

Manual on Labour Room Protocols

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First Trimester Screening

Vandana Walvekar, Preeti Deshpande

INTRODUCTION

The first trimester is the ideal time to screen for aneuploidies. In the past, invasive monitoring was only offered to women above 35 years age at delivery (advanced maternal age) or those with a previously affected child. Screening tests were then introduced.

TYPES OF SCREENING

First trimester screen was introduced in early 1990s with sonographic and serum markers. Nuchal translucency (NT) and pregnancy associated plasma protein A (PAPP-A) and human chorionic gonadotropin (hCG) were used for screen for Down's syndrome (**Table 3.1**).

The most effective multiple screen marker in the 2nd trimester is the quadruple screen comprising of alpha-fetoprotein (AFP), human chorionic gonadotropin (hCG), unconjugated estriol (uE3) and inhibin-A. This yields sensitivity for Down's syndrome of up to 81% with 5% false positive (**Table 3.2**).

Table 3.1 | Nuchal translucency and serum markers used in the first trimester screen

	NT	PAPP-A	Free beta hCG	Inhibin-A
Trisomy 21	Increased	Low	High	No change
Trisomy 18	Increased	Low	Low	Increase
Pregnancy loss <24 weeks	Increased	Very low	Very low	No change

Table 3.2 | Pattern of results with quadruple screen for foetal anomalies in second trimester

	AFP	uE3	hCG	Inhibin-A
Open NTD	Increase	No change	No change	No change
Down's syndrome	Decrease	Decrease	Increase	Increase
Trisomy 18	Decrease	Decrease	Decrease	No change

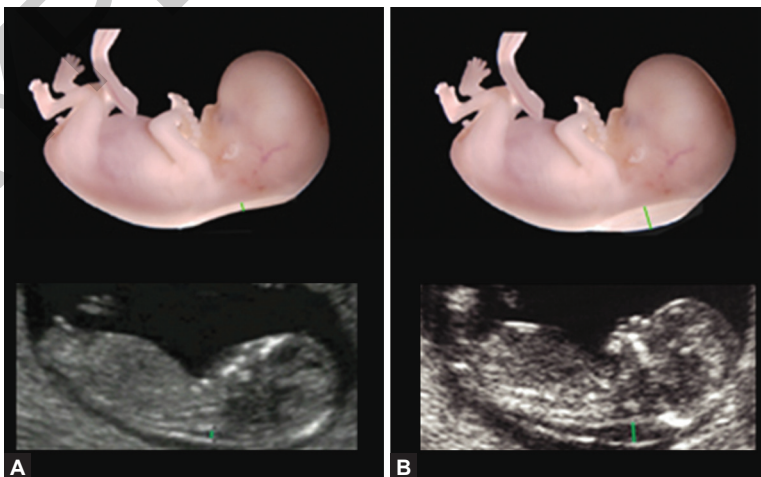
NUCHAL TRANSLUCENCY

The single most powerful marker today for differentiating Down's syndrome from euploid pregnancies is the nuchal translucency space. Nuchal translucency refers to the normal subcutaneous fluid filled space between the back of the foetal neck and overlying skin (**Figs 3.1A and B**). Normally this space is small. By adhering to the standard sonographic technique, it is possible to obtain accurate measurement of this area in vast majority of the fetuses between 10 weeks and 14 weeks (CRL 36–84 mm).

When performing nuchal translucency it is absolutely essential to ensure that the optimal technique is used.

- The foetus should be imaged in the midsagittal plane, ideally with the foetal spine down.
 - The image should be magnified so that only the foetal head, neck and upper thorax fills the viewable area.
 - The foetal neck should be neutral with care being taken to avoid measurements in hyperflexed and hyperextended position.
 - Skin at the foetal back should be clearly differentiated from underlying amniotic membrane, either by visualising separate echogenic lines or by checking how the skin moves with the foetus.
 - The calipers should be on the inner borders of the echolucent space and should be perpendicular to the long-axis of the foetus.
 - Ultrasound settings should be optimised to ensure clarity of the image and borders of nuchal space in particular.
- This may need a transvaginal scan.

