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REVIEW ARTICLE

Controversial Ultrasound Findings in Mid-Trimester Pregnancy

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ABSTRACT

US equipment became more and more important for the practicing obstetricians, and the demands for practicing US as part of the antenatal care becomes sometimes routine in certain areas. A lot of US workshops are practiced trying to put the guidelines for using the US in this domain, and every now and then new markers and US signs are added that could have some significance in relation to the fetal outcome.

Here a problem now exists, which is the gap between the ability to detect and the understanding of the significance of these findings, and this of course creates a great deal of improper counseling which leads to anxiety and confusions.

The aim of my lecture is to shed some light on some controversial US signs, like echogenic bowel, renal pyelectasis, cardiac echogenic foci, choroid plexus cyst, club foot, polydactyly, single umbilical artery and mild ventriculomegaly.

First I shall discuss the epidemiology—the pathophysiology, underlying risk for associated chromosomal anomalies and the most important is the significance of these signs, if present alone, so trying to suit out an evidence-based approach to their management and to provide the clinician with all the data that enables him to properly counsel the parents and eliminates the confusion created by the mere detection of these findings.

Keywords: Fetal echogenic bowel, Fetal renal pyelectasis, Fetal cardiac echogenic foci, Fetal choroid plexus cyst, Fetal club foot, Fetal polydactyly, Single umbilical art, Fetal mild ventriculomegaly.

INTRODUCTION

A lot of ultrasound (US) workshops are practiced trying to put the guidelines for fetal anatomy scan. Every now and then new markers and US signs are added that could have some significance in relation to the fetal outcome. A problem now exists, it is the gap between easiness of detection of these signs and the understanding of the significance of their presence, and this of course creates a great deal of improper counseling which leads to anxiety and confusions.

In the review we shall shed some light on some controversial US signs, discussing the epidemiology—the pathophysiology, underlying risk for associated chromosomal anomalies and the most important is the significance of these signs if present alone, so trying to suit out an evidence-based approach to their management and to provide the clinician with all the data that enables him to properly counsel the parents and eliminates the confusion created by the mere detection of these findings.

Echogenic Bowel (Fig. 1)

Definition: It is hyperechoic bowel compared to adjacent bone reported to be present in 0.2 to 1.4% of 2nd trimester US. It is related to aneuploidy-trisomy 21 (T21), congenital infection: CMV, toxoplasmosis, parvovirus; cystic fibrosis; intra-amniotic bleeding; IUGR; thalassemia.[1]

US diagnosis depends on detection of echogenic bowel which is equal to the surrounding bone with no respect to the grading of echogenicity.

What is the Pathophysiology in each Associated Finding[2]?

- *In T21*: Poor bowel motility resulting in poor water and thickened meconium
- *In fetal infection*: Meconium peritonitis with bowel edema, perforation with focal calcification at the perforation sites
- *In IUGR*: Areas of ischemia due to redistribution of blood flow away from the gut
- *In cystic fibrosis*: Abnormal pancreatic enzymes leading to change in meconium consistency leading to diffuse or focal echogenic areas with dilated bowel
- *In intra-amniotic bleeding*: Swallowing of blood.

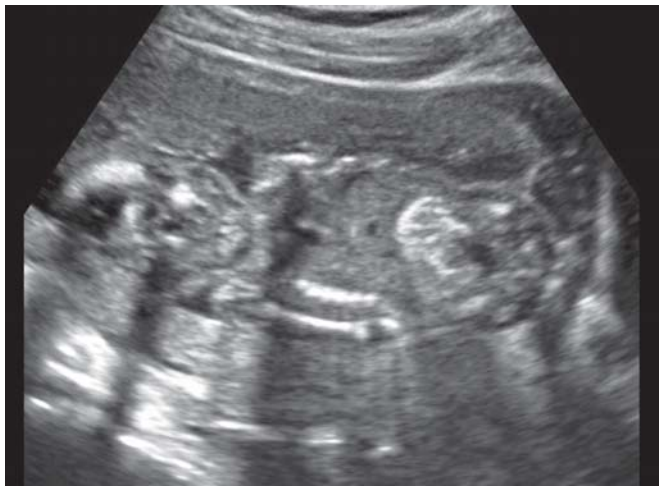


Fig. 1: Echogenic bowel

The prognosis of echogenic bowel depends mostly on whether or not there are associated fetal abnormalities.

