SOCIETY OF FETAL MEDICINE

Society of Fetal Medicine

SFM Bengal Chronicles

Short Stories

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From the President's Desk:

The SFM Bengal Chapter takes pride in publishing their fifth edition of the newsletter "SFM Bengal Chronicles."

The current issue has been titled the "Short Stories" to give you glimpses of certain conditions where fetal organs measure small for gestation. Readers may get more detailed information in the relevant literature but this newsletter may come handy to their day to day practice.

We start with small CRL for gestation, a topic that keeps on baffling the sonographers. It's a management conundrum when the dates are certain but the fetus is small right from the first trimester. Small bones are often a 'bone of contention' be they in the nose or in the limbs! Average operators like 'yours truly' are truly lost when they face a small cerebellum in isolation during anatomy scan. Identifying the corpus callosum or the cerebellar vermis has been a phew-moment for many of us until recently but now we have to blaze the trail for identifying and managing the smaller versions of them. Counting digits is still a challenge but picking up the tiny bits may be even more challenging.

The sincere efforts of the authors will be rewarded if this newsletter can at all inspire their readers in better scanning, better understanding.

Happy imaging. Happy learning. Long live SFM.

Dr. Kanchan Mukherjee
President, Bengal Chapter
Society of Fetal Medicine

Short CRL

Dr. Arkajyoti Mukherjee

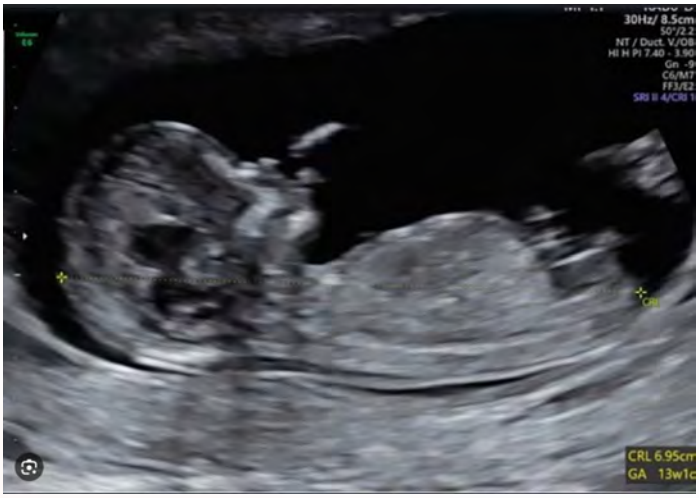
What is Crown rump length?

Crown rump length(CRL) is ultrasonographic measurement of embryo or fetus during first trimester ,from top of head(crown) to the bottom of buttocks(rump).

How to measure ?

ISUOG guidelines are there to measure CRL in a standardised way.

1. Fetus oriented horizontally on the screen so that the measurement line between crown and rump is at about 90◦ to the ultrasound beam.
2. The fetus should be in a neutral position (i.e. neither flexed nor hyperextended).
3. The image should be magnified to fill most of the width of the ultrasound screen.



Caption

4. Calipers should be placed on the end points of the crown and the rump, which need to be visualized clearly.

Why CRL is important?

1. It can be used to estimate gestational age.In this process of estimation it is assumed that the the embryo or fetus is growing at a rate which is more or less equal for each of them.But this is not true for all cases .
2. Assessment of fetal anatomy in a single swipe and useful to diagnose intracranial pathology, abdominal wall defect, megacystis etc.

What is 'short CRL' and how to diagnose?

Any deviation from the normal growth rate of fetus can have certain implications especially if the growth is lagging behind.Such slow growth can lead to short CRL.To diagnose 'short CRL' ,we must know the actual date of conception.In case of natural conception,if menstrual cycle is regular date of conception is supposed to be 14 days from first date of last menstrual period.In IVF,we know the transfer date and whether it is day-3 or day-5 embryo.Though there is no standard definition of short CRL ,it is usually diagnosed by observed/ mean expected value(CRL-MoM) <3SD or < 0.86.

What are the causes and effects of 'short CRL'?

Short CRL can either be due to improper implantation or intrinsic problem of the embryo(genetic/developmental).As a result of improper or faulty implantation embryo/fetus with short CRL are more prone to undergo spontaneous miscarriages or fetal demise and can develop into SGA or FGR later.Though there is no clear association between short CRL and spontaneous preterm birth, these fetuses are often delivered prematurely due to either maternal(eg.PIH) or fetal (eg.FGR) complications.Among the genetic problems, short CRL is evidently associated with trisomy 18 and to some extent with trisomy 13.But trisomy 21 usually has normal CRL .

Short CRL in Twin pregnancy

In case of twin pregnancy,apart from the absolute shortness discordance is also important. >10% CRL discordance can be useful predictor for adverse pregnancy outcomes. In monochorionic pair it can be a early sign of TTTS or s-FGR. In dichorionic twins, both genetic and implantation factors play important role like singletons.In terms of pregnancy outcomes in dichorionic twins,CRL discordance associated with peterm delivery <34 weeks,birth weight discordance and increased neonatal morbidity.

Cerebellar Hypoplasia: The Bullet Points

Dr Kanchan Mukherjee
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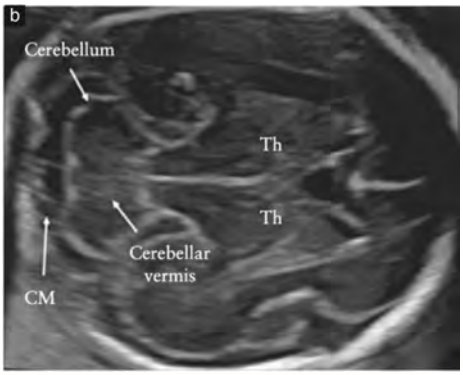
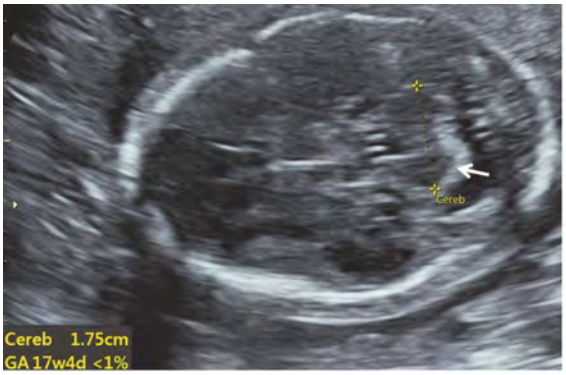
Definition:

Trans Cerebellar Diameter (TCD) less than 5th percentile for gestation but normal in shape
Often evolutive and may not present till late second trimester

Getting the images right:



Mid Trimester Imaging Of Cerebellum
(Courtesy ISUOG Guidelines 2022)



Cerebellar Hypoplasia at 21 weeks
(Reproduced with permission from Dr Ramamurthy's book)

Etiopathogenesis:

Heterogeneous condition, may be associated with Trisomies 9, 13 & 18
Disruption in the white matter of one or both cerebellar hemispheres due to disorders of glycosylation, anticonvulsant drugs (valproic acid) or cocaine
CMV infection
Posterior fossa haemorrhage

What else to look for:

Vermis may be small but normal in shape
Other intracranial anomalies (Neurosonography +/- MRI)
Extracranial anomalies (Detailed anomaly scan)
Chromosomal abnormalities (Amniocentesis for Karyotyping, Microarray)
Infections (Maternal blood for ToRCH IgG & IgM followed by Amnio for PCR if indicated
Polyhydramnios, fetal paralysis and seizures

Common associations:

Pontocerebellar hypoplasia: Autosomal recessive. A neurodegenerative disorder with small cerebellum, hypoplasia of brainstem (flat pons on midsagittal section)
Joubert syndrome: Autosomal recessive. Absent or hypoplastic cerebellar vermis with cleft between cerebellar hemispheres and communication the 4th ventricle and cisterna magna
Rhombencephalosynapsis: Sporadic condition. Absent vermis with fused cerebellar hemispheres, absent CSP, ventriculomegaly and migration disorders

Prognosis:

Generally poor
Delayed neurodevelopment
Deficient movement coordination
Neonatal death

Acknowledgments:

Imaging of Fetal Brain and Spine - B S Ramamurthy, 2019
Ultrasonography of the prenatal brain - Timor-Tritsch et al Third Edition, 2012
Fetal Medicine: Luc De Catte et al Third Edition, 2020

SHORT CORPUS CALLOSUM

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The fetal corpus callosum is a major commissure connecting the cerebral hemispheres.

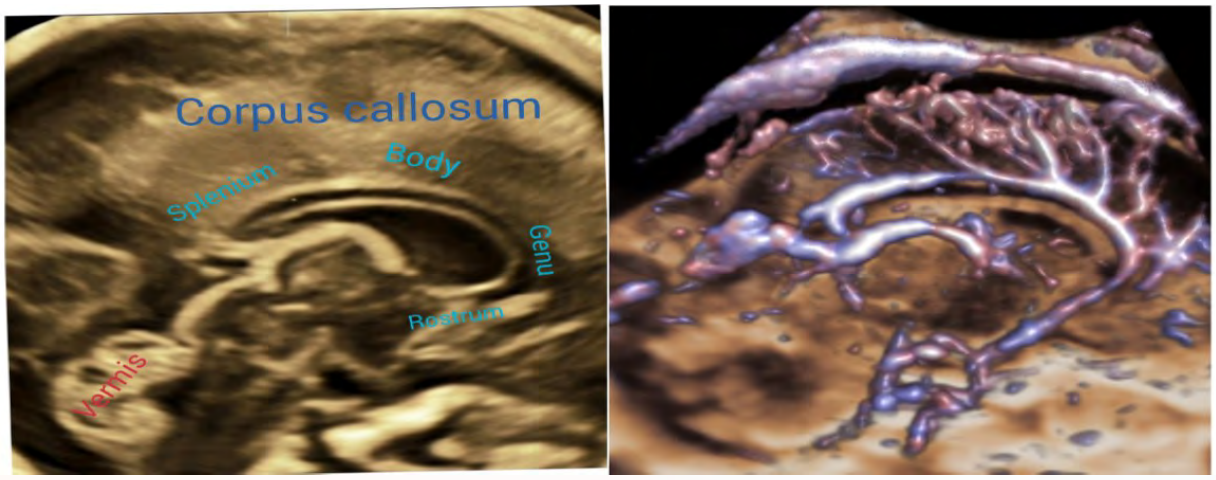
● It has four parts ;rostrum,genu,body and splenium from anterior to posterior .An isthmus portion has also been described in between body and splenium.It's formation begins with the genu and rostrum developing around the 11th week of pregnancy, followed by the body, isthmus, and splenium.

