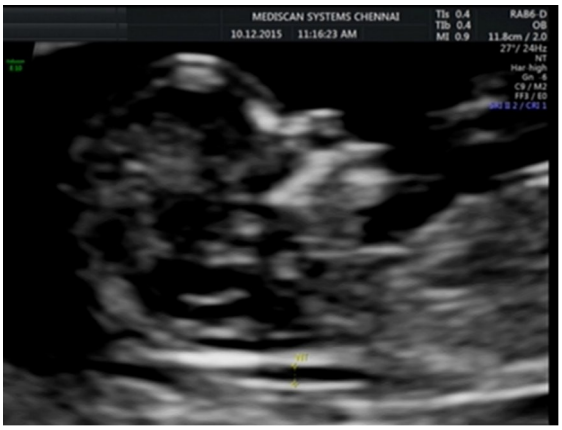
Screening for Downs syndrome in the first trimester

Screening for downs syndrome has undergone a sea change in the last decade. Screening for Downs syndrome in the 1970's was based on maternal age alone. In the next decade, association of downs syndrome with various biochemical markers was determined which formed the basis for the second trimester screening tests for Downs syndrome. However, these tests had a sensitivity of around 65% (Triple screening test) to 70%(Quadruple screening test). Pioneering work of Prof.Kypros and collogues in the UK, resulted in the advent of a newer tool for screening, the nuchal translucency which when combined with the biochemical parameters , which has stood the test of time , and has proven to be a much better screening tool (sensitivity of 90%). This review is designed to act as a ready reckoner for clinicians, with do's and dont's regarding screening for Downs syndrome in the first trimester (11-13+6 weeks / CRL 45mm-84mm).

Components:

1. MaternalAge: This parameter is computed from the maternal date of birth. The risk for having a baby with Down's syndrome increases with increase in maternal age.



CRL 45mm – 84mm

- Mid Sagittal plane
- Neutral position
- Image zoomed to occupy 75% of screen
- NT line clearly visualized and caliper placed between the lines

2. Nuchal translucency:The nuchal translucency is the fluid filled space between the fetal skin and the soft tissue overlying the cervical spine. There are strict criteria for measurement of the nuchal translucency provided by the fetal medicine foundation as detailed in the figure above. The sensitivity of the screening is closely linked to the quality of the NT imaged.

Quality control points:

- It is preferable that the person doing the NT scan should. Have undergone a verifiable training program and is certified by the FMF

- The lab which processes the samples should have a quality control process an audit process to reject improperly taken NT when it is done by a non FMF certified person

3. Biochemical parameters: free beta hCG and PAPP A :In pregnancies with trisomy 21, maternal serum concentrations of free b hcg is twice as high and papp-a value is reduced to half when compared to euploid pregnancies. These factors are affected by maternal demographic characteristics(age, mode of conception, ethnicity,maternal diabetes, weight).Vaginal bleeding does not affect the biochemical parameters.

Quality control points while looking at the screening report:

- Correct date of birth has been entered
- Maternal weight, diabetic status entered
- The report should contain MoM(multiples of median) for all the above parameters
- If the mother has had an hCGinjection , the biochemical screening can be done only after 5 days as administration of hCG will falsely elevate the serum values and high chance of a false positive result.

4.Prior h/o Downs syndrome: If a pregnant woman has had a prior baby with downs syndrome, the recurrence risk would depend on the type of trisomy 21. Ideally, these patient should have genetic counseling with the karyotype of the first child prior to screening. If screening is pursued, the information should be provided, as it would increase the apriority risk for the patient.

Quality control points:

- When there is previous h/o downs syndrome – genetic counseling is essential

- The screening report should reflect this information provided as it alters the baseline risk

5.Screening in assisted conception : When screening for pregnancies with assisted conception, the mode of conception (ICSI/IVF), date of embryo transfer, date of egg collection. If a donor egg has been used , the age of the donor MUST be provided.

Check list for conditions when FTS is not done :

- Higher order multiple pregnancies (triplet,quadruplets)

- Pregnancies where selective fetal reduction has been done

- Presence of an additional non-viable fetal pole in additional to the viable gestation

In these circumstances, screening based on maternal age, NT status can be done.

6.Screening in multiple pregnancy: First trimester combined screening is only done for singleton and twin pregnancies. Adjustments in the MoM has to be done for Chorionicity, as the levels of hcg and papp-a are twice as high in dichorionic twins compared to singletons. In monochorionic twins the levels are lower than in dichorionic twins.

Quality control points:

- Check if the report has chorionicity data

- hcg and papp-a MoM are computed for the pregnancy as a whole. The report should not have different MoM's for both fetuses

- In dichorionic twins, specific risks for trisomy 21 are provided for each fetus

- In monochorionic twins, one common risk is provided for the pregnancy

7.Pre-posttest counseling: It is good practice to provide information to the patient on the nature of the test.

Counseling points:

- This is a screening test which helps predict the probability of the fetus to have Downs syndrome with a sensitivity of 90% with a false positive rate of 5%. It does not confirm if the baby has Downs syndrome
- A risk of greater than 1:250 is considered screen positive. A positive screen test would mean that there is a higher than average chance of having a baby with Downs syndrome. Further confirmatory tests (chorionic villous sampling/amniocentesis) would need to be done
- A negative screen test would mean that there is a lower chance of the baby to have Downs syndrome.
- Appropriate post test counseling needs to be done interpreting the results, and further assessment can be planned.

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