One study showed 34% have poor perinatal outcome especially in early IUGR or elevated maternal alpha-feto protein.[3]

Larger study showed that 447 (65.5%) of 682 cases of echogenic bowel resulted in the birth of a normal healthy newborn.[4]

Evaluation and Management of Echogenic Bowel

The finding of echogenic bowel should prompt a work-up of:

1. History of intra-amniotic bleeding is listed with careful examination of the amniotic fluid and placenta
2. Detailed fetal anatomy scan
3. Amniocentesis is recommended even when isolated
4. CF carrier testing for both parents should be recommended
5. Maternal serological testing for CMV and toxoplasmosis, IgG, IgM and if in doubt of infection do PCR for amniotic fluid.

If all are normal, strict follow-up for evidence of IUGR and later some form of fetal evaluating testing is done. Doppler or BPP seems warranted because of the possible association with IU fetal demise.

Renal Pyelectasis (Fig. 2)

Pyel means 'Puelos' which further means 'basin' and ectasis implies to the distension of hollow organs.

Renal pyelectasis is the mild dilatation of the renal pelvis. Its incidence is in between 0.3 and 4.5% of antenatal US.

The cut-off value used most frequently is ant-post diameter > 4 mm for 2nd trimester and > 7 mm for thereafter.[5]

Often bilateral, if unilateral more on the left side. More in male fetuses, laterality does not seem to be useful in prognosis but a study showed that urinary tract pathology at birth was significantly higher in unilateral pyelectasis.

Pathophysiology of pyelectasis: It was related to aneuploidy, mainly T21.

First suggested by Benacerraf et al in 1990[5] and the association of pyelectasis with T21 is strongest when other anomalies are present,[6] but what about isolated mild pyelectasis?

Havutcu el al[7] in a retrospective study of 25,582 low risk cases, 301 cases of isolated pyelectasis > 5 mm were detected and none had aneuploidy.

In another study, Coplen and Jeanty[8] had 12,672 cases, 2.9% had mild pyelectasis > 4 mm, of which 83% were isolated, likelihood ratio of T21 was 3.79. They concluded that in the absence of other findings, isolated pyelectasis is not a justification for amniocentesis.

In another study, isolated renal pyelectasis has a sensitivity of 0.02 for the diagnosis of fetuses with Down syndrome. It would be necessary to screen 30,404 women in order to diagnose one case.[9]

Pyelectasis and Postnatal Abnormalities

In 60 to 70% of fetuses, the pyelectasis remains stable, improves or resolves, 1/3 has progression of their pyelectasis.

Wollenberg et al[10] showed that none of 20 children with a prenatal diagnosis of mild renal pelvis dilatation 7 to 9.9 mm during the 3rd trimester experienced a urinary tract infection or underwent surgery.

In contrast 5/22, 10 to 14.9 and 23/36 had severe hydronephrosis >15 mm had either a UTI or required surgery.

Management of Pregnancy with Pyelectasis

- Accurate measurement is required and repeated
- Careful search for concomitant abnormalities
- Fetal echocardiogram can be considered to evaluate the fetal heart comprehensively
- In the absence of other anomalies and soft markers or risk factors for aneuploidy, such as maternal age, amniocentesis, is not warranted
- Because 30% of cases with mild pyelectasis will proceed to hydronephrosis, follow-up of the renal pelvis diameter in the 3rd trimester is recommended
- It is recommended that all infants with persistent mild pyelectasis undergo some degree of postnatal evaluation or surveillance.

Choroid Plexus (CP) Cyst (Fig. 3)

Appears as well-circumscribed echolucent cyst within the Choroid Plexus (CP). It results from entrapment of CSF within