● Disturbances in the developmental process may lead to complete or partial absence of the corpus callosum (hypogenetic).

● Hypogenetic cases usually affect the posterior portion, including the posterior body and splenium.

● Normal measurements of the fetal corpus callosum can vary depending on gestational age, but typically the length is 20 mm at 20 weeks of gestation and the width should be greater than 2-3 mm

●The length increases by 2 mm every week till 35 weeks (For 50th Centile)



Mid sagittal section of fetal brain showing normal corpus callosum and normal pericallosal flow

●Short corpus callosum is considered when its length is below the 2 standard deviation for gestational age (Reference charts available).

Fetal corpus callosum nomogram

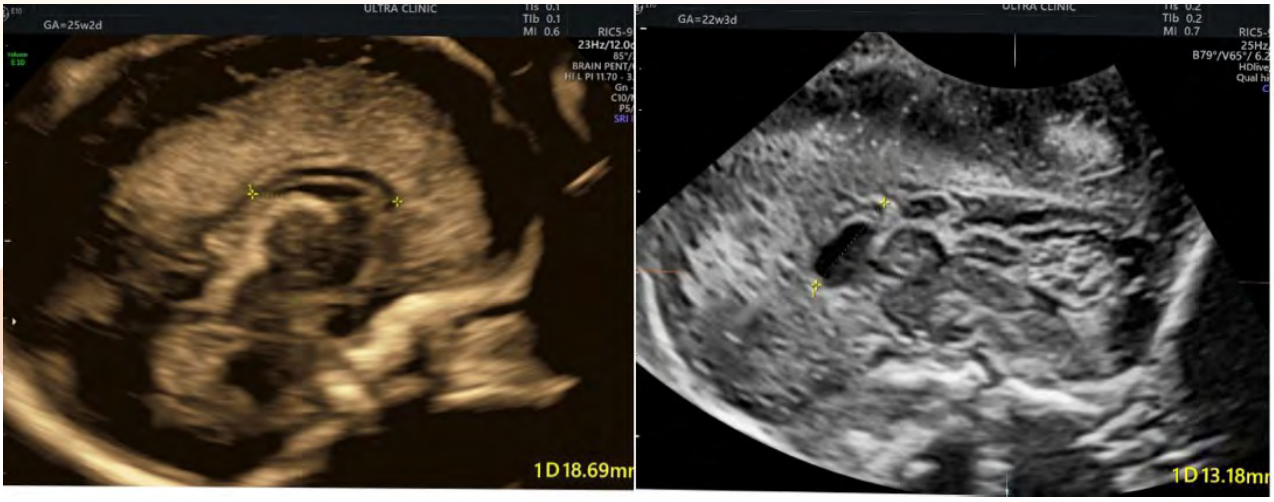
Table 1. Fetal Corpus Callosum Length (mm) by GA

GA, wk+d	n	Mean	SD	95% CI
19+0–19+6	7	18.78	1.33	17.45–20.10
20+0–20+6	75	21.02	1.43	19.59–22.46
21+0–21+6	1002	23.20	1.54	21.66–24.74
22+0–22+6	1322	25.30	1.65	23.65–26.94
23+0–23+6	217	27.31	1.76	25.56–29.07
24+0–24+6	31	29.24	1.86	27.38–31.10
25+0–25+6	34	31.07	1.97	29.10–33.04
26+0–26+6	26	32.81	2.08	30.73–34.89
27+0–27+6	29	34.45	2.18	32.26–36.63
28+0–28+6	24	35.97	2.29	33.68–38.26
29+0–29+6	33	37.38	2.40	34.98–39.78
30+0–30+6	33	38.68	2.51	36.17–41.18
31+0–31+6	43	39.85	2.61	37.23–42.46
32+0–32+6	38	40.89	2.72	38.17–43.61
33+0–33+6	20	41.80	2.83	38.97–44.62
34+0–34+6	6	42.56	2.94	39.63–45.50
35+0–35+6	4	43.19	3.04	40.14–46.23
36+0–36+6	3	43.66	3.15	40.51–46.81
37+0–37+6	3	43.98	3.26	40.72–47.24

CI indicates confidence interval.

● Usually there is absence or hypoplasia of the posterior part of the corpus callosum, including the posterior body and splenium in PACC

● PACC can be confirmed or excluded on direct visualization and measurement of the corpus callosum itself in the midsagittal view



Short corpus callosum; splenium is absent in the first image while body and splenium both absent in the second image,both images representing PACC

● Simple hints for suspicion of an abnormal corpus callosum (PACC) lies in the abnormal shape and size of the CSP in the axial plane of the fetal head .

● Hypoplasia of the septum pellucidum is more pronounced with extensive agenesis extending to the body and Genu of the corpus callosum.

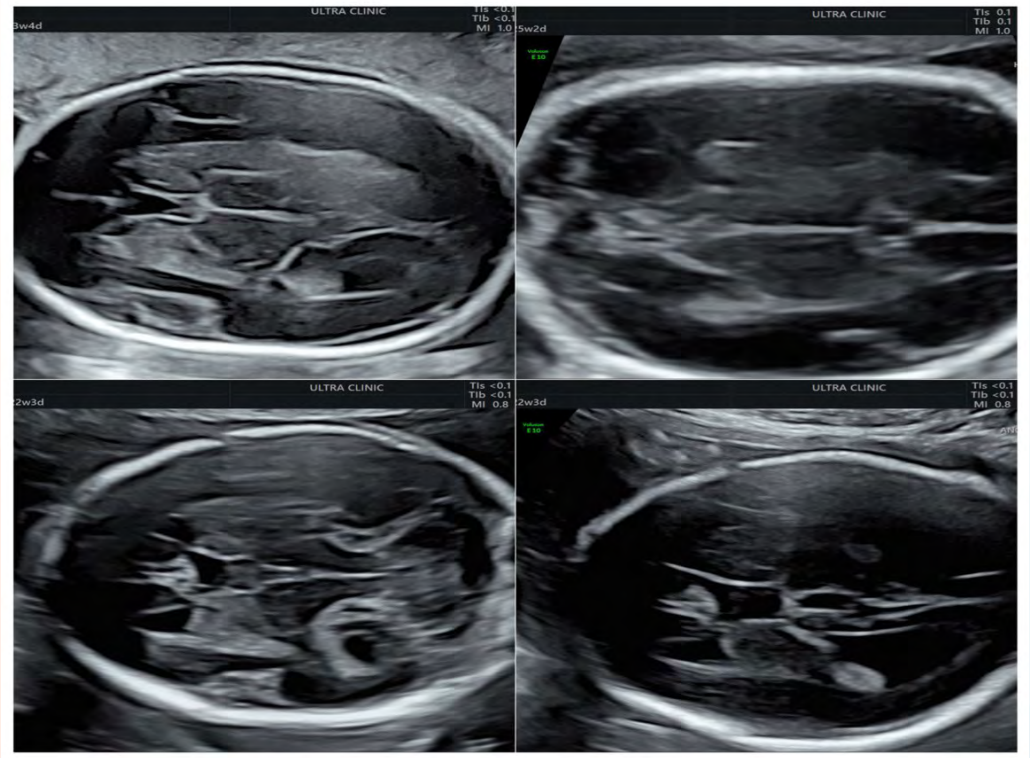
● The shape of the cavum septi pellucidi (CSP) is important in diagnosing PACC. Its Fetal corpus callosum nomogram Short corpus callosum; splenium is absent in the first image while body and splenium both absent in the second image,both images representing PACC

absence or abnormal shape may indicate the absence of the anterior part of the corpus callosum.

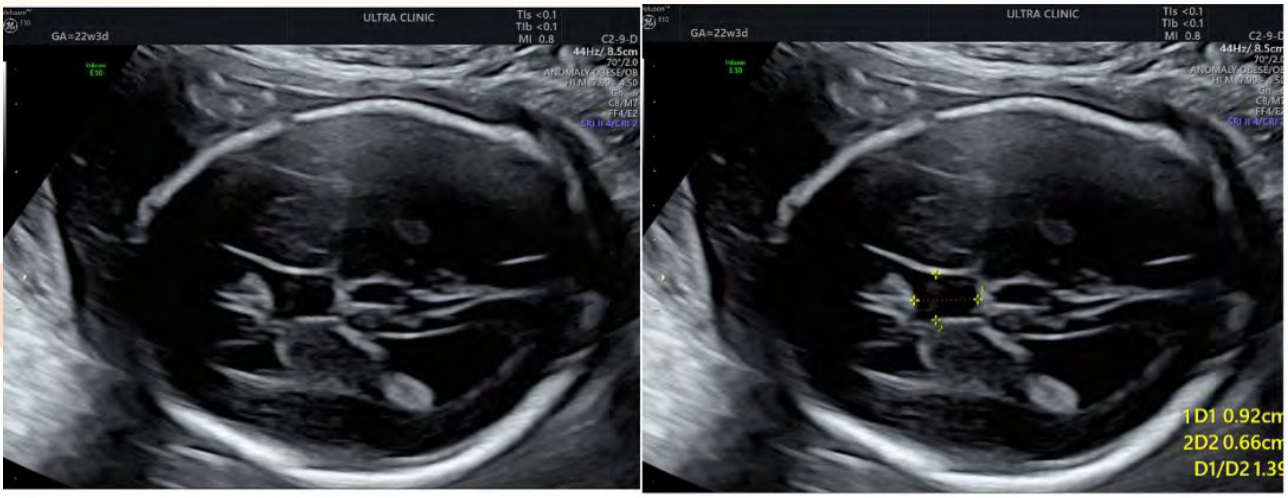
● CSP ratio refers to the ratio of the distance between the length and the width of the CSP. In cases of PACC, the CSP ratio is usually less than 1.5

●In cases of PACC, the pericallosal artery may follow closely along the anterior part of the corpus callosum.However, when the corpus callosum disappears posteriorly, the pericallosal artery may take an upward posterior oblique direction, showing an abnormal course.This sign, observed on color Doppler ultrasound, can be of great value in detecting PACC.

