The use and understanding of soft ultrasound markers

The use and understanding of ultrasound soft markers and their screening relative risks is an important option in the care of pregnant women. On the other hand, the absence of a soft marker does not indicate a reduced risk of chromosomal abnormality.
Identification of soft markers for fetal aneuploidy requires correlation with other risk factors, including history, maternal age, and maternal serum testing results.
Soft markers are not diagnostic for fetal abnormalities.

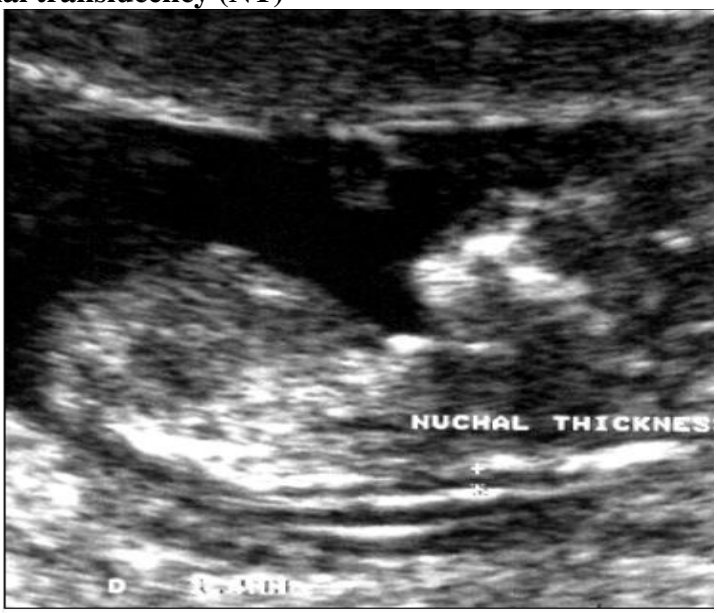
Definition of soft ultrasound markers
Soft markers are minor ultrasound abnormalities, considered variants of normal, which do not constitute a structural defect.
They may be associated with chromosomal or none chromosomal abnormalities.

Soft markers include:
Those associated with increased risk of aneuploidy and in some cases none chromosomal problems
Nuchal translucency (NT)
Nasal bone hypoplasia
Nuchal pad edema
Echogenic bowel
Echogenic focus in the heart (golf ball sign)
Choroid plexus cysts
Mild ventriculomegaly

Those associated with an increased risk of non-chromosomal abnormalities when seen in isolation
Mild renal pyelectasis
Single umbilical artery
Enlarged cisterna

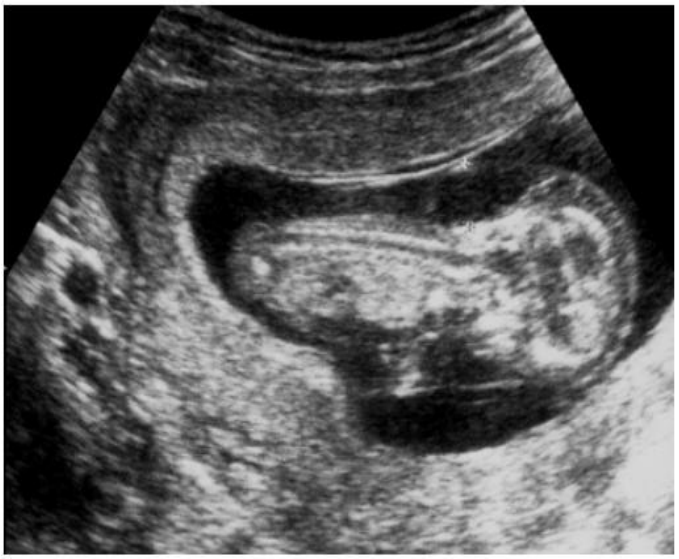
Those of undefined association
Clenched fists
Rocker bottom feet
Sandal gap
Strawberry shaped skull
Shortened long bones

Nuchal translucency (NT)