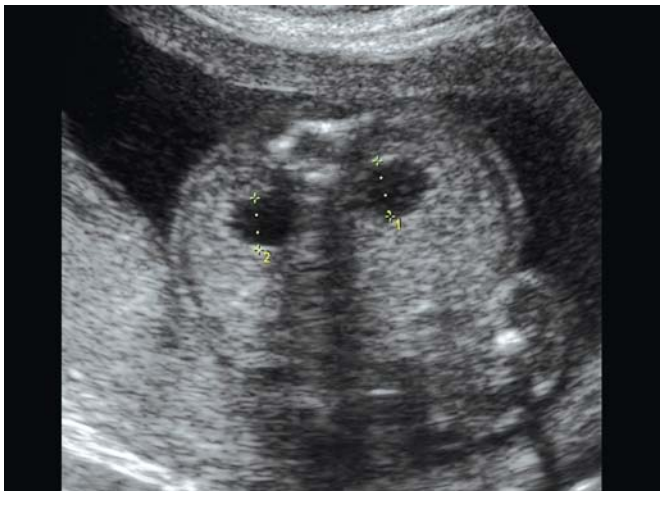


Fig. 2: Renal pyelectasis

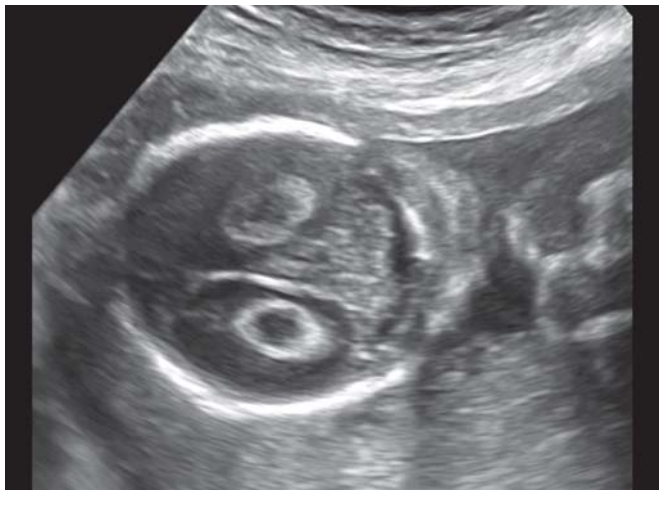


Fig. 3: Choroid plexus cyst

tangled villi of the CP and as the stroma in the CP decreases with increasing age, this fluid is released and cyst resolve, incidence is around 1% in mid-trimester.

It could be single, multiple, uni- or bilateral, and 95% disappear before 26 weeks.[11] It is associated with increased risk of aneuploidy mainly T18. About 71% of trisomy, 18 fetuses have CP cysts but usually associated with additional sonographic abnormalities.

No evidence of relation between aneuploidy and location of the cysts (unibilateral), size of the cyst, morphology of the cyst.

Dilemma arises with isolated CP cysts with no other specific features apart from these cysts. In a meta-analysis of more than 2000 cases of isolated CPC showed that T18 was found in 1/128.[11] In other meta-analysis,[12] it was concluded that amniocentesis is only offered if isolated CP with age > 36 or with abnormal serum multiple marker screen.

In a large prospective study,[3] 16000 cases were examined and 302 choroid plexus cyst were diagnosed, 263 of them were isolated; the e-study concluded that only choroid plexus cyst with additional risk factor warrants amniocentesis.

- In a similar meta-analysis,[14] the number of examined cases were 106,732, and isolated choroid plexus cyst in patients < 35 years were 1,017 (1%), and the conclusion was detection of isolated CPCs in women < 35 years of age does not increase the risk of T18, and amniocentesis is not warranted.
- Management of CPC:
  - Detailed fetal anatomy, looking for any additional abnormalities
  - Careful examination of the hands are very helpful
  - Fetal echocardiogram can be considered
  - Amniocentesis is offered only if:
    i. Maternal age in isolated CP > 35 years
    ii. Presence of any other sonographic abnormalities
    iii. Positive multiple marker screen
  - For a karyotypically normal fetus, CPCs are not associated with adverse pregnancy outcomes.

Cardiac Echogenic Foci (EF) (Figs 4A and B)

They are defined as discrete echogenic foci located in the chorda tendinea not attached to the ventricular walls and moving with the AV valve—mainly related to the mitral valve also can be seen in the right ventricle.[15]

Origin

- They are thought to represent calcifications within the fetal papillary muscle
- Collection of fibrous tissue with increased echogenicity
- In some cases, they represent true microcalcifications within the cardiac muscle.

It is present in 4% of cases and described as golf ball, more in Asian patients and lowest in black population, can be single or multiple, can appear in either ventricle more common in the left ventricle.[15]

It was first related to aneuploidy in early 1990s, however, the exact pathophysiologic link remains uncertain. This relation was confirmed in many other studies.[15] However, most of the studies were done on high risk cases. In a recent study on 12,373 cases, 267 echogenic foci were diagnosed, 149 of them were isolated, there was no cases of T21 among any case of these with age < 35.[16]

In an another prospective study, there were 12,672 cases included, 479 cases of EF were diagnosed, 90% were isolated, only one case had T21 (positive LH ratio of 2.66). This study concluded that amniocentesis is not warranted in low-risk cases with isolated EF.[17]