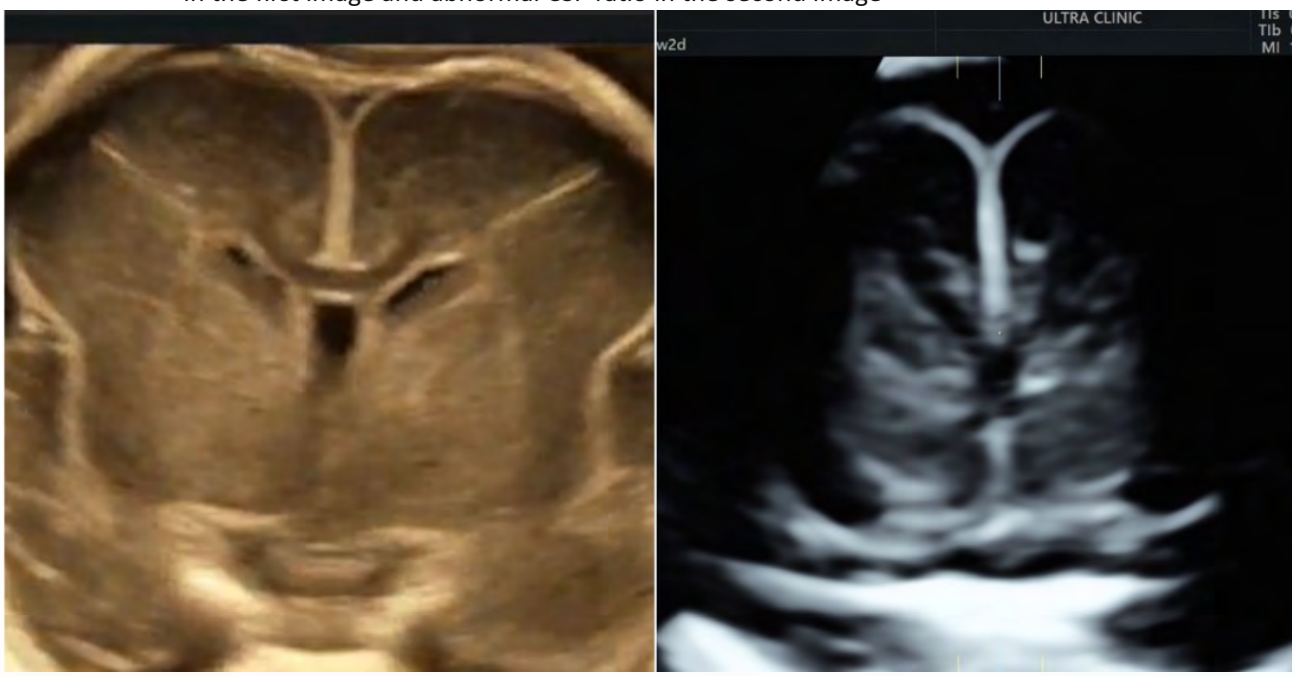
● Tela choroidea to Anterior Cerebral Artery Distance (TACAD) is a novel marker on color Doppler to identify fetuses with complete and partial agenesis of corpus callosum, where the said distance is much lesser than in the normal foetuses.



Axial section of fetal head showing normal shape of CSP at top left image,while other images showing abnormal shapes diagnosed to have PACC



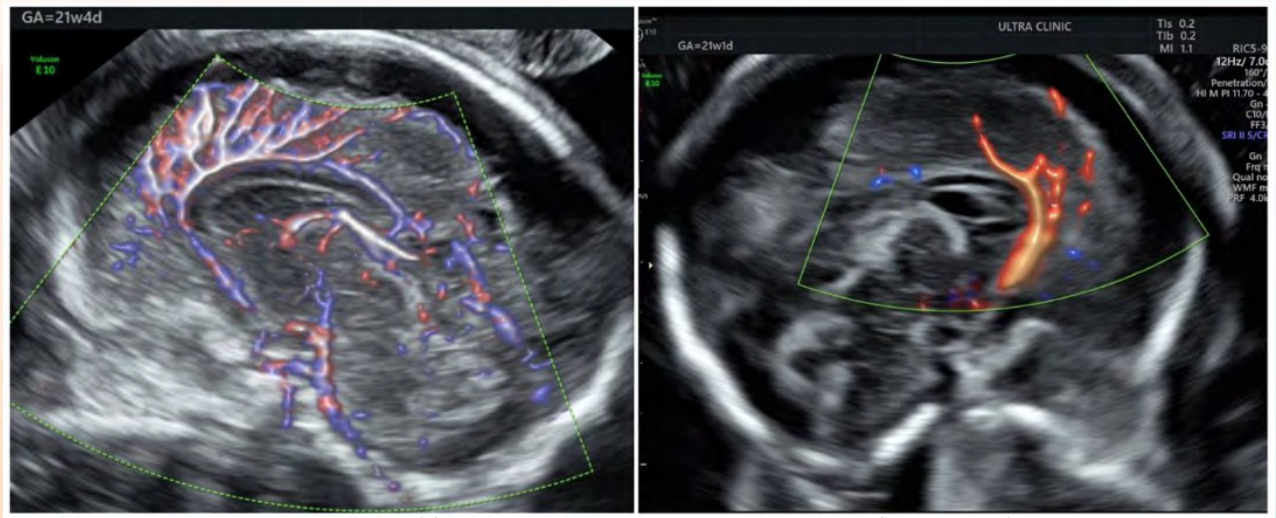
Axial image of fetal brain of diagnosed PACC showing borderline ventriculomegaly in the first image and abnormal CSP ratio in the second image



Coronal section of fetal brain showing normal appearance of CSP in the first image and abnormal appearance in the second image having PACC

●Other sonographic signs may be seen depending on severity and sporadically like- Colpocephaly, referring to the abnormal enlargement of the occipital horns of the lateral ventricles or teardrop configuration of the lateral ventricle Borderline ventriculomegaly Widened interhemispheric fissure,referring to an increased distance between the cerebral hemispheres. Dorsal cyst referring to the presence of a cystic structure at the posterior part of the corpus callosum. Posterior fossa abnormalities having an increased association.

●Some subtle signs including late sulcation and migration anomalies like in some cases, lissencephaly, gyral anomalies, and neuronal heterotopia ,observed through fetal MRI ,can be associated with PACC.



Mid sagittal section of fetal brain showing normal pericallosal flow in the first image while there is an abnormal short upturned course in the second image having PACC

● Accurate diagnosis of callosal anomalies requires expertise and may involve referring the mother to specialized centers for direct visualization using sagittal and coronal planes.
● Fetal MRI can help identify associated brain abnormalities not detected by ultrasound.
●The clinical relevance and prognosis of callosal agenesis vary; some individuals may have no neurological problems, while others may experience developmental delays or seizures.
● Isolated PACC cases have been reported with both normal psychomotor development and significant neuro developmental delay.
● Protracted follow-up until around 6 years of age is crucial to assess the long-term neuro developmental status and provide better prognostic information. The outcome of isolated PACC is variable, requiring careful monitoring and assessment during early childhood to determine its impact on neurodevelopment.
●In conclusion, advances in neurosonography and the use of fetal MRI have improved the detection of Partial Agenesis of the Corpus Callosum (PACC). Typical ultrasound findings, along with the evaluation of CSP shape, CSP ratio, and the course of pericallosal artery, aid in diagnosing PACC and associated anomalies.

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SHORT LONG BONES

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INTRODUCTION

Skeletal dysplasias (also called osteochondrodysplasia) are a large, heterogeneous group of conditions involving the formation and growth of bone and include osteodysplasia, chondrodysplasia, and dysostosis.

BACKGROUND

● Etiology – Skeletal dysplasias are primarily caused by genetic variants, but they may also be related to extrinsic causes, including maternal exposure to drugs (eg, thalidomide) and maternal diseases (eg, diabetes mellitus with poor glycemic control, autoimmune diseases) .

● Classification system – A nosology and classification system categorizes genetic bone disorders into 461 different diseases classified into 42 major groups based on their clinical, radiographic, and/or molecular phenotype . Pathogenetic variants affecting 437 genes have been identified in 425 of the 461 (92 percent) disorders.

● Prevalence – Overall, skeletal dysplasias account for approximately 5 percent of genetic disorders identified in the newborn period.

● Perinatal mortality – Approximately 50 percent of skeletal dysplasias are lethal perinatally . The overall frequency of perinatal deaths due to skeletal dysplasias is approximately 9 per 1000 births, with 23 percent stillborn and an additional 32 percent who do not survive beyond the first week of life .