NORMAL NUCHAL TRANSLUCENCY

Figure1 Normal NT



INCREASED NUCHAL TRANSLUCENCY

Figure2 Increased NT

It is the maximum thickness of the subcutaneous translucency between the skin and the soft tissue overlying the cervical spine. It has been shown to be an effective screening test for aneuploidy.
It is measured between 11 – 14 weeks of pregnancy. It is a soft marker screening for chromosomal abnormalities (trisomy 18 and 21), structural or thoracic compression (diaphragmatic hernia) and cardiac abnormalities.
In the first trimester, NT combined with serum screening and maternal age has an estimated detection rate of 85% and a 5% false positive rate for screening for trisomy 21.
Nuchal translucency should not be confused with cystic hygroma or Nuchal pad thickness.

Nasal bone hypoplasia
Association with aneuploidy
Nasal bone hypoplasia at 11 – 13 weeks has now emerged as an ultrasound soft marker for trisomy 21 with a high Relative Risk (8.5 – 51). Nasal hypoplasia has not been associated with other aneuploidy. Preliminary results suggest it may be a feasible tool but refining of the technique and more understanding of its association with abnormalities is required before wide spread clinical applications.
Absence or nasal bone hypoplasia has not been found to be associated with structural abnormalities.
If the nasal bone is felt to be small or absent, referral to a tertiary level is recommended.

Nuchal Pad thickness (6mm or over)
It is the skin thickness in the posterior aspect of the fetal neck. It should be measured between 15 – 20 weeks of gestation.

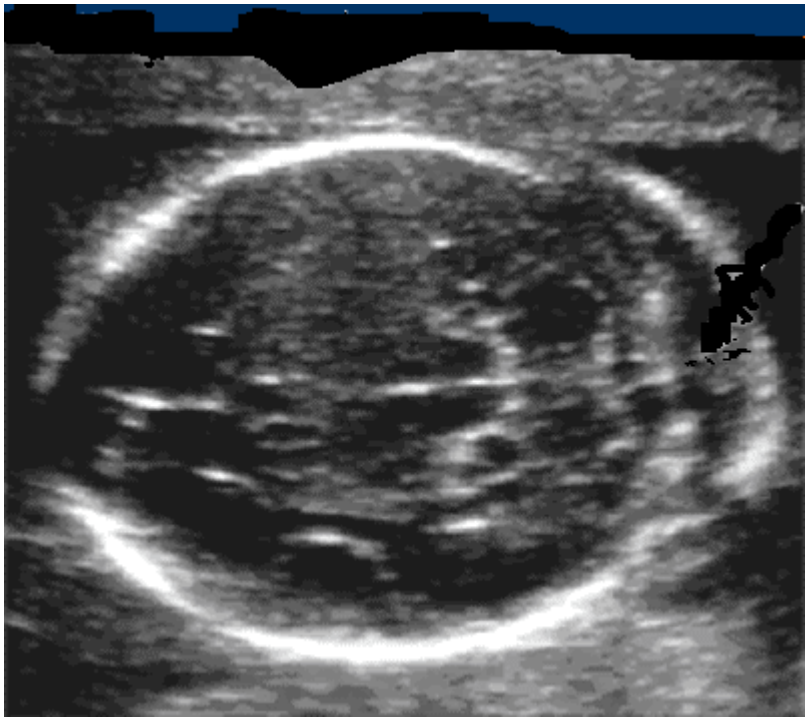


Figure3 Nuchal pad thickness

Nuchal pad should not be confused with cystic hygroma where the skin has fluid filled loculations.
The risk for Downs's syndrome increases 17 fold. Referral to expert opinion is recommended and Karyotyping offered.
Nuchal pad thickness may be associated with congenital heart abnormalities and detailed cardiac scan should be carried out at 22 – 24 weeks.