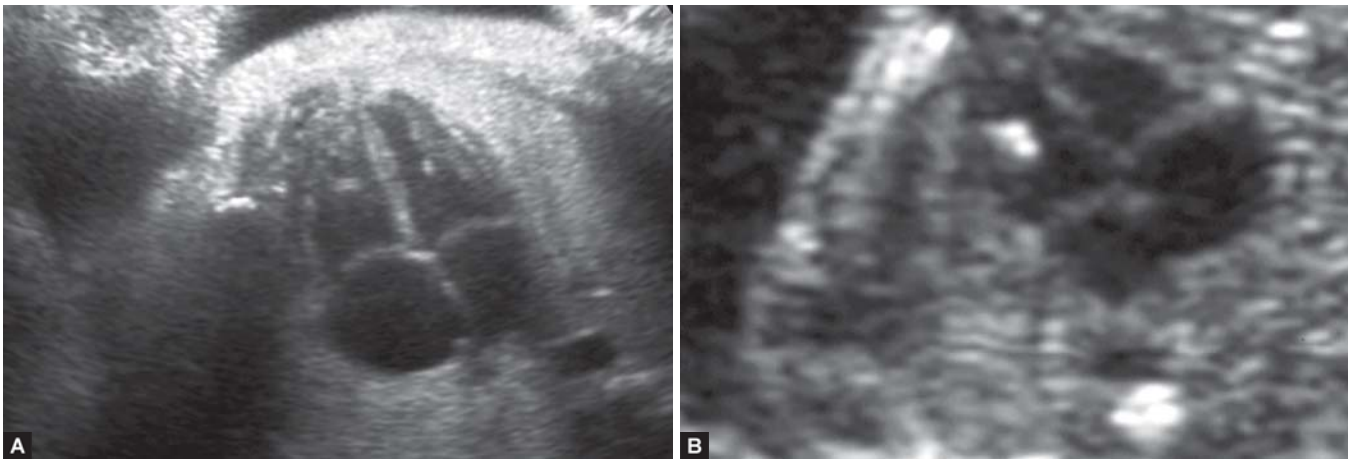
So, it was amazing to see a paper recently published with an interesting title. It is time to reconsider our approach to EF and choroid plexus.[18]

Relation to Cardiac Functions Pre- and Postnatal

- In the absence of aneuploidy, EF has not been associated with structural cardiac abnormalities[19]
- There is no much evidence of increase in childhood myocardial dysfunction when compared with the general population.

Management of EF

1. Detailed fetal anatomy to search for any associated anomalies



Figs 4A and B: Echogenic focus in the heart

2. In situation like:
   - Old age > 35 years
   - Associated abnormalities or soft markers
   - Or history of chromosome abnormality, an amniocentesis is done to rule out aneuploidy
   - Isolated EF is considered as incidental finding and not warrant amniocentesis and even further evaluation of EF is not necessarily either prenataly or postnataly.

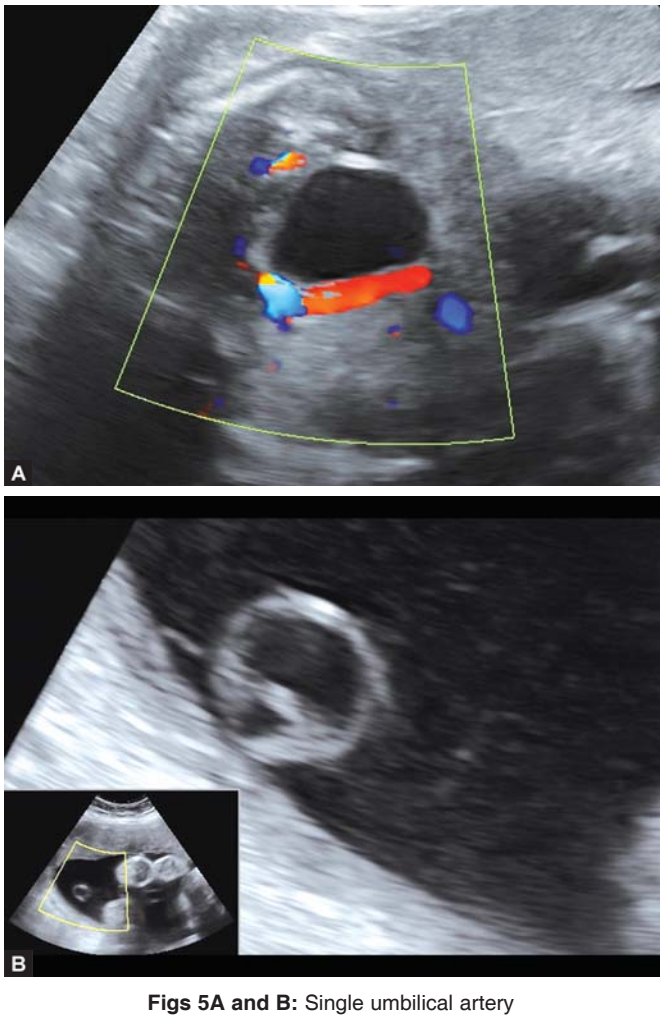
Single Umbilical Artery (SUA) (Figs 5A and B)