INITIAL ULTRASOUND EVALUATION

Screening —

International Society of Ultrasound in Obstetrics & Gynecology (ISUOG) practice guidelines state that femur length (FL) should be measured on ultrasound examinations performed at ≥14 weeks .

The FL is imaged such that both ends of the ossified metaphysis are visible, and then the longest length of the femur diaphysis is

Definition of short femur — A short femur is typically defined as below the 5th percentile for gestational age, or less commonly below two standard deviations (SD) from the mean for the gestational age.

Evaluation of the fetus with a mildly shortened femur — The differential diagnosis for a mildly shortened FL includes normal variation, constitutional short limb, a false-positive measurement, fetal growth restriction (FGR) , and aneuploidy (primarily trisomy 21). The following key points help in differential diagnosis when a short femur is detected on ultrasound:

●The majority of isolated mildly short femurs represent normal variation or constitutional short stature, and has been termed "constitutional short femur." Over time, children with constitutional short stature will demonstrate normal interval growth of the long bones, but along a line below the normal centiles.

●As many as 13 percent of isolated mildly short femurs diagnosed at 18 to 24 weeks are reclassified as normal on follow-up . This suggests the original value was a measurement error rather than an interim catch up growth spurt.

●Parental ethnicity impacts height and should be considered in interpretation of FL percentile. Mean FL is shorter in Asian populations compared with White populations and shorter in White populations compared with Black populations.

●The possibility of aneuploidy, in particular Trisomy 21, should be considered as a mildly short femur is a soft marker of fetal aneuploidy, although the predictive value is low when this is an isolated finding and the patient is otherwise at low risk for fetal aneuploidy. The high detection rate for Trisomy 21, using non-invasive prenatal screening (NIPS) by analyzing cell-free DNA, should be offered to rule out this possibility when amniocentesis is declined.

●The possibility of FGR should be considered. The diagnosis of FGR is supported by other sonographic evidence of growth restriction (eg, small abdominal circumference, abnormal placental morphology, abnormal Doppler parameters) and low pregnancy-associated plasma protein-A (PAPP-A) and placental growth factor (PlGF). An isolated short femur may be the presenting sign of FGR, but over time, other measurements, such as abdominal circumference and sometimes the head circumference, will also begin to drop below the normal growth curves for gestational age.

Findings suggestive of pulmonary hypoplasia include:

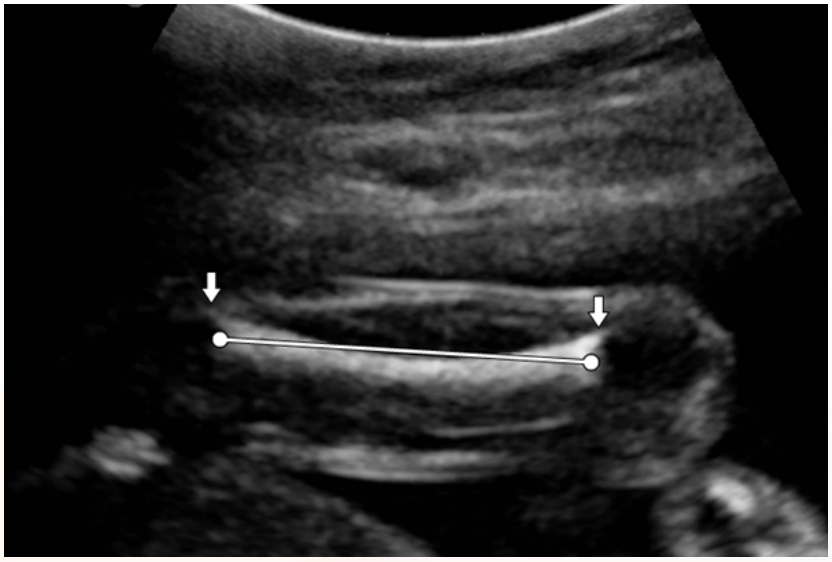
- Thoracic circumference <5th percentile, measured at the level of the four-chamber heart view
- Thoracic to abdominal circumference ratio <0.6
- Short thoracic length (from the neck to the diaphragm compared with nomograms)
- Ribs that encircle less than 70 percent of the thoracic circumference at the level of the four-chamber cardiac view
- Markedly narrowed anteroposterior diameter (sagittal view)
- Concave or bell-shaped contour of the thorax (coronal view)
- Heart to chest circumference ratio >50 percent
- Femur length (FL) to abdominal circumference ratio <0.16; this ratio is even more predictive when associated with polyhydramnios.

Postnatal/post-termination evaluation — Despite the rare occurrence of individual skeletal dysplasias, assessment of radiographic findings, molecular analysis, and pathology specimens enables postnatal assignment to a specific group within the 2010 and 2015 Nosology and Classification of Genetic Skeletal Disorders system in up to 99 percent of cases .

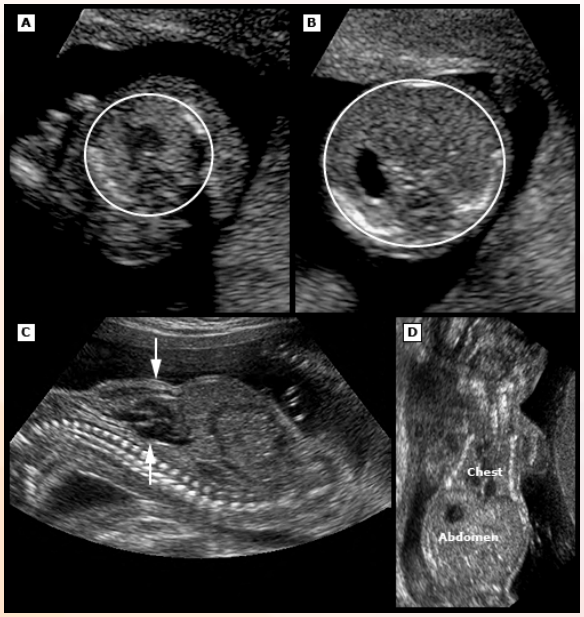
Fetal autopsy should be offered to identify the etiology of the skeletal dysplasia, especially if the diagnosis is uncertain or the results will affect future reproductive plans. For example, if there is an increased risk of recurrence, some parents may choose to have preimplantation genetic testing, egg/sperm or embryo donation, early prenatal diagnosis, or avoid subsequent pregnancy.

It is preferable for the autopsy to be performed by a perinatal pathologist. If the parents decline a full postmortem evaluation, then a minimally invasive evaluation including external evaluation and imaging as well as DNA/fibroblasts/tissue banking may be of value.

With parental consent, external and internal examinations are performed, and skeletal radiographs and photographs are taken. Histopathologic examination of bones, relevant tissue, and the placenta should be performed. The femur is the most useful bone for examination, as it offers bone and cartilaginous tissue in addition to two large growth plates. Bone and cartilage may be kept deeply frozen for later studies. Tissue should be referred for DNA extraction and banking, as well as fibroblast banking for further studies, including microarray analysis, genetic variant analysis for a specific gene disorder when a specific diagnosis is suspected, as well as gene panel and WES/WGS when no specific diagnosis is suspected. If ES is used, parental DNA should also be obtained to improve the diagnostic yield.



Femur (diaphysis) length measurement: The transducer is optimally aligned; the long axis of the femur is aligned perpendicular to the beam with both ends of the diaphysis visualized. The calipers are placed at each end of the ossified diaphysis without including the specular reflection of the distal epiphyseal cartilage (thick arrows). To ensure the maximum length is obtained, the specular reflectors from the smooth surface of the lateral aspect of the femoral epiphyseal cartilage (thick arrows) should be visible at both ends but not included as part of the measurement of the diaphysis (line).



(A and B) Lethal pulmonary hypoplasia, subtype unknown, diagnosed at 13 weeks of gestation on the basis of a small chest circumference. The chest circumference (circle in A) is significantly smaller than the abdominal circumference (circle in B). Pathological diagnosis was dyssegmental dysplasia.
(A) Cross-section of the thorax.
(B) Cross-section of the abdomen.
(C and D) Lethal pulmonary hypoplasia on the basis of a small thorax.
(C) Thanatophoric dysplasia at 23 weeks. Sagittal ultrasound demonstrates the markedly narrow anteroposterior diameter of the thorax (between arrows). The heart fills almost the entire thorax. The abdomen appears relatively protuberant compared with the constricted thorax.
(D) Osteogenesis imperfecta type 2 at 21 weeks. Coronal ultrasound demonstrates the bell-shaped contour of the thorax and narrow transverse diameter relative to the abdomen.

Qualitative assessment of long bones — Assessment of long bones includes:

●Shape (bowing, angulation, contour, metaphyseal flaring)
Bowing/bending/angulation of the femurs is a finding in most skeletal dysplasias, but the four most common are campomelic dysplasia, thanatophoric dysplasia (TD), achondroplasia, and osteogenesis imperfecta. Conditions that are associated with isolated bowed femurs include Stuve-Wiedemann and Schwartz-Jampel syndromes, amongst others.
Metaphyseal flaring is associated with Kniest syndrome.
●Mineralization and presence of fractures
Decreased mineralization of the long bones is most reliably diagnosed by the presence of fractures; decreased or absent acoustic shadowing is a less reliable marker.
●Absence of individual long bones (fibula, tibia, radius)
●Joint deformities. Multiple joint contractures in association with kyphoscoliosis and micromelia are typical of diastrophic dysplasia.
●Premature ossification of the epiphysis in association with multiple ossification centers ("stippled epiphysis") is characteristic of chondrodysplasia punctata but may also be associated with warfarin embryopathy and maternal systemic lupus erythematosus and other autoimmune diseases.
●Spine — The spine is assessed for segmentation anomalies, kyphoscoliosis, platyspondyly, demineralization, myelodysplasia, and caudal regression.
●Hands and feet — Common deformities of the hands and feet include clubfoot, rocker bottom foot, clubhand, short fingers (brachydactyly), or an abnormal number of digits.
●Calvarium — In most skeletal dysplasias with prenatal onset, the long bones are disproportionately short, and the calvarium is normal or large.
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●Face — Common facial abnormalities include midface hypoplasia, saddle nose deformity, hypertelorism, cleft lip and palate, frontal bossing, micrognathia (mandibular hypoplasia), and retrognathia (abnormal posterior positioning of the mandible or maxilla).
●Ribs — Ribs are assessed for abnormal appearance or number. Short ribs, encircling less than 70 percent of the thorax, are associated with lethal skeletal dysplasias.

