 4 (0.6%) parvovirus. In 11 of the fetuses with CMV, echogenic bowel was the only sonographic abnormality noted. All four of the fetuses with parvovirus had asso-

ciated abnormalities. It is unclear how a viral infection results in the echogenic appearance of the bowel. It may be caused by direct intestinal damage from inflammation or meconium peritonitis or indirectly by ascites, anemia, or growth restriction (38, 54).

Thalassemia. The high frequency of echogenic bowel in first and second trimester fetuses suggests bowel wall edema, due to severe anemia and hypoxia may be the cause (55).

## Outcome

Combining data from five large North American studies of second trimester fetuses with hyperechogenic bowel, shows that in almost 60% of the 230 cases no abnormalities were found after birth (14, 16, 18, 28). Among the remaining, however, there was an abnormally high incidence of karyotype abnormalities, intra-uterine growth retardation, and perinatal death. The incidence of aneuploidy varied from 3 to 27%, with Down's syndrome accounting for the majority, and other trisomies and sex chromosome anomalies, such as Turner's syndrome, for most of the others. In some, hyperechogenic bowel was the only detectable sonographic abnormality, which supports an argument for karyotyping these fetuses. In a retrospective study Nyberg et al. found hyperechogenic bowel in 7% of second trimester fetuses with Down's syndrome and in over half it was an isolated finding (29). Nevertheless, hyperechogenic bowel is neither very sensitive nor specific as a marker of trisomy 21 in the second trimester fetus (18, 29, 30, 56).

Intrauterine growth retardation was evident in around 15% of fetuses with hyperechogenic bowel, even after excluding those with karyotype anomalies. Moreover, this group of patients contributed to the 10% of cases in whom perinatal death was recorded. This is a complex area with probable links between hyperechogenic bowel, uteroplacental insufficiency, prematurity and functional neonatal intestinal obstruction. Blott et al described eight premature, growth retarded infants with hyperechogenic bowel, absent umbilical artery end diastolic flow velocities, and neonatal intestinal obstruction due to meconium (57). These observations have been subsequently confirmed by a prospective case control study in which enteral feeding was also shown to be significantly delayed in the surviving infants (58). Other rarer associations with hyperechogenic fetal bowel have been reported: mechanical intestinal obstruction due to imperforate anus, intestinal atresia, or volvulus (14, 59, 60); congenital cytomegalovirus infection (18, 29, 61, 62), and maternal systemic lupus erythematosus (18, 22, 63). We have observed it in association with bloodstained amniotic fluid which would have been swallowed by the fetus. Hyperechogenic bowel can also be a marker of meconium ileus attributable to cystic fibrosis (CF), but its sensitivity and specificity in this context are uncertain (14, 15, 64, 65). In prospective evaluations of pregnancies at risk for CF, hyperechogenic bowel has been documented in up to 60% of affected fetuses (66). However, several studies of second trimester fetuses with hyperechogenic bowel have not identified a single infant with CF (16-18, 28). Lack of formal testing and relatively short follow up periods may account for this but hyperechogenic bowel by itself is probably only a weak marker of CF. The presence of hyperechogenic bowel before 20 weeks of gestation may in fact be misleading and false positive results have been

reported (67). When combined with bowel dilatation, the finding is probably much more suggestive of meconium ileus (14, 16, 68). Given this spectrum of associated pathologies, it is not surprising that perinatal death is linked to hyperechogenic bowel in the fetus. The risk of an adverse fetal outcome seems to be greater the more echogenic the bowel and is highest when the density is comparable with bone (17, 18, 28).

## Management

What practical steps are necessary in the second trimester fetus with hyperechogenic bowel? A detailed parental history is clearly important because of the links with karyotype anomalies, intrauterine infection, and CF. The sonographic fetal survey must be complete to exclude associated structural problems and features such as intestinal dilatation and fetal ascites. Serial ultrasound assessments may detect resolution of the hyperechogenicity and can be used to monitor fetal growth and placental function. More invasive investigations such as parental carrier testing for CF and fetal karyotyping are probably justified, but more detailed studies are necessary before we can be certain of the risk benefit ratio and so that high risk subgroups can be defined. Infants with a history of persistently hyperechogenic bowel and particularly those with growth retardation and/or documented abnormalities of umbilical artery blood flow are at risk of functional neonatal intestinal obstruction. A greater demand for parenteral nutrition should be anticipated in such cases and rectal washouts or water soluble contrast enemas may be necessary to release meconium plugging and to exclude mechanical obstruction. A sweat test should be performed subsequently.

## Conclusion

A reproducible definition of hyperechogenic bowel is urgently needed so that large, controlled, prospective studies with standardised equipment settings and methods of collection can replace the largely retrospective data currently available. This would permit accurate estimates of incidence/prevalence and reliable data on various adverse outcomes. A more objective measure of fetal bowel echogenicity is required before this can be achieved. A recently published multicentre French study of 182 cases of hyperechogenic fetal bowel is completely consistent with the pooled North American data in terms of the incidence and spectrum of associated pathologies (69).

The small group of fetuses with intrauterine infection also included, however, two cases of toxoplasmosis.

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