It is the most common anomaly of the cord, incidence of about 0.5 to 2.5% of all deliveries.

Pathogenesis: Aplasia or atrophy of one artery, more left artery than the right. More common in twins. The marginal and velamentous cord insertions have been reported to occur in 18 and 9.3% among fetuses with SUA compared with 6 to 8% and 1.1% respectively in singletons.[20]

Diagnosis

- Transverse section of free loop of the cord
- Two umbilical arteries as they course on either side of the bladder



Figs 5A and B: Single umbilical artery

- Diameter of the umbilical cord in a two vessel tends to larger than the three vessel cord and also reported that umbilical artery diameter > 4 mm or a v/a ratio < 2 may be diagnostic of SUA.[20]

Multiple segments should be examined to exclude fusion of the two arteries. It could be isolated or combined with other abnormalities, or oligohydramnios, polyhydramnios, IUGR.

The most common associated anomalies with SUA are cardiac and genitourinary.[21] Associated congenital anomalies in a fetus with SUA confer increased risk of aneuploidy estimated to be 31%.

SUA, at 11 to 14 weeks, has a high association with trisomy 18 and other chromosomal defects. The increased morbidity and mortality associated with pregnancies complicated by SUA is attributable to increased rates of associated anomalies and aneuploidy.[21] In a very recent publication by Dagklis et al they showed that the finding of SUA should prompt the sonographer to search for fetal defects and if these are found the risk for chromosomal abnormalities is increased. In cases of apparently isolated SUA there is no evidence of increased risk of chromosomal abnormalities.[22]

Management of SUA

- Detailed fetal anatomy scan
- Fetal echocardiography
- Invasive testing is offered in presence of abnormalities or presence of polyhydramnios or IUGR
- In isolated SUA, no invasive testing is warranted
- Serial growth scans are warranted
- Antenatal fetal surveillance specially color Doppler of the umbilical artery.

Clubfoot (Figs 6A and B)

It is abnormal relationship of foot/ankle to tibia and fibula. It is talipus equino varus; equino means planter flextion and varus means inward displacement of the foot. Incidence is around 0.1 to 0.4%, males are more affected, 60% are bilateral. Best US imaging clue is long axis of foot in same plane as long axis of tibia and fibula. Clubfoot may occur in isolation or in association with numerous other conditions, like general musculoskeletal disorders, arthrogryposis, genetic syndromes, neural tube defects and spine defects, early amniocentesis.[23] It is associated with other structural malformations in 10 to 14%.

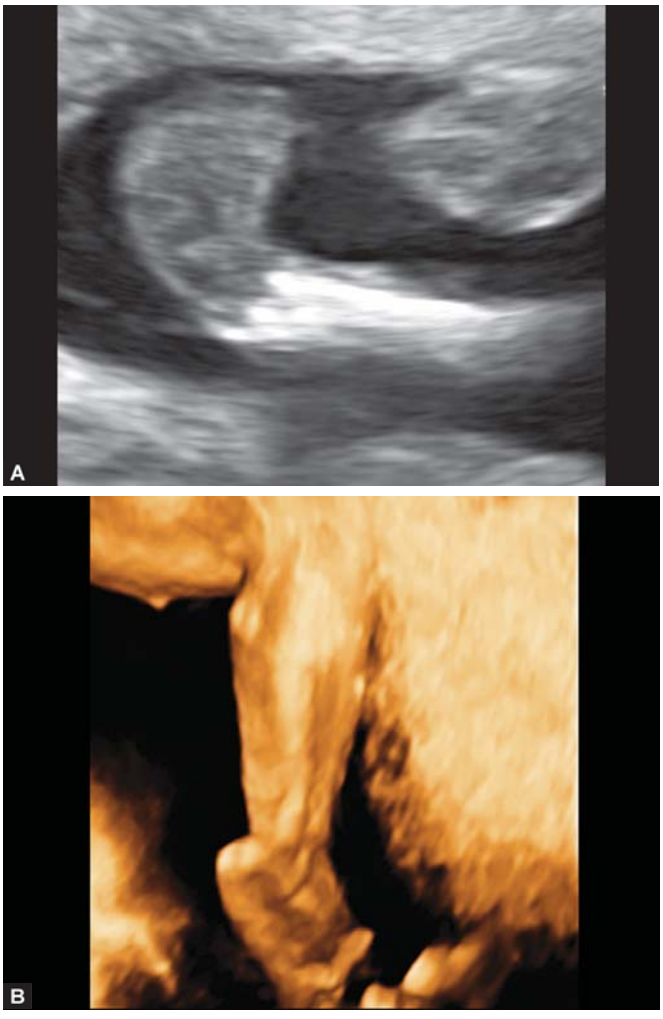
There is a significant risk of karyotype abnormality specially trisomy 18 in 6 to 22%.[24]