●Scapula — Hypoplastic or absent scapula is commonly noted in campomelic dysplasia but may also occur in Cousin syndrome, Kosenow syndrome, and Antley-Bixler syndrome.
●Pelvic bones — Although important to evaluate, the pelvic bones are difficult to assess on conventional two-dimensional (2D) ultrasound and additional three-dimensional (3D) techniques may be required to appreciate the shape of the iliac bones and the sacrosciatic notches.

Predicting lethality

Overview — One of the most important determinations that needs to be made prenatally is whether the condition is lethal: resulting in intrauterine death or in neonatal death (from respiratory failure caused by pulmonary hypoplasia). After a lethal prognosis is established, evaluation of key sonographic features is performed to attempt to determine a specific diagnosis.
Prediction of lethality on prenatal ultrasound has been reported to be highly accurate, ranging from 81 to more than 99 percent . In the largest prospective study using a standardized ultrasound approach to the evaluation of these disorders, lethality was accurately predicted in 96.8 percent of 500 cases in the International Skeletal Dysplasia Registry.
The literature indicates that death occurs in this group before or during the neonatal period, typically due to respiratory failure. However, in one study of a cohort of 38 infants with typically lethal skeletal dysplasias, including thanatophoric dysplasia, achondrogenesis, and osteogenesis imperfecta type IIA, the survival rate was 50 percent in the neonatal period and 28.9 percent at one year of life . This group of infants required aggressive medical intervention, including intubation in 78.9 percent, mechanical ventilation in 92.1 percent, and tracheostomy placement in 23.7 percent. Because of such data, it has been suggested that a diagnosis of lethality should be replaced by the term "lethal or life-limiting" to more fully encompass the potential postnatal clinical course with aggressive medical support . Contemporary data should be considered when counseling parents about the most common of the so called "lethal" skeletal dysplasias, acknowledging some limitations of the diagnosis of "lethality." As part of this counseling, the clinician should discuss with parents whether they want heroic measures to treat the newborn and their decision should be respected.
First trimester prognostic findings — In general, the earlier in gestation a skeletal dysplasia is detected, the worse the prognosis. The majority of cases identified in the first trimester represent lethal skeletal dysplasias . In the first trimester, the combination of increased nuchal translucency, short femurs, abnormal skull shape, lack of or low degree of mineralization, and small chest is highly predictive of a lethal skeletal dysplasia . When increased nuchal translucency is associated with skeletal dysplasia, approximately 85 percent of cases are lethal skeletal dysplasias .
Second and third trimester prognostic findings — It is important to use multiple sonographic parameters to obtain the most accurate diagnosis of lethality (caused by the pulmonary hypoplasia associated with the small chest circumference).

Prenatal ultrasound assessment of suspected skeletal dysplasia

Obtain the following	General comment	Specific comments
Accurate gestational age	LMP or early dating ultrasound	If unable to obtain accurate dating, consider BPD to FL ratios
Measure all long bones	Are any bones missing? Determine the pattern and degree of limb shortening	Rhizomelia, mesomelia, acromelia, micromelia (mild, severe, severe/bowed)
Measure foot length	Calculate femur to foot length ratio	<0.9 abnormal
Assess the shape and contour of long bones	Bowing, angulations, fractures	If fractures, query occasional or numerous
Determine if decreased mineralization	Determine if diffuse or focal	If focal, specifically determine if the calvarium or spine or specific bones appear "absent"
Determine if this may be a lethal condition	Obtain axial, coronal, sagittal images of the thorax	Look for narrow AP diameter on sagittal Look for bell-shape thorax on coronal
	Obtain chest circumference	Chest circumference <5th percentile suspicious
	Determine if ribs appear short	Ribs should encircle >70 percent thoracic circumference
	Obtain chest to abdomen circumference ratio	Chest to abdomen ratio <0.6 concern for lethality
	Obtain femur length to abdominal circumference ratio	<0.16 concern for lethality
	Consider obtaining lung volume	
Skull	Shape, size, mineralization	Assess for cloverleaf deformity, macrocranium, compressibility
Facial profile		Look for frontal bossing, micrognathia, flat nasal bridge, cleft lip/palate
Vertebrae/spine	Degree and pattern of demineralization, shape, alignment	Is there platyspondyly?
Abnormal posturing of joints		Query kyphoscoliosis, fixed contractures
Hands and feet	Postural deformities, abnormal number of digits	
Scapulae size and shape	Hypoplastic or dysplastic	Think campomelic dysplasia
Growth parameters	Placental and well-being parameters	Is there intrauterine growth restriction?

LMP: last menstrual period; BPD: biparietal diameter; FL: femur length; AP: anterior-posterior.

UpToDate

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SHORT CERVIX

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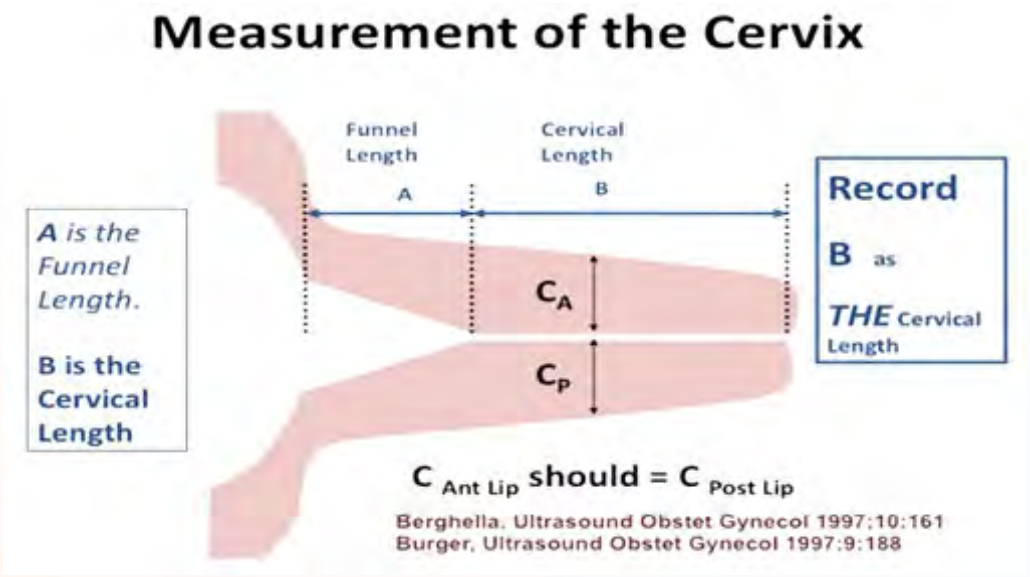
WHO defines preterm birth as those which deliver between 20 - 36 weeks.

The cervix plays a central role in maintaining a pregnancy. During most duration of a normal pregnancy, the cervix remains firm and closed in spite of distension of the uterus and a progressive increase in fetal size.

Importantly, USG cervical length is more informative than a history of previous preterm in predicting preterm birth.

USG cervical length is not a screening test for spontaneous preterm delivery as only a few patients who will experience a spontaneous preterm birth develop a short cervix in the mid trimester of pregnancy.

Transabdominal sonography requires a full bladder for adequate visualization of the cervix; as a result, a distended bladder can compress and artificially lengthen the cervix. Therefore, TVS is the recommended technique for evaluation of the uterine cervix in pregnancy.



Technique for assessment of cervical length by transvaginal ultrasound

Before examination - Maternal bladder should be empty
Patient position - Semi-recumbent with abducted legs
Probe selection - High-frequency transvaginal probe covered with disposable sheath and lubricated with gel on both sides (free of air bubbles)
Probe insertion - Place probe at anterior fornix with longitudinal axis orientation for sagittal imaging. Gentle pressure is needed for better identification of cervix.
Structures to be seen- external os, endocervical canal, internal os (limited by edge of mucosa)
Decreasing pressure – so that both cervical lips have same width
Magnification - Cervix should occupy 50–75% of screen
Measurement - Place calipers between functional IOS & EOS, forming a straight line between them
Repeating measurements - record 3 different measurements and choose the shortest technically correct one
Duration - Allow sufficient time to obtain 3 correct measurements which allows for observation of dynamic changes over time
Additional findings - Funneling, amniotic fluid debris, sludge, membrane separation, vasa previa, low lying placenta, morbid adherent placenta
Avoid pitfalls - Full bladder or excessive transducer pressure may artificially elongate cervical length. Thickened lower segment or uterine contractions may mimic funneling: identify cervical mucosa properly. Avoid confusing cervical mucus with funnel by identifying course of membranes at level of IOS.