Echogenic bowel

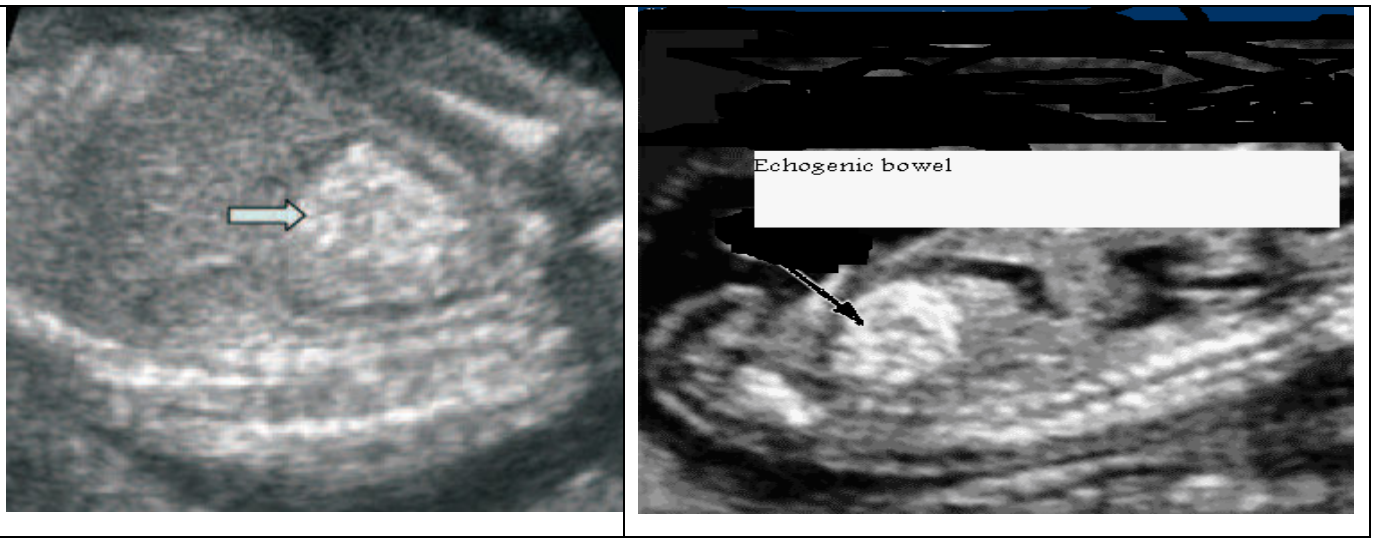


Figure4 Echogenic bowel

Definition

Echogenic bowel is an area of the fetal bowel with single or multiple foci of echogenisity equal or greater than the surrounding bone.

Association with aneuploidy
There is a high risk for association with trisomy 13, 18 and 21. The Likelihood Ratio is 6.

Association with structural abnormalities
Echogenic bowel has been associated with an increased risk for:
Cystic fibrosis
Congenital infection (cytomegalovirus [CMV], herpes, parvovirus, rubella, varicella, and toxoplasmosis)
Intra-amniotic bleeding
Congenital malformations of the bowel
Perinatal complications, including intrauterine growth restriction

Management
Because of the high association with the above chromosomal and none chromosomal abnormalities, referral to a fetomaternal medicine unit is recommended for the following procedures:
Detailed review of fetal anatomy, growth, and placental characteristics
Testing for congenital infections (maternal serum titers, fetal amniotic culture, or polymerase chain reaction [PCR] for viral DNA)
Fetal Karyotyping and DNA testing for cystic fibrosis
Paternal testing for carrier status for cystic fibroses
Neonatal testing if amniocentesis was declined or showed negative results

Echogenic foci in the heart, Echogenic Intracardiac Focus (EICF)