Management of Clubfoot

Most cases of clubfoot, which are related to chromosomal anomalies like T18 will demonstrate other structural abnormalities.

Sonographic detection of clubfoot warrants a detailed anatomic survey also careful examination of the uterus for fibroids or a septum.

Once it is achieved, and in the absence of oligohydramnios or IUGR, no need to do serial growth scans or antenatal testing



Figs 6A and B: Club foot

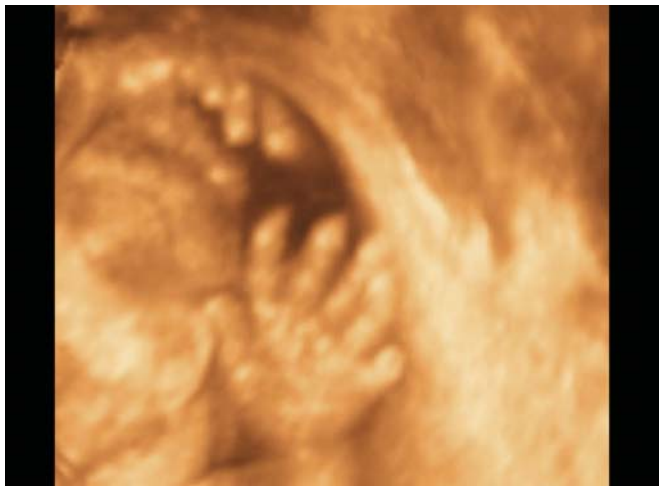


Fig. 7: Postaxial polydactyly

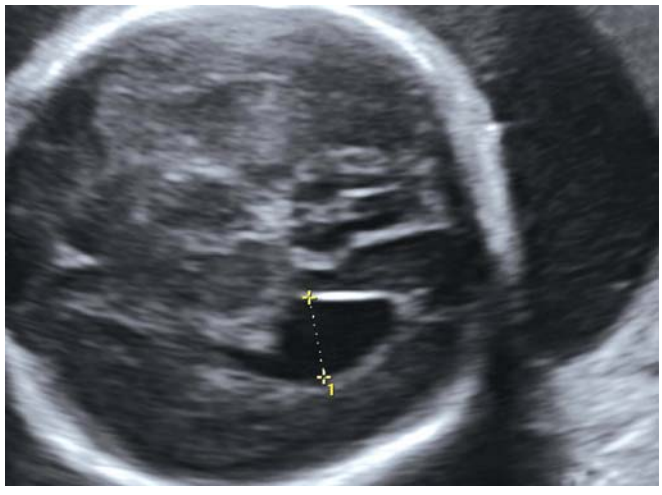


Fig. 8: Mild ventriculomegaly

because isolated clubfoot has not been associated with adverse pregnancy outcomes.

Postnatal successful surgery is obtained in 52 to 91% of cases enabling most children participate in normal activities.[24]

Polydactyly (Fig. 7)

It is classified into:

- Preaxial: Radial—tibial
- Postaxial: Ulnar-fibular—more common in black and two types are recognized: Type A extra digit is well-developed whereas in type B the extra digit is rudimentary and without skeletal structure.[25]

Polydactyly may be present as part of a syndrome or as an isolated finding.

