بسم الله الرحمن الرحيم
Prenatal Screening for Fetal aneuploidy

Screening is the process of surveying a population, using a specific marker or markers and defined screening cut-off levels, to identify the individuals in the population at higher risk for a particular disorder.
• **First trimester screening for aneuploidy**
  
  *Fetal nuchal translucency*
  
  *Nasal bone sonography in the first trimester*
  
  *Doppler ductus venosus*
  
  *Tricuspid regurgitation*

• **Second trimester genetic ultrasound**
  
  *Structural anomalies*
  
  *Soft marker screening*
In the 1990s, screening by a combination of maternal age and fetal **NT thickness** at **11–13+6 weeks** of gestation was introduced.

This method has now been shown to identify about 75% of affected fetuses for a screen-positive rate of about **5%**.

In 2001, it was found that in **60–70% of fetuses** with trisomy 21 the **nasal bone** is not visible by ultrasound at **11–13+6 weeks** and preliminary results suggest that this finding can increase the detection rate of the first trimester scan and serum biochemistry to more than **95%**.
Nuchal translucency (NT) is the sonographic appearance of a subcutaneous collection of fluid behind the fetal neck. In the first trimester, the term translucency is used irrespective of whether the collection of fluid is septated, whether it is confined to the neck, or it envelopes the entire fetus.
Pathophysiology of increased NT:

- Cardiac dysfunction secondary to structural malformation
- Venous congestion in the head and neck
- Altered composition of the extracellular matrix
- Failure of lymphatic drainage because of impaired fetal movements in various neuromuscular disorders
- Fetal anemia
- Fetal hypoproteinemia
- Fetal infection.
• Fetal NT can be measured successfully by transabdominal ultrasound examination in about 95% of cases; in the others, it is necessary to perform transvaginal sonography. The results from transabdominal and transvaginal scanning are similar.

• At 11–13+6 weeks, all major chromosomal defects are associated with increased NT thickness (Snijders et al 1998). In trisomies 21, 18 and 13 the pattern of increase in NT is similar and the average NT in these defects is about 2.5 mm above the normal median for crown-rump length.

• In Turner syndrome, the median NT is about 8 mm above the normal median.
• Fetal NT increases with crown–rump length and therefore it is essential to take gestation into account when determining whether a given NT thickness is increased.

• During the second trimester, the translucency usually resolves and, in a few cases, it evolves into either nuchal edema or cystic hygromas with or without generalized hydrops.

• The single most powerful marker available today for differentiating Down syndrome from euploid pregnancies is the first trimester sonographic measurement of the fetal nuchal translucency (NT) space.
measurement of fetal NT

- The optimal gestational age for the measurement of fetal NT is between 11 weeks and 13 weeks 6 days. The minimum fetal crown-rump length (CRL) should be 45 mm, and the maximum should be 84 mm.
- Only the fetal head and upper thorax should be included in the image for measurement of NT.
- The magnification should be as large as possible. A good sagittal section of the fetus, as for the measurement of fetal CRL, should be obtained and the NT should be measured with the fetus in the neutral position.
**chromosomal defects** increases with NT thickness:

- 50% trisomy 21.
- 25% trisomy 18 or 13.
- 10% Turner syndrome.
- 5% triploidy.
- 10% other chromosomal defects (Snijders et al 1998).

There are no clinically relevant effects on NT measurements by ethnic origin, parity or gravidity, cigarette smoking, diabetic control, conception by assisted reproduction techniques, bleeding in early pregnancy or fetal gender.
Increased NT

Increased NT is also associated:

1. Major defects of the heart and great arteries,
2. Skeletal dysplasias

- The prevalence of these abnormalities is related to the thickness of NT.
• Recently, multiple studies have demonstrated that fetal NT has the potential of being a very powerful predictor of fetal aneuploidy.

• Prospective studies in 200,000 pregnancies, (900 fetuses with trisomy 21), have demonstrated that NT screening can identify 75% of fetuses with trisomy 21 and other major chromosomal abnormalities.

• An NT above the 99th percentile has a sensitivity of 31% and specificity of 98.7% for major congenital heart defects when fetal chromosomes are normal.
Finding an increased NT at 11 to 14 weeks’ gestation when fetal chromosome patterns are normal warrants offering a detailed ultrasound examination at 18 to 20 weeks, with an assessment of the fetal heart including a four chamber view and view of the outflow tracts as a minimum.
Absence or hypoplasia of fetal nasal bone

- In 1866 Down noted that a common characteristic of patients with trisomy 21 is a small nose. The fetal nasal bone can be visualized by sonography throughout pregnancy.
- This examination requires that the image be magnified so that only the head and the upper thorax are included in the screen.
- At 11–13+6 weeks the nasal bone is not visible by ultrasonography in about 60–70% of fetuses with trisomy 21 and in about 2% of chromosomally normal fetuses.
• A mid-sagittal view of the fetal profile is obtained with the ultrasound transducer held parallel to the longitudinal axis of the nasal bone. In the correct view, there are 3 distinct lines.