Nuchal translucency may be increased in Down's syndrome, aneuploidies, adverse pregnancy outcome, congestive cardiac failure, abnormalities in extra cellular matrix and delayed development of the lymphatic system. The largest study for nuchal translucency screening was performed by the Foetal Medicine Foundation based in London and published in the Lancet 1998 with 96,127 patients. The overall Down's syndrome detection rate was 77% with a false positive 5%.¹

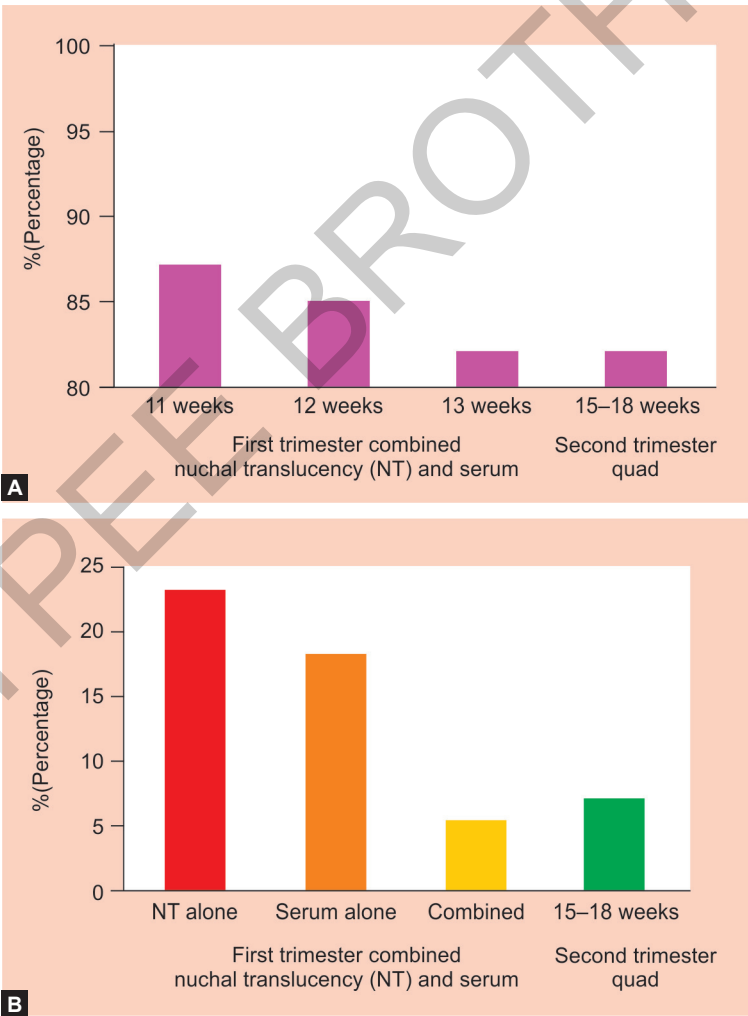


Figures 3.1A and B Nuchal translucency. (A) Normal; (B) Abnormal

Combined First Trimester Screening Nuchal Translucency with Serum Markers

First trimester serum markers are independent of nuchal translucency (NT). Hence, a combined serum and sonographic screen protocol has been developed which would be more effective than ultrasound screening alone.

Two large prospective studies have validated the performance of combined screening. The biochemistry, ultrasound, nuchal translucency (BUN) study evaluated 8,216 patients and demonstrated a Down's syndrome detection rate of 79% with a 5% false positive.² The first- and second-trimester evaluation of risk (FASTER) study evaluated 38,033 patients and demonstrated even better Down's syndrome detection rates and showed that the performance varied which the gestational age (**Figs 3.2A and B**).



Figures 3.2A and B Comparison of first and second trimester screening for Down's syndrome

For a 5% false positive rate, the Down's syndrome detection rates using combined serum and sonographic screening were 87%, 85% and 82% at 11, 12 and 13 weeks of gestation.³ Nuchal translucency increases 15–20% each weeks from 10 weeks to 14 weeks. Therefore there is no single cut off and 95th percentile of gestational age/multiples of median are used.

Recently there has been much debate regarding the 1st trimester screen program versus 2nd trimester screen approaches.

First trimester combined screen detection rates are similar to second trimester quadruple marker detection rates. The 1st trimester combined screen has lowest false positive rate. The combination of 1st trimester screen with nuchal translucency and serum marker comes close to performance of 2nd trimester quadruple marker serum screen. Nuchal translucency without being combined with serum markers has significantly inferior performance characteristics.³

SEPTATED CYSTIC HYGROMA

Increased nuchal translucency is a high-risk factor for foetal aneuploidy and adverse pregnancy outcomes. Septated cystic hygroma is said to be present when the nuchal translucency is enlarged and extends along entire length of foetus with septae. There is a 50% chance of associated foetal aneuploidy, Down's syndrome, Turner's syndrome, trisomy 18, structural malformations, cardiac malformations and skeletal dysplasia. There is also increased risk of intrauterine foetal death. Chorion villus biopsy and anatomical assessment at 18 weeks is recommended.