Once we diagnose polydactyly, detailed ultrasonographic survey of all fetal organs should be performed in all cases in which this anomaly is found. Amniocentesis should be offered if there is no familial history of polydactyly. Patients should be informed that fetuses with an isolated finding of polydactyly usually have a favorable outcome, however, parents should also be informed that at present it is not possible to definitely exclude the possibility of a rare anomaly, such as Bardet-Biedl syndrome.[25]

Mild Ventriculomegaly (MVM) (Fig. 8)

Ventriculomegaly affects 1 to 2% in 1000 births. Mild ventriculomegaly or so-called border line ventriculomegaly range between 10 and 12 mm and 10 and 15 mm.[26] Clinicians involved in prenatal diagnosis are asked almost daily to offer counseling for this condition which is border line between normality and pathology.

When we are confronted with this situation we should first check:

- Is it stationary or a progressive lesion?
- Is it isolated or combined with other anomalies?
- We should exclude aneuploidy—agenesis of the CC
- What is the relation with chromosomal anomalies?

It was reported to be 10 to 12% in isolated cases that is why some recommend amniocentesis.

Postnatal Prognosis

In one study,[27] they had 60 cases with isolated MVM 10 to 12 mm, followed up to 18 months and they postulated that parents counseling is difficult, however, normal neuro development between 18 months and 10 years are basis for reassuring. Their conclusions were:

1. Most infants with a prenatal diagnosis of isolated MVM have normal neurological development at least in infancy

2. Rate of abnormal or delayed neurodevelopment in infancy is about 11%
3. There is lack of good quality postnatal follow-up studies making antenatal counseling for this abnormality difficult.

In a recent review for all the cases with mild ventriculomegaly which was followed up,[28] the data collected points out to this conclusion. There are limitations of existing studies of mild VM. Although they address many of the relevant questions regarding the prognosis and management of fetal isolated mild VM, there is a lack of good quality postnatal follow-up studies. The resulting uncertainties make antenatal counseling for this abnormality difficult.

CPC-EIF-E Bowel—Hydronephrosis in 11 to 13 weeks Scan

Within the context of the 13 weeks fetal anatomy scan, the prevenlace of Down's syndrome is higher when these findings are seen[29] as proved by Dagklis et al who had 3D volumes of 228 fetuses with Down's syndrome and 797 of euploid fetuses at 11 to 13 weeks. They concluded that the prevalence of these signs is higher in DS.

CONCLUSION

The so-called controversial US signs should be called alert signs because using our knowledge from the literature we can now know how to tackle these signs with high degree of precision.

Clinicians are advised to follow well-designed studies to state the clinical significance before embarking on clinical actions. We should always remind ourselves that service without quality is worse than no service at all. We should be shielded with the most up-to-date knowledge concerning these US signs going hand in hand with our ability to detect them, so as to provide the parents with the most appropriate counseling as well as the most correct management is to commenced.