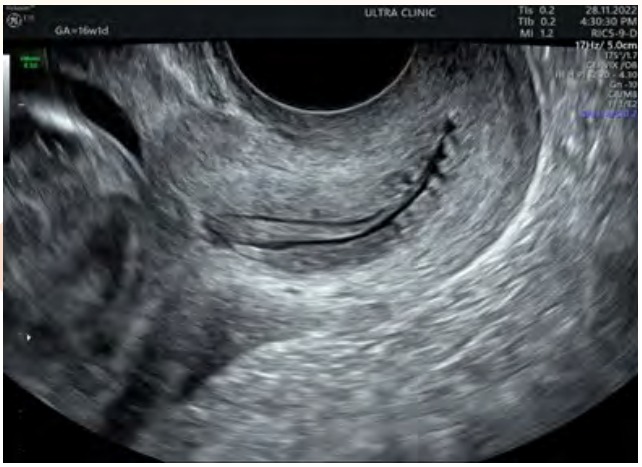


Image : Normal cervix with clearly seen internal os, external os, and endocervical canal

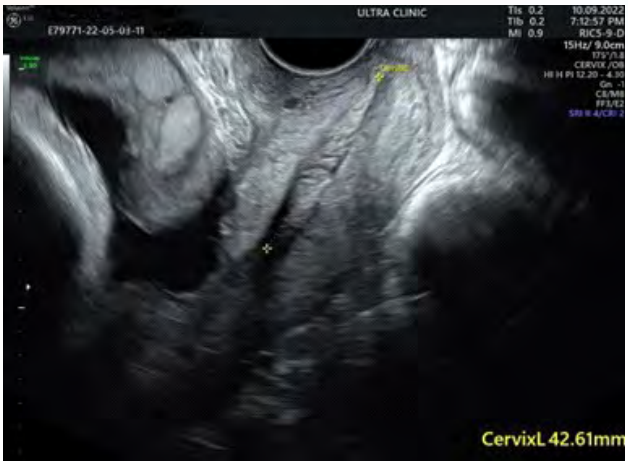


Image : TVS image of a normal cervix with slightly hyperechoic cervical mucosa

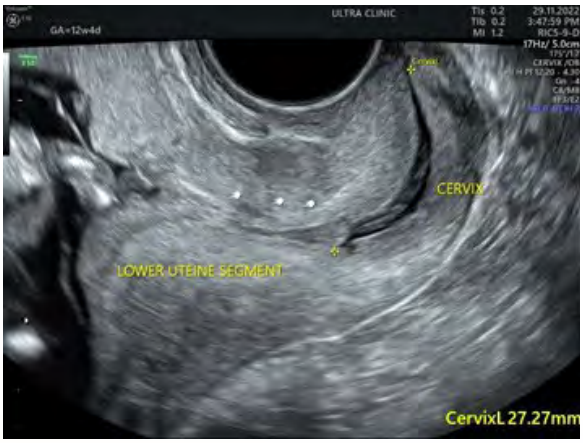


Image : TVS during 1st trimester : the thickened underdeveloped lower uterine segment not to be included in the measurement

In general, the shorter the cervical length measurement and the earlier the gestational age at shortening, the higher the rate of spontaneous preterm birth. It is always advisable to screen asymptomatic women by cervix measurement between 18 and 24 weeks of gestation, as part of the anomaly scan.

Pre pregnancy measurements of cervical length are not useful for predicting preterm birth in a subsequent pregnancy.
Cut-off to define short cervix - In general practice, since more than 10 years, a cut-off of 25 mm has been used in the majority trials as the best method to predict preterm birth before 24 weeks of gestation.

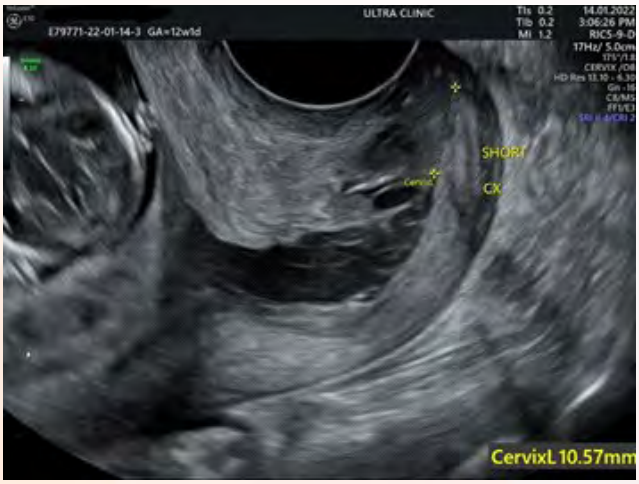


Image : Short cervix with open IOS

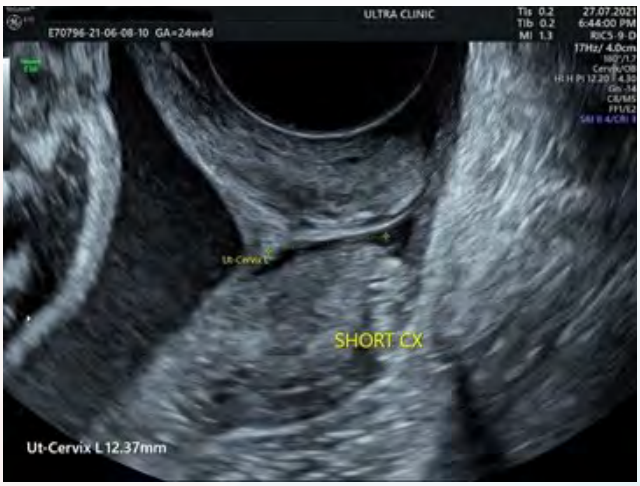
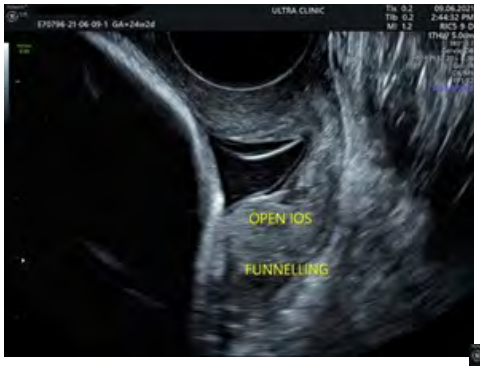
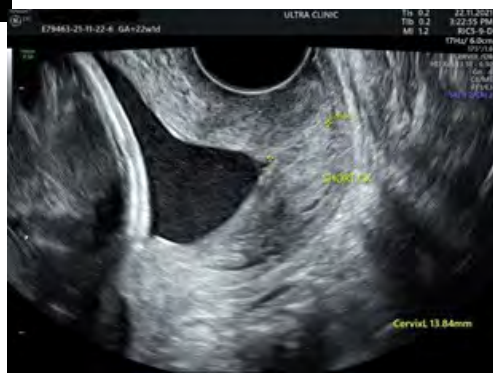


Image : A short cervix is virtually always straight

Funnelling – It is the protrusion of the amniotic sac into the upper cervical canal. Its appearance differs according to the severity of cervical shortening. If funneling is present, its length should not be included in the cervical length measurement

Trust Your Vaginal Ultrasound (mnemonic)





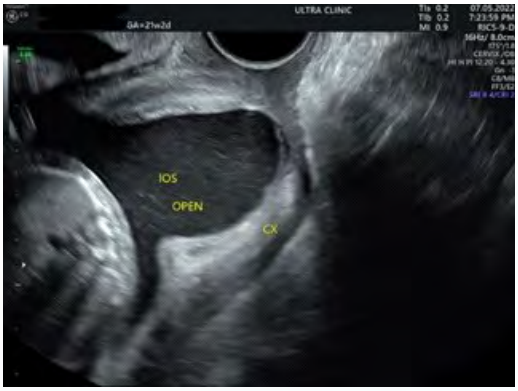
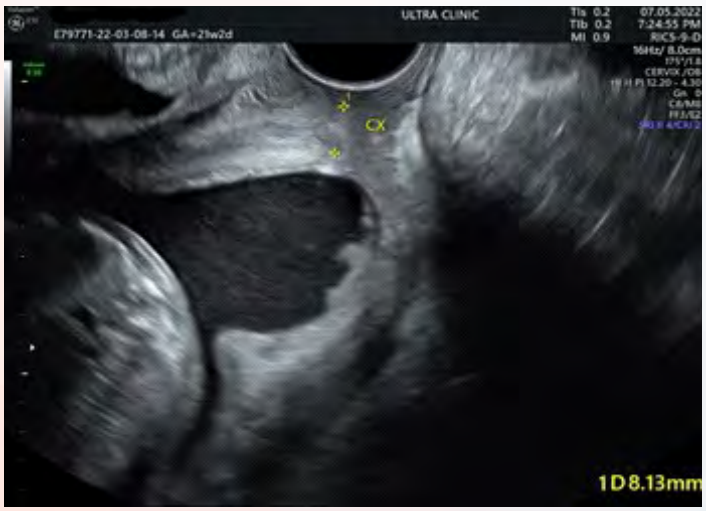


Image – TYVU progression

Amniotic Fluid Sludge - hyperechogenic dense aggregates of particulate matter in the amniotic fluid, often seen in close proximity to the internal os during TVS. Sludge may contain pus, microbes, blood clots, vernix or meconium, and has been associated with intra-amniotic infection and increased risk for preterm birth



SHORT FETAL VERMIS

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Introduction

The study of the posterior fossa is a standard protocol in fetal CNS evaluation. The cerebellar vermis is an important structure in the posterior fossa, evaluation of which is very important to diagnose and differentiate posterior fossa disorders. This write-up will discuss the topic on short vermis in brief.

Embryology

The dorsal pontine flexure divides the area membranacea into anterior and posterior parts. The cerebellum and the vermis develop from the anterior membranacea and extend inferno-laterally to cover the roof of the fourth ventricle. Development of the vermis begins with the fusion of cerebellar hemispheres in the midline by the ninth week and extends caudally with the closure of the vermis being completed by the 15th week. In some cases, the posteroinferior aspect of the vermis may be open till the 18th week of gestation.