• The first 2 lines, which are proximal to the forehead, are horizontal and parallel to each other, resembling an equal sign (=). The top line represents the skin and the bottom line, which is thicker and more echogenic than the overlying skin, represents the nasal bone.
Recent reports have suggested that an absent fetal nasal bone or nasal hypoplasia is a marker for aneuploidy, both in the first and second trimesters, and that the absence of the nasal bone is not related to NT thickness. Therefore, they could be combined relatively simply to provide a more effective method of early screening for trisomy 21.

Several studies have demonstrated a strong association between an absent nasal bone at 11–14 weeks of gestation and trisomy 21, and other chromosomal abnormalities.
Doppler in the ductus venosus

The ductus venosus is a unique shunt directing well-oxygenated blood from the umbilical vein to the coronary and cerebral circulations by preferential streaming through the foramen ovale into the left atrium. Blood flow in the ductus has a characteristic waveform with high velocity during ventricular systole (S-wave) and diastole (D-wave), and forward flow during atrial contraction (a-wave).

- In the second and third trimesters of pregnancy abnormal flow with absent or reverse a-wave is observed in impending or overt cardiac failure.
At 10–13+6 weeks abnormal ductal flow is associated with chromosomal defects, cardiac abnormalities and adverse pregnancy outcome. There is no or only a weak association between increased fetal NT and the incidence of abnormal ductal flow. These findings indicate that assessment of the ductus venosus can be combined with measurement of fetal NT to improve the effectiveness of Early sonographic screening for trisomy 21.
Examination of ductal flow is time-consuming and requires highly skilled operators and at present it is uncertain if this assessment will be incorporated into the routine first-trimester scan. However, it could be used in specialist centres to re-evaluate the risk in patients with borderline results after screening by fetal NT and maternal serum biochemistry.
Second trimester genetic sonogram

Aim of study:
- Structural or Major abnormalities
- Minor abnormalities or soft markers
Structural or Major abnormalities

- Central nervous system anomalies
- Cystic hygroma
- Diaphragmatic hernia
- Cardiac defects
- Gastro-intestinal abnormalities
- Genitourinary anomalies
- Non immune hydrops
- Extremity abnormalities
Second trimester genetic sonogram

- Many fetuses with trisomy 18 and 13 have multiple major structural anomalies; however, this may not necessarily apply to Down syndrome.
- Only 25% of second trimester fetuses with Down syndrome have ultrasonographically detectable major congenital anomalies.
“Soft” sonographic markers

“Soft” sonographic markers are:

- variations in normal anatomy that, except for their relationship to aneuploidy (especially trisomy 21), are unlikely to be clinically significant.
- Compared with structural anomalies, markers are often transient and nonspecific findings which can also occur frequently in euploid fetuses.
- General statement: As the number of identified marker increases, the risk of aneuploidy increases as well.
Nuchal skin-fold thickness

Redundant nuchal skin folds are present in 80% of newborns with Down syndrome.

Sonographic assessment of fetal nuchal skin-fold thickness was first proposed by Benacerraf et al. in 1985. Measurements are typically performed between gestational weeks 15 and 21 using a transverse axial image that is directed in the suboccipital-bregmatic plane.

- values of $\geq 6$ mm considered abnormal
Choroid plexus cysts

The cranial lateral ventricles contain sonolucent cerebrospinal fluid. Within the lateral ventricles lies the brightly echogenic choroid plexus that normally fills the atrium, and may contain cysts.

- CPCs are a relatively common finding during the second trimester. The prevalence among normal fetuses is variable and ranges from 0.3% to 3.6%.
- Cysts may be unilateral or bilateral, single or multiple, and small or large. Commonly they are multilocular in appearance.
Extremity abnormalities

- Clubfoot
- Rocker-bottom foot
- Clinodactyly
- Sandal gap
- Radial aplasia
- Flexion deformities and movement disorders
- Polydactyly
Single umbilical artery

- In fetuses with isolated SUA, there is usually no increased incidence for a chromosome abnormality. However, as with isolated CPCs, this stipulates that a detailed sonogram by experienced personnel should rule out other anomalies. Once the SUA is believed to be isolated, in the absence of high-risk factors, invasive prenatal diagnostic procedures for chromosomal analysis may not be routinely indicated, because most fetuses with isolated SUA are karyotypically normal.
- When IUGR or multiple malformations are detected in association with SUA, prenatal karyotyping should be offered.
- When SUA is diagnosed sonographically, patients should be informed that their neonates may be at risk for subtle Anomalies which may be found only at time of birth.
Echogenic intracardiac focus

An echogenic intracardiac focus (EIF) is commonly seen on second trimester sonography, and it is present in 3% to 4% of normal fetuses.

- It is a discrete, brightly echogenic spot.
- In a low-risk population when the EIF is isolated and no other sonographic major or minor anomalies are identified, it is considered a “normal variant”, and no further evaluation (including fetal karyotyping) is generally recommended.
Thanks for your attention