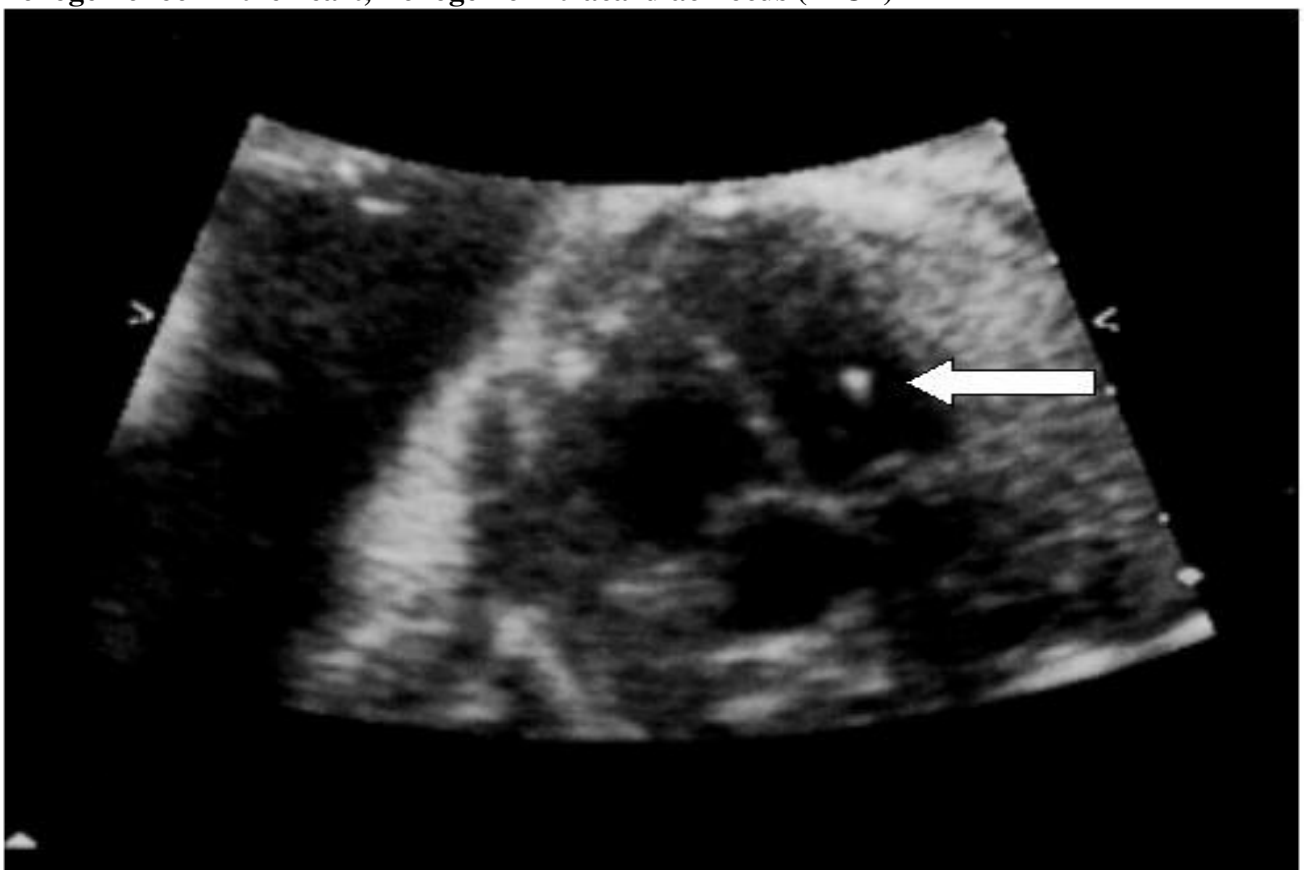


Figure5 Echogenic foci of the heart

Definition
It is a focus of an echogenic small area in the fetal heart with echogenisity comparable or greater to the surrounding bone.

Association with aneuploidy

In the high-risk population, the association has a likelihood ratio (LR) of 2.8 and a weaker LR of 2 in low risk population.
If EICF is found in isolation in low risk population <1/600 there is no need for further action. In high-risk population, (> 1/600) then referral for expert opinion and Karyotyping should be offered.

Association with structural abnormalities
There is no association with structural cardiac abnormalities or cardiac function if the cardiac scan is otherwise normal
In low risk population, most EICF disappear by term or after a short time after delivery.