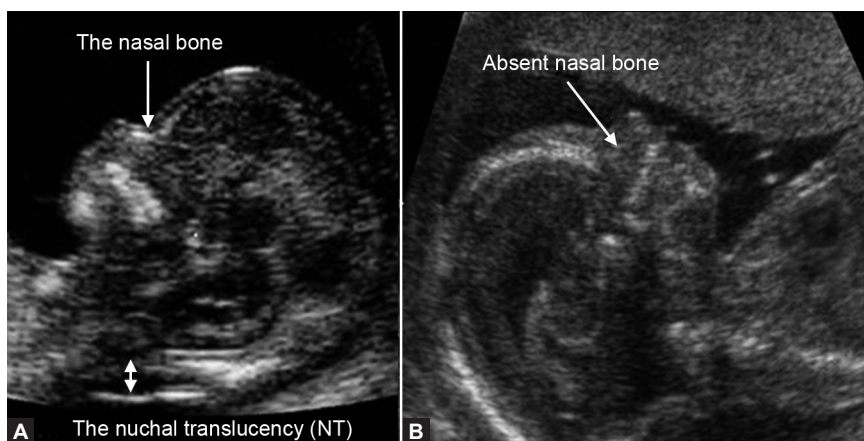
The FASTER trial suggests that if nuchal translucency is more than 3 mm then a chorion villus sampling should be done since the risk of aneuploidy is 1:6. It should also be noted that nuchal fold thickness is a different parameter that is measured in a second trimester scan (at ~18–22 weeks) and it should not be confused with nuchal translucency (which is measured in the 1st trimester).⁴

NASAL BONE

In a study by Cicero et al. 701 fetuses with increase nuchal translucency were evaluated (**Figs 3.3A and B**).⁴ The foetal nasal bone could not be seen in 73% of Down's syndrome. However, the absence of nasal bone could not be related to nuchal translucency and therefore the two could not be combined as a single screening modality. The study was subsequently expanded and detection rate was increased to 67% with absent nasal bone. However, all studies have had a high-risk population.

Adequate imaging of foetal nasal bone can be technically challenging.

- The nasal bone should be visualized on USG, along midsagittal plane with a perfect foetal profile.
- The foetal spine should be posterior which neck in slight flexion.
- Two echogenic lines at foetal nose profile should be visualised. The superficial echogenic line is real nasal skin and deeper echogenic line represents the nasal bones should be echolucent at its distal end.
- Care should be taken not to perform this evaluation with USG beam parallel to the plane of the nasal bones.



Figures 3.3A and B (A) Normal nasal bone; (B) Absent nasal bone

The largest study of 1st trimester foetal nasal bone USG in an unselected general population has been evaluated did not confirm the useful role of this evaluation. It has a limited role in screening. Therefore current data suggests that nasal bone screen can be used as a second line screening tool in a high-risk population.

DUCTUS VENOSUS

First trimester ductus venosus screen has been described as an adjunctive test for foetal aneuploidy screening. Forward triphasic pulsatile ductus venosus flow is normal whereas reversed flow at atrial contraction is associated with aneuploidy and cardiac malformation.

Ductus venosus flow can be used to improve detection and decrease false positive rate. But the ductus venosus is small; 2 mm at 10–14 weeks. Therefore it is difficult to get accurate wave form. Doppler should be performed only as a secondary screening test by experienced sonologist than to modify the final risk for aneuploidy.

First Trimester Tricuspid Regurgitation (Flow Chart 3.1)

Abnormal tricuspid regurgitation has been noted with aneuploidy. For assessing tricuspid regurgitation:

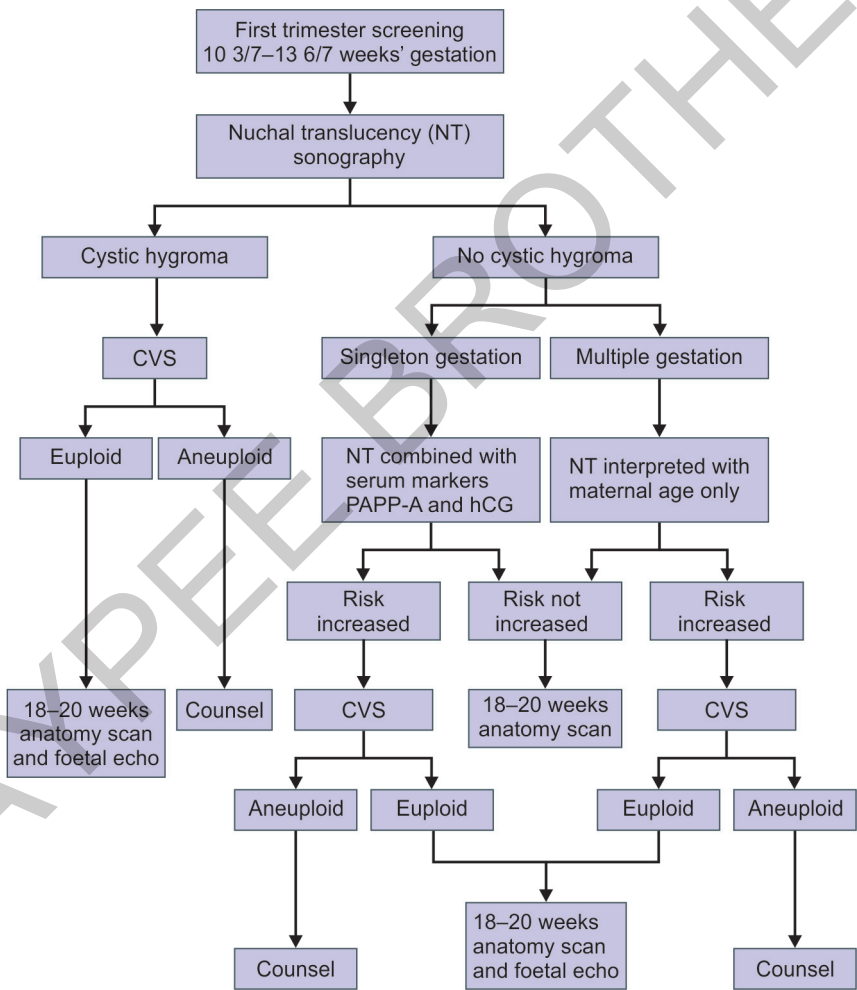
- The foetus should be oriented with the chest wall anterior and foetal heart should be insonated parallel to the ventricular septum.
- Tricuspid regurgitation is significant if the regurgitation jet of at least 60 cm/s is noted extended over half of the systole.

In a study, tricuspid regurgitation was present in 68% of Down's syndrome and 33% trisomy 18. There was low interobserver variability.⁵ Tricuspid regurgitation may have a role as second line test to increase detection of Down's syndrome to 92% and reduce false positive to 2.7%.

CONCLUSION

The American Congress of Obstetricians and Gynecologists (ACOG) has released a practical bulletin for ‘Screening for foetal aneuploidies’. According to this bulletin prenatal genetic screening is designed to assess whether a patient is at high-risk of having a foetus affected with a genetic disorder such as Down’s syndrome. Women with a positive screen result should always be offered counseling and diagnostic testing.⁶ If a first trimester screen is done then a chorionic villus sampling must be available to avoid anxiety. Hence, there is also

Flow chart 3.1 Screening decision options during the first trimester



(Data from Fergal D Malone: First trimester screening for aneuploidy. *Ultrasonography in Obstetrics and Gynaecology*. Peter W Callen, 5th edition, 2008)
Abbreviations: CVS, chorionic villus sampling; hCG, human chorionic gonadotrophin; NT, nuchal translucency; PAPP-A, pregnancy associated plasma protein A

a concept of integrated screening with nuchal translucency and double marker (1st trimester) and quadruple marker (2nd trimester).

The Royal College of Obstetricians and Gynaecologists (RCOG) supports increased access to noninvasive testing to improve antenatal screening for Down's syndrome. In 2001, the UK National screening committee advised that all pregnant mothers should be offered one of the available screening tests for Down's syndrome. The Committee recommended that by 2007–10, these tests should have a false positive rate < 3% and an accurate detection rate of >75%.¹ The increasing availability of the foetal nuchal translucency test together with analysis of blood hormone levels, commonly known as the first trimester combined test, signals a move in this direction.⁷

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- Provides, at a glance, algorithms and management guidelines for difficult situations encountered in everyday practice in the labour room
- Includes a diverse range of scenarios, from the simple to the complicated, graded by frequency and severity, and which are of practical importance
- The chapters are written by the senior teachers, who are amongst the well-known authorities with several decades of experience in this field
- Aims to offer practical tips, with stress on evidence-based practice points
- Serves as a day-to-day companion during the busy obstetric practice
- Helps to refine the vast skillset that today's busy practitioner needs to possess while battling in the trenches.



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