Ultrasound appearance

On ultrasound the vermis is seen as a bright hyperechoic kidney-shaped structure in the posterior fossa sitting on the brainstem, its echogenicity is due to pial reflection and dense folia. The ventral border has a small “v” shaped notch called the fastigium. An indentation is seen along the dorsal aspect of the vermis in its upper aspect, this represents the primary fissure, this fissure divides the vermis into anterior and posterior lobes. (Fig.1).

Vermian morphometry

Vermian morphometry is important in diagnosing various pathologies, on routine scan eyeballing with appreciating the important landmarks (fastigium, primary fissure) is helpful as a part of the initial assessment, for further evaluation vermian size is measured by taking the length (craniocaudal dimension) and its AP diameter from fastigium to the highest point on the dorsal surface. There are studies that have measured the area and circumference of the vermis to determine its size. In addition, there is the brainstem-vermis angle taken between the dorsal aspect of the brainstem and the ventral aspect of the vermis, normal angle varies between 5.5–12.5°. Appearance, size, and the angle help in the differential diagnosis.

Normal Vermis

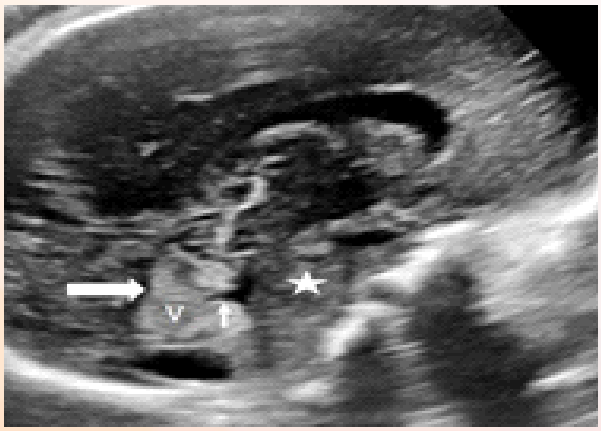

Fig.1 Hyperechoic normal vermis (v) , brainstem(star), Fastigium(arrow) , primary fissure (thick arrow).

Short Vermis

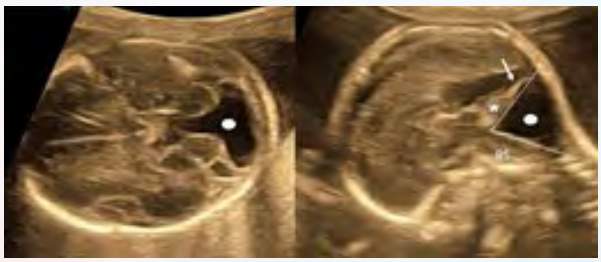

Fig.1 Dandy walker malformation- Cystic dilatation in posterior fossa(circle), splaying the cerebellar hemispheres and compressing the vermis , fastigium and primary fissure are absent, increased brainstem vermis angle.

NASAL BONE HYPOPLASIA: AN OVERVIEW

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Nasal bone hypoplasia, a condition characterized by the underdevelopment of the nasal bones, has garnered substantial attention due to its association with various genetic syndromes. This essay delves into the multifaceted aspects of nasal bone hypoplasia, including its genetic underpinnings, embryological insights, diagnostic methodologies and clinical significance.

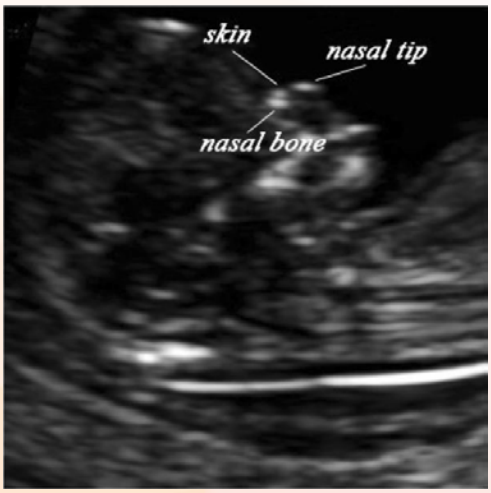
Diagnostic Definition

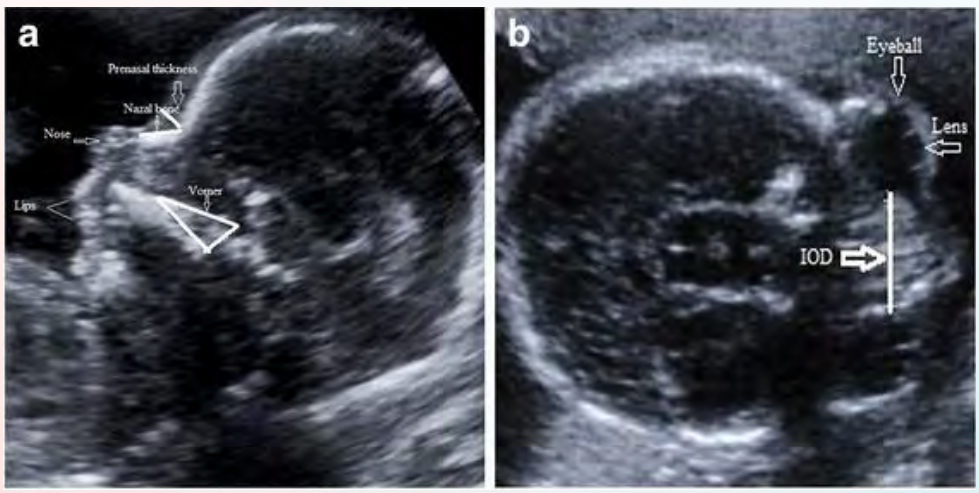
Nasal bone hypoplasia is often defined by its absence or measurements falling below the 2.5th percentile. This parameter, influenced by genetics, race, and gestational age, contributes to the comprehensive evaluation of fetal development. Accurate and timely diagnosis is of paramount importance, as nasal bone hypoplasia is frequently associated with additional malformations. Chromosomal aberrations were found in 7.1% of isolated cases and a staggering 57% of cases with supplementary malformations. This underscores the significance of early detection, timely interventions and genetic counselling.

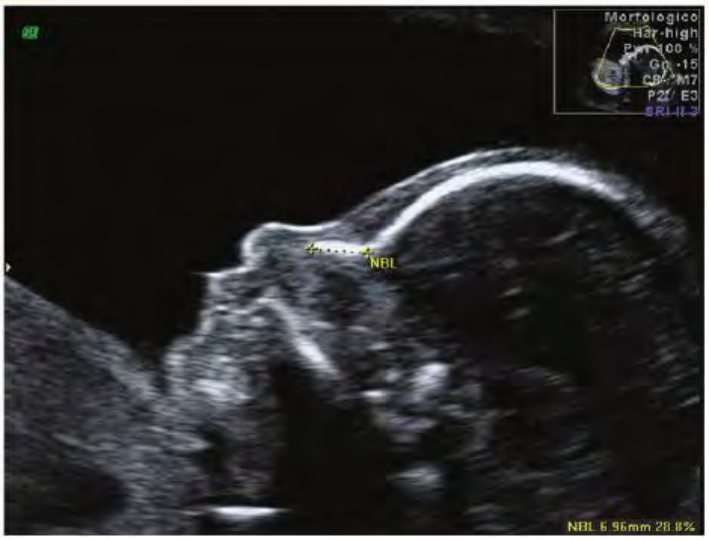
Diagnostic Protocol and Measurement

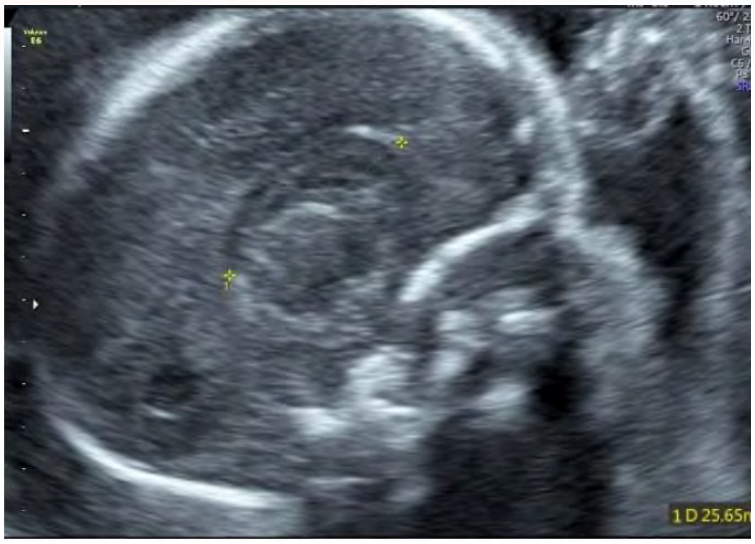
Precise measurement of fetal nasal bone length is a cornerstone in diagnosing nasal bone hypoplasia. The nasal bones are evaluated in the mid-sagittal plane of the fetal profile, with the ultrasound transducer at an angle between 45° and 135° to the facial plane. The image was magnified so that the fetal head and upper thorax were present on 75% of the screen. The nasal bone and nasofrontal

synostosis, which appear as an anechoic area on the glabellar region. The caliper position was adjusted in such a way that each movement corresponded to a 0.1 mm-displacement. The method and reference range outlined by Sonek et al. guide clinicians in ensuring accurate measurements. The echogenic appearance of the nasal bone, resembling an "equal sign," aids in differentiating normal development from hypoplasia or absence. Further parameters, including prenasal thickness, nasal tip distance, and the length of the corpus callosum, contribute to a comprehensive evaluation. Nasal bone length is also correlated with biparaital diameter as well as inter orbital distance.









