**SOGP GUIDELINES FOR FIRST TRIMESTER SCREENING FOR CHROMOSOMAL ABNORMALITIES**

SOGP MFM guidelines committee has the mandate to develop practice guidelines and consensus statements that provides the health care professionals with the evidence-based approach to the use of Obstetric ultrasound. It not only shows the best practice approach and shares the limitations on the subject.

The aim of this guidelines is to provide clinicians with evidenced based consensus related to first trimester scan between 11-14 weeks and how it influences pregnancy outcomes. For the sake of clarity level of recommendations are given in Table 1.

First trimester scan is an integral part of antenatal care. It is routinely used to determine fetal viability, confirm gestational age and ascertain chorionicity in twins and has been used in the last three decades for aneuploidy screening. 1, 2,3,4 [11-2B]

Chromosomal abnormalities complicate 3% of all pregnancies. 1,2,3 and are a major cause of perinatal death and childhood handicap. 3 Down’s syndrome is the commonest of all aneuploidy.  5 Seventy percent of the babies with Down’s syndrome are born alive and have reasonable life expectancy with varying degree of neurological handicap. 3,5 Therefore, Screening for this condition remains vital.

**2:0The aim of the screening?**

The main aim of the first trimester screening is to identify pregnancies more at risk of chromosomal abnormalities by using strategies that have high detection rate without increasing the false positive rate. 5, 6 Women that are identified as high risk by the screening tests are offered diagnostic testing. 5 Diagnostic tests like CVS and Amniocentesis are both based on testing the chromosomes on fetal cells and are relatively safe but carries a small risk of miscarriage. 3 Based on the results of the tests the parents can make an informed choice regarding continuation of pregnancy or otherwise and optimize pregnancy outcomes. 5

In the last three decades there has been tremendous improvements in the screening and diagnostic testing and hence this improves the ability to diagnose these problems in pregnancy. 5, 7

**3.0: Screening strategies:**

**3.1: Maternal age:**

The risk of aneuploidies is related to advanced maternal age.3 It was the earliest maker for chromosomal abnormalities. When used alone maternal age can only identify 30% of pregnancies by offering invasive procedures to around 6% of pregnant women. 5,8 Based on this observation maternal age is considered to be a poor marker for aneuploidy screening. 5, 7 Therefore invasive testing should not be offered on maternal age alone. 6

**3.2: First Trimester Screening by Nuchal Translucency Screening:** It was Langdon Down who suggested that babies with Down have increased swelling behind the neck of the fetus. This observation was later conceptualized Nicolaides et al in the 90s for the use of Nuchal Translucency for the aneuploidy screening in the first trimester. 9 Following this ground breaking work, several subsequent studies confirm these findings. 10,11,12

Snijider R 10 has published a comprehensive multicenter study involving 22 centers incorporating maternal age and Nuchal translucency. The authors found using a cut off of 1 in 300, the modality could identify 80% of Trisomy 21 and 77.8% of other chromosomally abnormal pregnancies. With the risk cut off of 1 in 300 or higher was found in 82.2% of trisomy 21. 10

**3.3: When is the Ultrasound performed? 10**

This ultrasound is performed between 11-13 weeks and 6 days. An individualized risk is given to the pregnant women based on maternal age, crown rump length and Nuchal translucency measurement. Background risk of any pregnancy depends upon:

1. Maternal Age.
2. Previous History of Down’s syndrome.

Individualized risk is calculated by incorporating Nuchal translucency measurement will enable the couple to make informed choice.10, 13

There are wide differences in the detection rate. This can be due to the variation in the expertise in obtaining this measurement.12 Fetal Medicine foundation has an established criteria for taking the measurements.10

**Criteria for performing Nuchal Translucency scan:**

1. Is performed between 11-13 weeks and six days.
2. The fetal crown rump length should be between 45-84mm.
3. A mid sagittal view of the face should be obtained with appropriate magnification.
4. The fetus should be done in a neutral, with the head in line with the head and spine.
5. Care should be taken to distinguish fetal skin and amnion.
6. During the scan more than one measurement of the NT is taken and the widest measurement is used for risk assessment.
7. While taking the measurements the calipers are placed on the line.
8. NT 2.5 mm or more requires further evaluation

Raised Nuchal Translucency is associated with Chromosomal abnormalities, Structural defects particularly cardiac defects and rare genetic syndromes. 14, 15 Therefore, the women with raised NT need to referred to the Fetal Medicine Specialist. [Level 11-3C] **Therefore, women with raised NT should not be offered termination directly but further evaluation.**

**3.4: Who should be performing the ultrasound scan?**

Centers with **appropriately trained individuals** following strict criteria of obtaining measurements and adhering to quality control measures have better results. **[11-2A] 1,6**

In order to achieve optimum results, the individuals should have:

1. Received appropriate training in the diagnostic ultrasound and aware of the safety.
2. Individuals are aware of the first trimester screening programs and that **mentioning only Nuchal translucency measurement is no longer acceptable.**