Choroid plexus cysts (CPCs)

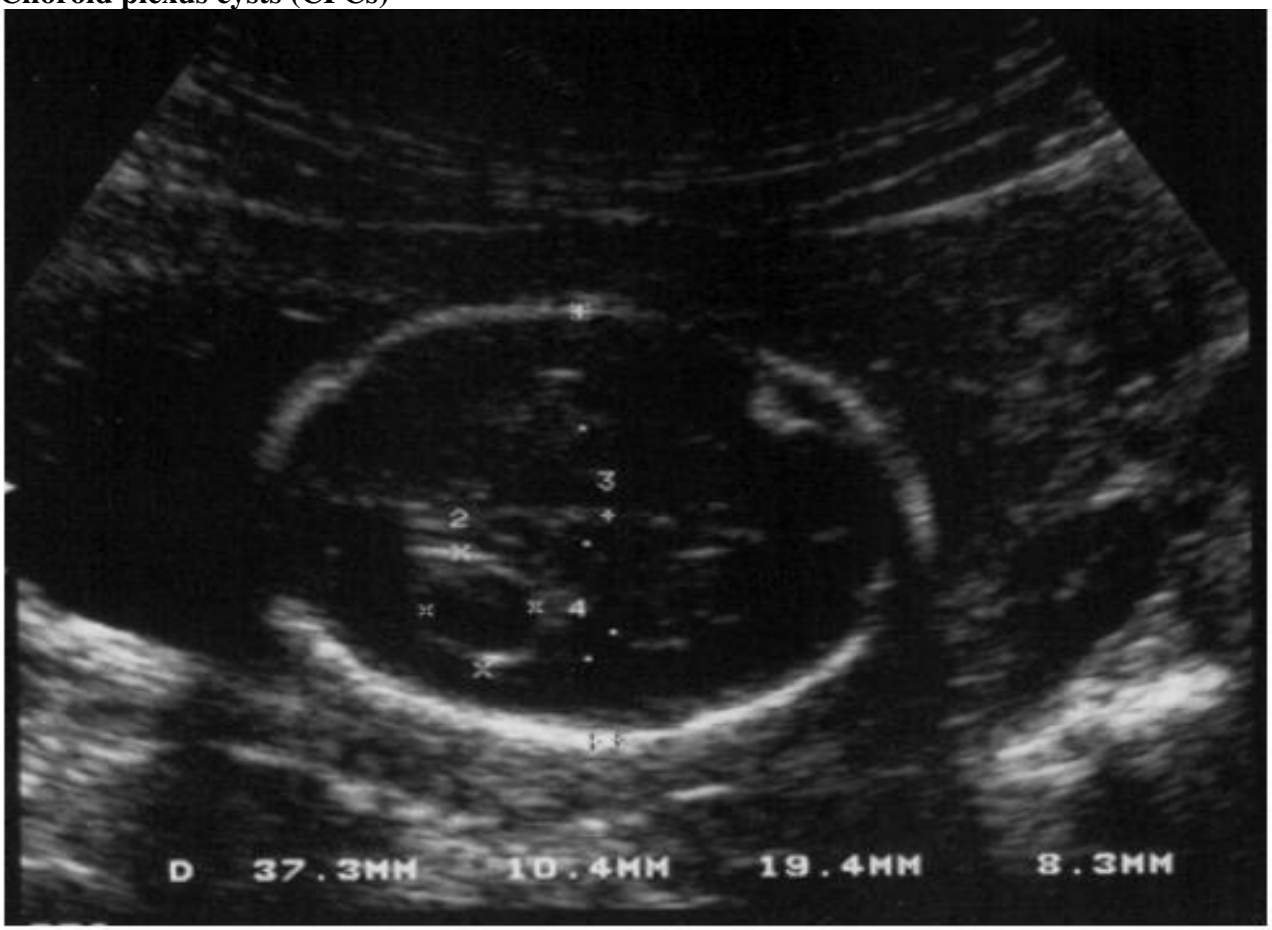


Figure6 Choroid plexus cyst

Definition
Choroid plexus cysts (CPCs) are sonographically discrete fluid filled small cysts (< 3 mm) in the choroid plexus within the lateral cerebral ventricles. It is seen in 1-2% of fetuses scanned at 16 weeks and will almost always disappear by 26 weeks.
Association with chromosomal abnormalities
They are more associated with trisomy 18 (Edwards syndrome) than trisomy 21.
Association with none chromosomal abnormalities
In chromosomally normal babies, associations with structural abnormalities have not been demonstrated.
Management
The presence of isolated CPCs in mothers who are above 35 or those with an abnormal serum screen should be offered Karyotyping for trisomy 18 and 21.
The presence of CPCs in association with other ultrasound abnormalities should be referred for expert opinion and offered Karyotyping.
Isolated CPCs in women below 35 years age, with normal biochemical screening does warrant further actions or ultrasound follow up.