REFERENCES

1. Al Kouatly H, Chasen S, Streltzoff J, Chervenak F. The clinical significance of fetal echogenic bowel. Am J Obstet Gynecol 2001;185:1035-38.
2. Strocker Am, Snijders RJ, Carlson DE, Greene N, Gregory KD, Walla CA, et al. Fetal echogenic bowel: Parameters to be considered in differential diagnosis. Ultrasound Obstet Gynecol 2000;16:159-23.
3. Sepulveda W, Sebire NJ. Fetal echogenic bowel: A complex scenario. Ultrasound Obstet Gynecol 2000:16:510.
4. Simon-Bouy B, Muller F. French collaborative group. hyperechogenic fetal bowel and Down syndrome: Results of French collaborative study based on 680 prospective cases. Prenat Diagn 2002;22:189-92.
5. Benacerraf BR, Mandell J, Estroff JA, Harlow BL, Frigoletto F. Fetal pyelectasis—a possible association with Down syndrome. Obstet gynecol 1990;76-58-60.
6. Chudleigh PM, Chitty LS, Pembrey M, Campbell S. The association of aneuploidy and mild fetal pyelectasis in an unselected population: The results of a multicenter population. Ultrasound Obstet Gynecol 2001;17:197-201.
7. Havutcu A, Nikolopoulos G, Adinkra P, Lamont R. The association between fetal pyelectasis on second trimester ultrasound scan and aneuploidy among 25586 low risk unselected women. Prenat Diagn 2002;22:1201-06.
8. Coco C, Jeanty P. Isolated fetal pyelectasis and chromosomal abnormalities. Am J Obstet Gynecol 2005;193:732-38.
9. Smith Bindman R, Chu P, Goldberg JD. Second trimester prenatal ultrasound for the detection of pregnancies at increased risk of Down syndrome. Prenat Diagnosis Sep 2007;27(9):884.
10. Wollenberg A, Neuhaus J, WilliV, Wisser J. Outcome of fetal renal pelvic dilatation diagnosed during the third trimester. Ultrasound Obstet Gynecol 2005;25:483-88.
11. Walkinshaw SA. Fetal choroid plexus cysts are we there yet? Prenat Diagn 2000;20-657-62.
12. Yoder PR, Sabbaghare, Gross SJ, Zelop CM. The second trimester fetus with isolated choroid plexus cysts: A meta-analysis of risk of trisomies 18 and 21. Obstet Gynecol 1999;93:869-72.
13. Reinsch R. Choroid plexus cysts—association with trisomy: Prospective review of 16059 patients. Am J Obstet Gynecol 1997;176:1381-83.
14. Demasio K, Canterino J, Ananth A, Fernandez C, Smulian J, Vinzileos A. Isolated choroid plexus cyst in low risk women less than 35 years old. Am J Obstet Gynecol 2002;187: 1246-49.
15. Huggon IC, Cook AC, Simpson JM, Smeeton N, Sharland G. Isolated echogenic foci in the heart as a marker of chromosomal abnormality. Ultrasound Obstet Gynecol 2001;17:6-11.
16. Anderson N, Jyott R. Relationship of isolated fetal intracardiac echogenic focus to trisomy 21 at the mid-trimester sonogram in women younger than 35 years. Ultrasound Obstet Gynecol 2003;21:354-58.
17. Coco C, Jeanty P. An isolated echogenic heart focus is not an indication for amniocentesis in 12,672 unselected patients. Ultrasound Med 2004;23(4):489-96.
18. Bethune M. Time to reconsider our approach to echogenic intracardiac focus and choroid plexus cysts. Aust N Z J Obstet Gynaecol Apr 2008;48(2):137-41.
19. Wolman I, Jaffa A, Geva E, Daimant S, Strauss S, Lessing JB, et al. Intracardiac echogenic focus: No apparent association with structural cardiac abnormality. Fetal Diagn Ther 2000;15: 216-18.
20. Sepulveda W, Dezerega V, Carstens E, Guitierrez J. Fused umbilical arteries: Prenatal sonographic diagnosis and clinical significance. J Ultrasound Med 2001;20:59-62.
21. Rembouskos G, Cicero S, Longo D, Sacchini C, Nicko-laides KH. Single umbilical artery at 11-14 weeks gestation: Relation to chromosomal defects. Ultrasound Obstet Gynecol 2003;22(6):567-70.
22. Dagklis T, Defigueiredo D, Staboulidou I, Casagrandi D, Nicolaides KH. Isolated single umbilical artery and fetal karyotype. Ultrasound Obstet Gynecol 2010;36(3):291-95.
23. Malone F, Maino T, Bianchi D, Johnston K, Dalton M. Isolated club foot diagnosed prenatally: Is karyotyping indicated? Am J Obstet Gynecol 2000;95:437-40.
24. Offerdal K, Jebens N, Blaas H, Eikness. Prenatal ultrasound detection of talipes equinovarus in a non-selected population of

49314 deliveries in Norway. Ultrasound Obstet Gyecol 2007;30:838-44.
25. Zimmer EZ, Bronshtein M. Fetal polydactyly during early pregnancy: Clinical applications. Am J Obstet Gynecol 2000;183(3):755-58.
26. Senat V, Bernad P, Schwarzler P, Britten J, Ville Y. Prenatal diagnosis and follow up of 14 cases of unilateral ventriculomegaly. Ultrasound Obstet Gynecol 1999;14(5):327-32.
27. Signorelli M, Tiberti A, Valseriati D, Molin E, Cerri V, Groli C, Bianchi U. Width of the fetal lateral ventricular atrium between 10-12 mm: Simple variation of the norm. Ultrasound Obstet Gynecol 2004;23:14-18.
28. Melchiorre K, Bhide A, Gika AD, Pilu G, Papageorghiou AT. Counseling in isolated mild fetal ventriculomegaly. Ultrasound Obstet Gynecol Aug 2009;34(2):212-24.
29. Dagklis T, PLasencia W, Maiz N, Duarte L, Nicolaides K. Choroid plexus cyst, intracardiac echogenic focus, hyperechogenic bowel and hydronephrosis in screening for trisomy 21 at 11+0 to 13+6 weeks. Ultrasound Obstet Gynecol 2008;31:132-35.