According to research by scientists in the Philippines, fetal nasal bone length at the following weeks of gestation is considered normal:
11th week of pregnancy: 1.96mm;
12th week of pregnancy: 2.37mm;
13th week of pregnancy: 2.90mm;
14th week of pregnancy: 3.44mm;
15th week of pregnancy: 4.05mm.
20 weeks of pregnancy: 4.50mm or more is normal

Any nasal bone < 2mm at 11 -14 weeks is consistent with hypoplasia and if it is less than 3.50mm at 22 weeks of pregnancy, the risk of the baby having Down syndrome is very high.
If BPD/NBL ratio is >10 the value is essentially below 5th centile.

Embryological Insights and Development

The intricate process of nasal bone development unfolds within the dense mesenchyme overlying the cartilaginous nasal capsule. Histological observations indicate that nasal bones start to form around 9-10 weeks of gestation, progressively becoming evident in ultrasound and subsequently in radiographs. Most accounts suggest the presence of a single ossification center for each nasal bone, although reports of a second, medial endochondral center remain debated. The abnormal development of these ossification centers disrupts the intricate orchestration of bone formation, leading to nasal bone hypoplasia. The fragility of nasal bones during early stages limits their identification, often becoming distinguishable only in the third trimester.

Genetic Associations and Syndromes

Nasal bone hypoplasia has been notably linked to chromosomal aberrations (microdeletion and duplication) involving trisomy of chromosomes 21, 18, and 13. However, the implications extend beyond these well-known cases. Emerging research has highlighted its occurrence in rarer genetic syndromes. Gu et al. described rare chromosomal aberrations in cases with nasal bone hypoplasia and congenital malformations, such as Cri-du-chat syndrome (del 5p15.33p14.3 and dup 5q35.3), Smith–Magenis syndrome (del 17p11.2), duplication 17q23.3q25.3 (rare pathogenic CNV) and deletion 9q31.2 (CNV of potential significance)

Nasal bone hypoplasia is often observed in syndromes with a characteristic facial dysmorphism like Pallister–Killian syndrome with a diaphragmatic hernia and characteristic flat profile and small nose.

Conclusion

In summary, nasal bone hypoplasia stands at the intersection of genetics, embryology, and clinical diagnostics. Its association with various syndromes underscores the significance of accurate and timely diagnosis. The developmental intricacies of nasal bone formation and the elucidation of diagnostic protocols contribute to a deeper understanding of this condition. Fetal nasal bone length measurement, alongside other parameters, serves as a crucial diagnostic tool, guiding healthcare practitioners in offering optimal care and guidance to expecting parents. As research continues to unravel the complexities of nasal bone hypoplasia, further insights into its pathogenesis and clinical implications are expected to emerge, enhancing the quality of prenatal care and management.

SHORT DIGITS- HOW FAR DO WE UNDERSTAND THE IMPLICATIONS?

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Fellowship in Fetal Medicine

"Details make perfection, and perfection is not a detail"

Who understands the worth of this famously said adege by Leonardo da Vinci more than us, the Fetal medicine lovers? The ISUOG guidelines do tell us that finger counting is not a part of a routine anomaly scan, but importance of having a closer look at the digits is undeniable as far as the literature suggests.

So in my article today, I talk about one of the myriad of digit abnormalities, " brachydactyly", a general term that refers to the disproportionately short fingers and toes. It is one of the 10 categories of hand malformations classified by Temtamy and McKusick in their original work on the genetics of hand malformations. At present, "The nosology of genetic skeletal disorders: 2023 revision"(American Journal of Medical Genetics, part A, Vol.191,Issue 5) has grouped the isolated brachydactylies in Group 18 and those with syndromic associations in Group 19. Prognosis is highly variable, and depends on the nature of associated anomalies if it forms a part of a syndrome.

Bell's classification, modified by Temtamy and McKusick in 1978 consists of 5 types- A to E and there are 4 subgroups- A1 to A4. Out of these, types A3(shortened middle phalanx of little finger) and D (shortening of distal phalanx of thumb) are more frequent, for which the prevalence is about 2%.

Before we move on to a discussion about the genetics in details, let me tell you all about an interesting old study(2004, Maymon et al) that had concluded that all 5 digits of fetuses with Down's Syndrome were shorter than those of euploid fetuses. So they had advocated the integration of fetal digit measurement into the antenatal assessment of selected high-risk cases. This definitely demands more evidence, but surely can be an arena for further research.

Now, the isolated brachydactylies generally have an autosomal dominant mode of inheritance. Prenatal invasive testing is usually not indicated as per literature. Plastic surgery is needed only if it affects the hand function or for cosmetic reasons, but sometimes only physical therapy is sufficient.

More perplexing are the syndromic ones, where the associated anomalies decide the outcome. Invasive prenatal testing can be helpful for prognostication and we should seek guidance from our geneticist friends to understand the implications and nature of the causative mutation in the family. The associated syndromes reported so far are many, like Langer-Giedion syndrome, DOORS(Deafness, onychodystrophy, osteodystrophy, retardation and seizures) syndrome, Brachydactyly—intellectual disability syndrome(HDAC4-related), Brachydactyly, obesity and intellectual disability syndrome (PRMT7-related), Coffin-Siris syndrome (associated with developmental disability and characteristic facial features), Heart-hand syndrome type IV (associated with Cardiomyopathy) and so on and so forth.

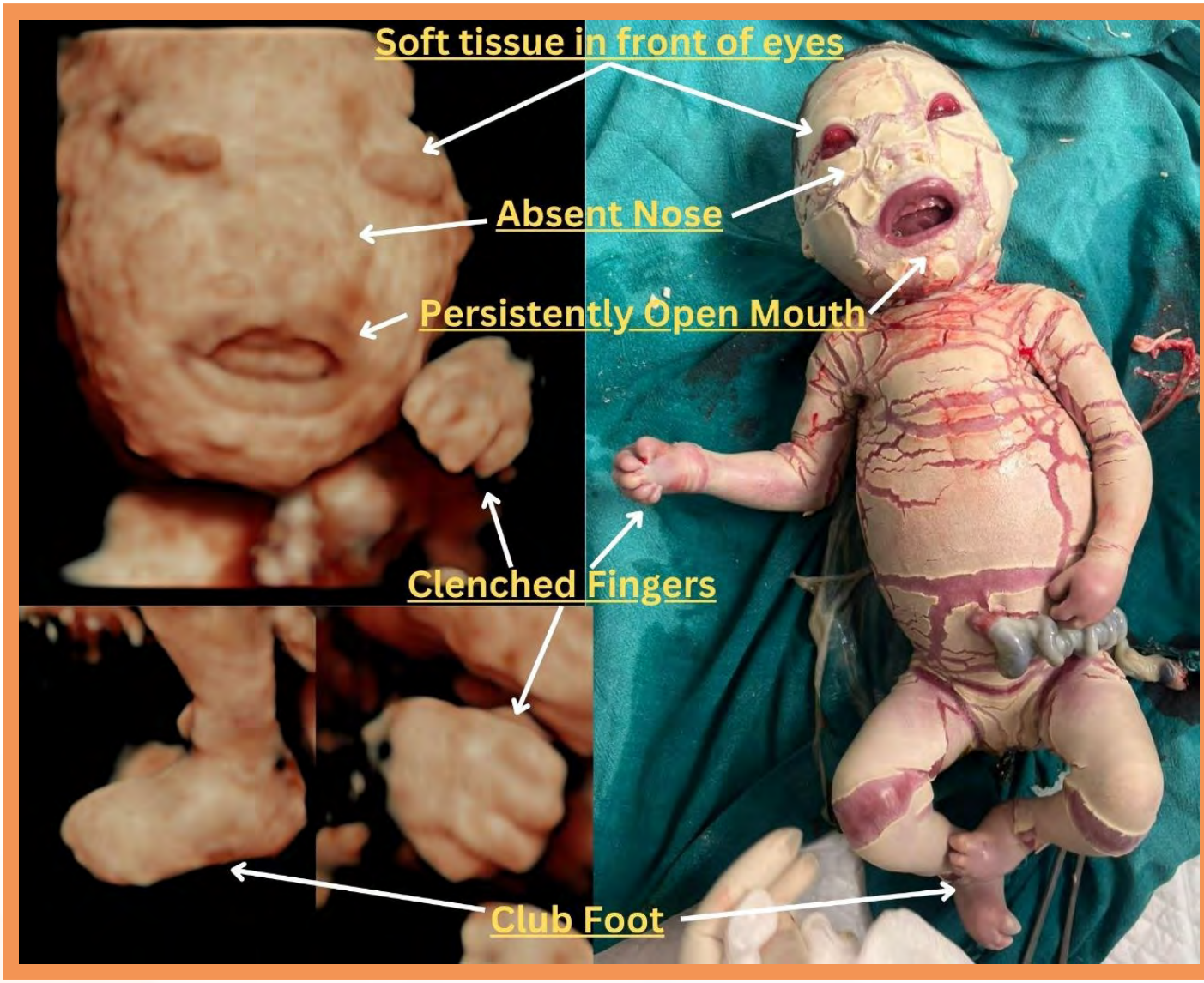
Thus, this discussion definitely clarifies 3 things-

1) The examination of digits is not something that should be disregarded, and paying attention to details helps us be more accurate as fetal medicine practitioners.

2) The syndromic cases need genetic counselling and prenatal invasive testing.

3) A multidisciplinary approach involving Fetal medicine specialist, Obstetrician, Plastic Surgeon, Geneticist is helpful for prognosticating the deformity.

The question remains, if isolated brachydactyly should have a molecular diagnosis or not. On this point, there is still somewhat conflicting evidence in literature. This issue needs further discussion, as evidently some syndromes that we have discussed, do not have sonographically identifiable anomalies other than brachydactyly. I choose to leave this question open for our esteemed readers.



1st Prize Image

Dr. Tulika Joshi
Ranchi

We thank our esteemed authors who despite their busy schedules spent valuable time to write for our newsletter.

We are grateful to our media partner **Conferences International**, without whose support we couldn't have published this newsletter.