Renal pyelectasis

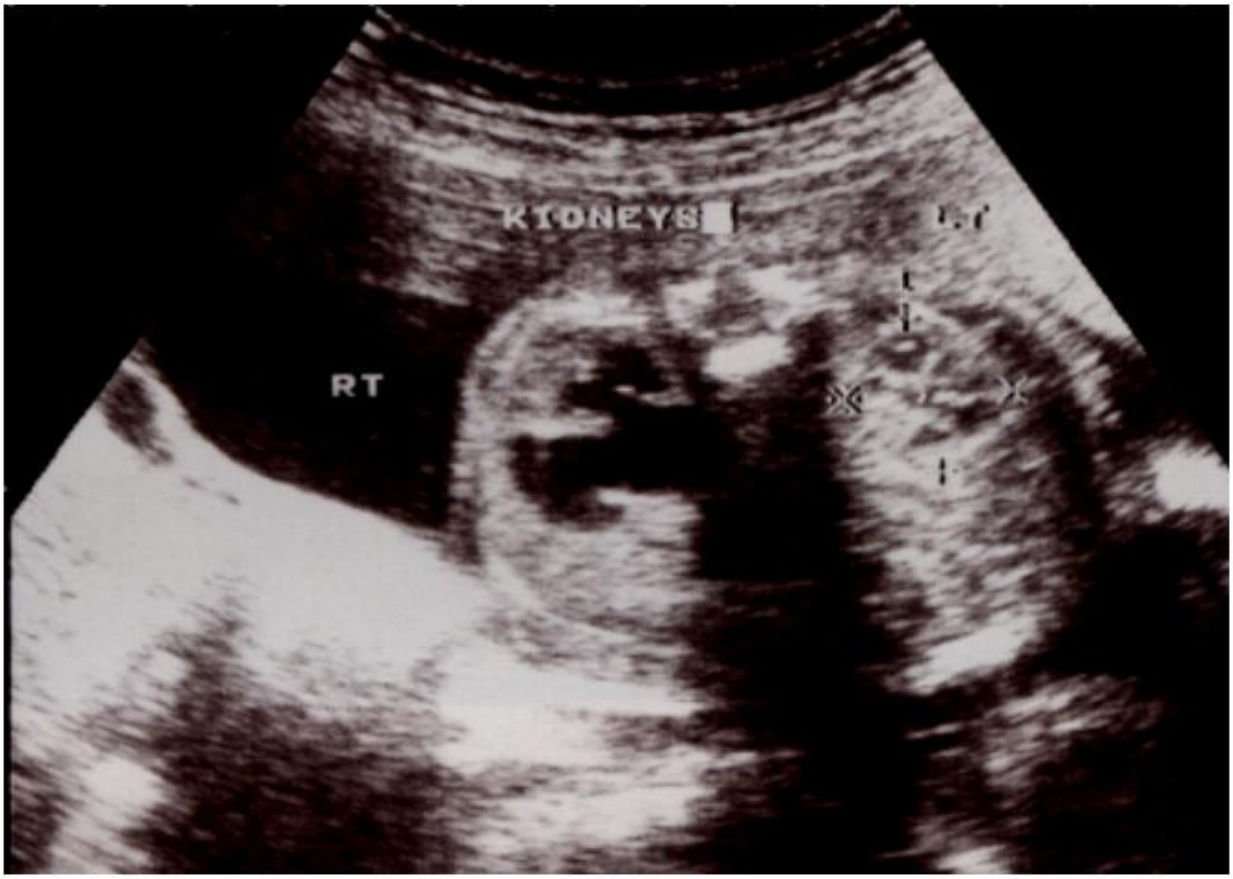


Figure7 Renal pyelectasis

Definition

Mild pyelectasis is defined as a hypoechoic spherical or elliptical space within the renal pelvis that measures 5 - 10 mm with no calyseal involvement.

Association with Fetal Aneuploidy

The presence of an isolated mild pyelectasis in the absence of other risk factors, does not justify an invasive diagnostic procedure, as the risk of Down syndrome remains small.

Association with nonchromosomal structural abnormalities

Fetal pyelectasis is associated with congenital hydronephrosis or vesico-ureteric reflux. Renal pelvis measurements > 10 mm should be considered equivalent to congenital hydronephrosis with appropriate follow-up by ultrasound scans. All fetuses with renal pelvic measurements 5 mm should have a neonatal ultrasound and pediatric follow up.

Single umbilical artery