**3.5: Pre-Screening Counseling:**

A detailed non directive counseling is mandatory prior to embarking on aneuploidy first trimester screening with or without biochemistry.6 The objective is to make the pregnant woman understand the implications of such testing including the risk of a positive result and further testing with invasive procedures. Views of the couple regarding termination of pregnancy should be known prior to embarking on such screening.6 Couple have a right to accept or decline the screening and care providers respect their wishes.5 [111A]

**3.6: Who should be screened in Pakistan?**

In Pakistan as there are limited number of operators with expertise in this scan, therefore screening is offered to:

1. Advanced maternal age of 35 years or above.
2. Previous baby with Chromosomal abnormalities
3. Previous structural abnormalities.
4. Bad Obstetric history with previous Intrauterine fetal demise, neonatal deaths & recurrent Miscarriages.
5. In cases with medical conditions like Diabetes, Thyroid disorders & Autoimmune disorders.
6. Twin/Multifetal Gestation.
7. Maternal history of exposure to teratogens, or use of category C/D drugs
8. ICSI/IVF conception.

**3.7: What are the additional benefits of Nuchal Translucency Scan??**

In addition to the screening for chromosomal abnormalities, scan is used for the diagnosis of major structural abnormalities. It is performed by operators with appropriate expertise. [Level 11-3A] The table below gives an idea of which abnormalities can be diagnosed at that stage.16, 17

**3.8: Detection of first trimester anomalies:**

| Always detected | Sometimes detected | Not detectable |
| --- | --- | --- |
| Acrania/ Anencephaly | Open Spina Bifida | Ventriculomegaly |
| Holoprosencephaly | Hypoplastic left heart | Agenesis of Corpus callosum |
| Encephalocele. | Lower urinary tract obstruction | Isolated cleft lip |
| Exomphalos/ Gastroschisis | Arthrogryposis or fetal akinesia deformation sequence | Multicystic kidneys |
| Body stalk anomaly | Amputation of limbs | Hydronephrosis |
| Polydactyly |  |  |

**4: ROLE OF NIPT IN THE FIRST TRIMESTER SCREENING:**

Paradigm of prenatal screening has shifted with the introduction of cell free DNA screening. This technology is most sensitive and specific screening test for the common fetal aneuploidies like Trisomy 21, 13, and 18 and can be performed any time after 9-10 weeks of gestation.5 It is based on the principle of fetal cell in maternal blood. It has the highest detection rate in comparison with other conventional screening tests.6 It has a detection rate of 99.7% for trisomy 21, 98.2% for trisomy 18 and 99% for trisomy 13.18 However it is not very sensitive for sex aneuploidy or deletions and duplications.18

Pre-test counselling for cell free DNA-based screening should include informed decision-making regarding testing for fetal sex, sex chromosome aneuploidy and other deletions/duplications and its role in twin pregnancy.

**4.1: Who should be offered NIPT:**

* The test can be offered to high-risk women. First trimester screening has a vital role and hence cannot be replaced by cell free DNA.19
* Cell free DNA can be used as a second-tier screening test for women considered to be at high-risk women for aneuploidy.20,21

**4.2: What are the limitations of this test??**

* Cost
* In twin pregnancies has limited role.
* When fetal congenital anomalies are diagnosed based on ultrasound then invasive or genetic testing is offered rather than NIPT. Genetic Counseling can be offered in places where available but not mandatory.
* Inconclusive or failed test: This could be due to low fetal fraction, which can be found in aneuploid fetuses. It occurs in 1-8%.5
* It has the potential of false positive or false negative results. False-Positive Results: Placental Mosaicism, Demise of Co-Twin, Maternal Karyotype Abnormality.5
* NIPT results cannot be used for termination of pregnancy. So invasive procedures need to be offered to those with positive results.

**Recommendations:**

* First trimester screening should be offered to all women with risk factors. Low risk can be offered this scan where it is practically possible.
* Prior counseling is mandatory for both Nuchal translucency screening and Non-Invasive prenatal testing.
* Counseling should include the implications of a positive result including invasive testing and termination of pregnancy.
* If the couple lady opts for aneuploidy screening, then it is strongly advised not to offer multiple screening strategies. As this may lead to contradictory results.4
* Nuchal Translucency screening is offered by experienced operators to women between 11 weeks and 13 weeks 6 days.1
* Women with raised Nuchal Translucency 2.5 and above, need to be referred to the MFM Specialist for counseling and diagnostic procedures.6
* Raised NT perse is not an indication for termination of pregnancy.
* Women need to be made aware that Non-invasive prenatal testing is not equivalent to Diagnostic procedures like Amnio or CVS.
* Those with low risk on first trimester scan need to be counseled that they would need Second trimester scan between 19-22 weeks.
* Those with raised Nuchal Translucency or any other abnormality, should be referred to a Specialist for counseling and diagnostic testing. 14
* In case of sonographic features on the ultrasound scan, the option of invasive testing should be discussed. NIPT is only offered if the couple declines Amniocentesis/CVS.

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