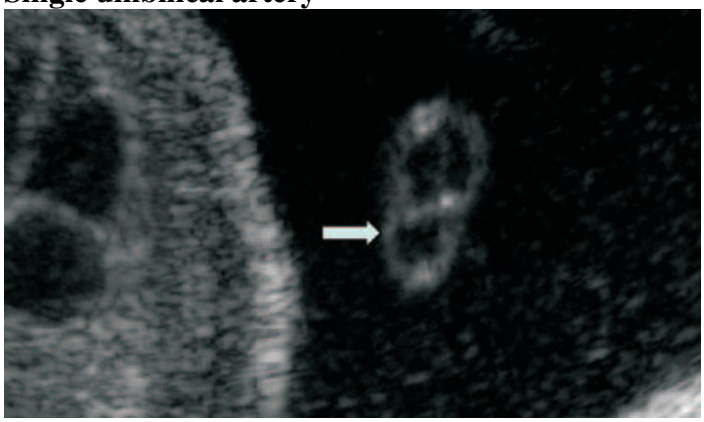


Figure8 Single umbilical artery

Association with aneuploidy

There is no significant association with fetal aneuploidy

Association with structural anomalies

An isolated single umbilical artery has been associated with cardiac, renal abnormalities and fetal growth restriction (FGR). It requires detailed fetal anatomy scan, fetal cardiac echo and serial growth scans.

Short long bones (femur and humerus)

Definition

Short femur and humerus length is defined as a measurement less than the third centile for the gestational age. Isolated short femur or humerus length is associated with aneuploidy and should be referred for tertiary level evaluation.

Short long bones may be associated with general skeletal malformation or FGR. Ultrasound screening for other long bones and serial growth measurements should be undertaken

Mild ventriculomegaly

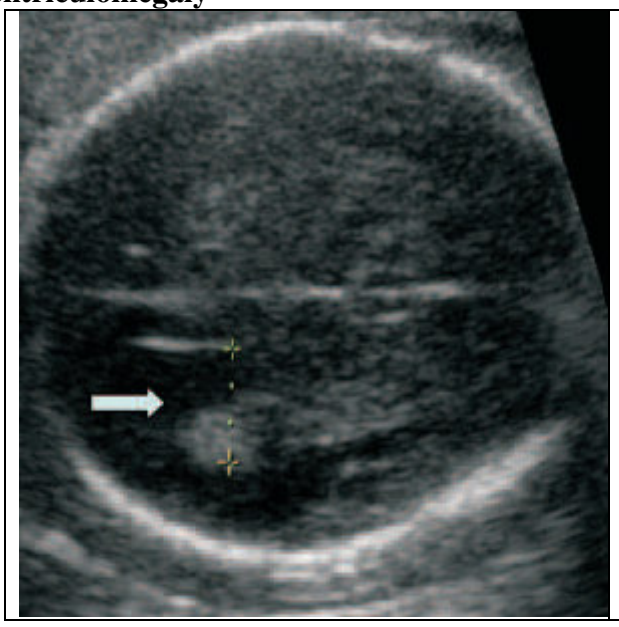


Figure9 Mild ventriculomegaly

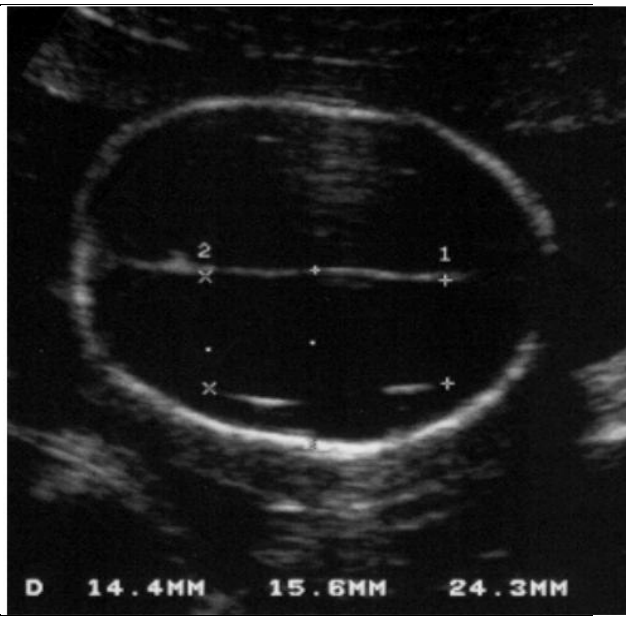


Figure10 Major Ventriculomegaly

Mild ventriculomegaly is defined as a measurement of the cerebral ventricles of between 10 to 15 mm. Normal ventricle measurements are 6 – 10 mm and major ventriculomegaly is > 15 mm.

Association with chromosomal aneuploidy

There is high LR of 9 for the risk of aneuploidy if an isolated mild ventriculomegaly is detected.

Association with none chromosomal abnormality

There is a strong association with central nervous system abnormality if the cerebral ventricles are 10mm or over.

Management

If the cerebral ventricles measure 10 mm or greater, then expert view is sought. A detailed anomaly scan, laboratory investigations for congenital infection or fetal aneuploidy should be carried out. MRI is a potential additional imaging technique.

In the neonatal period, the newborn should be followed up because of the potential for subsequent abnormal neurodevelopment.

Disadvantages of soft markers

1- The exact significance of ultrasound soft markers is still uncertain.
2- It is operator dependent and therefore may be missed.
3- The detection of soft ultrasound markers requires training and high-resolution ultrasound equipment.
4- The counseling, training and expertise required is currently difficult to achieve.
5- Some soft markers are transient and the significance is uncertain.
6- With better equipment, more markers may become more evident which may cause more concern to the prospective parents.
7- Unless caution is exercised and it is combined with other markers for abnormalities, it may lead to unnecessary interventions.

Other soft markers without undefined associations are not discussed in this article.

Conclusion and summary

Ultrasound is a valuable tool in obstetric management. However, it cannot be used for the diagnoses or exclusion of aneuploidy. It provides useful means to screen and adjust the risk for chromosomal anomalies. Soft ultrasound markers are variables of the normal that do not in themselves constitute a structural abnormality. Ultrasound markers are also common among karyotypically and structurally normal fetuses.

Most of the studies for soft ultrasound markers have concentrated on high risk pregnant populations. Prospective studies are needed to confirm the value of isolated soft markers in low risk populations.

The detection of any abnormal finding on ultrasound should prompt an immediate detailed ultrasound evaluation by an experienced sonographer. Referral to a tertiary center and Karyotyping should be considered it there is more than one abnormal ultrasound finding, if the patient is over 35 years of age, or if the biochemical screening is abnormal.

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