Review Article

FIRST TRIMESTER SCREENING

Zehra N. Kavak, M.D.

Department of Obstetrics and Gynecology, School of Medicine, Marmara University, Istanbul, Turkey.

ABSTRACT

All women, whatever their age, face a small risk of delivering a baby with a physical and/or mental handicap. In some cases the handicap is due to a chromosomal abnormality such as Down syndrome. The only way to know for sure whether or not the fetus has a chromosomal abnormality is by having an invasive test done, such as chorionic villus sampling (CVS) or amniocentesis. However, these tests carry a risk of miscarriage of about 1% (1). The most recent and accurate way of estimating the risk of the fetus having a chromosomal abnormality is carried out at 11-13 weeks and depends on the:

a) age of the mother

b) amount of fluid behind the neck of the fetus (nuchal translucency) (Fig. 1)

c) presence of any fetal abnormalities

d) fetal heart rate

e) level of two hormones (β-HCG and PAPP-A) in the mother's blood.

After the scan, on the basis of all the above factors, the estimated risk for Down syndrome can be discussed with the patient.

Irrespective of whether the patient decides to have an invasive test, it is recommended that she has a scan at 20 weeks to check for physical abnormalities (2).

Key Words: Nuchal translucency, First trimester screening

During the second and third trimester of pregnancy, abnormal accumulation of fluid behind the fetal neck can be classified as nuchal edema. Nuchal edema has different etiologic factors; chromosomal abnormalities are found in about one-third of the fetuses. Edema is also associated with fetal cardiovascular and pulmonary defects, skeletal dysplasias, congenital infection and metabolic and hematologic disorders (1).

In the first trimester of pregnancy, we use the term translucency, because this is the ultrasonographic feature observed. In most cases, we can obverse the resolution of the translucency during the second trimester, in a few cases however, it evolves into either nuchal edema or cystic hygromas with or without generalized hydrops (1).

Nuchal translucency can be measured successfully by transabdominal ultrasound examination in about 98% of cases (1). There are a number of benefits: 1) Dating the pregnancy accurately. This is particularly relevant for women who cannot recall the date of their last period, have an irregular cycle, conceived while breastfeeding or soon after stopping the pill. By measuring the crown-rump length (CRL) of the fetus, the gestational age and therefore the

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Correspondance to: Zehra N. Kavak, M.D. – e.mail address: nesekavak@superonline.com

expected date of delivery can be accurately calculated. 2) Assessing the risks of Down syndrome and other chromosomal abnormalities. 3) Diagnosing multiple pregnancy. Approximately 2% of spontaneous conceptions and 10% of assisted conceptions result in multiple pregnancy. Ultrasound scanning can identify if twin babies are sharing the same placenta which can lead to problems in the pregnancy. In such cases it would be advisable to monitor the pregnancy more closely. 4) Diagnosing certain major fetal abnormalities. Major abnormalities may be visible at this gestation but a 20 week anomaly scan is still essential. 5) Diagnosing early pregnancy failure. Unfortunately, in about 3% of women who have a nuchal scan it is found that the fetus has died, often several weeks before and without any warning. Couples will receive full counselling as to the possible causes of this problem and the options for subsequent measures that may be necessary (1). The average time for evaluation of each patient should be at least 10 minutes. During this examination period, we should pay attention to some important points which are as follows:

1. We should try to obtain a good sagittal view of the fetus for measurement of the fetal crown-rump length.

2. The fetus should occupy at least three-quarters of the image.

3. The maximum thickness of the subcutaneous transluceny between the skin and the soft tissue overlying the cervical spine should be measured by placing the callipers on the lines.

4. The nuchal translucency should be measured with the fetus in the neutral position.

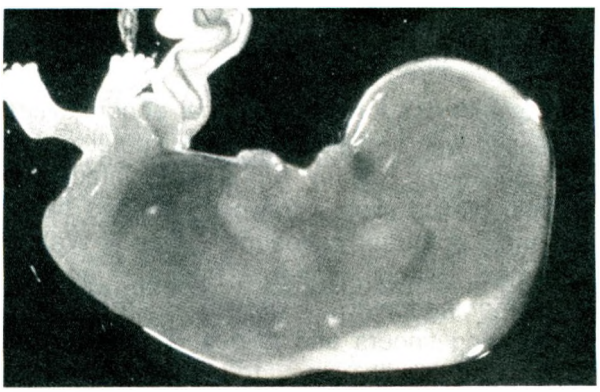

Fig. 1.: Amount of fluid behind the neck of the fetus.

5. We must distinguish carefully between fetal skin and amnion because, at this gestation, both structures appear as thin membranes (2).

The ability to measure nuchal translucency and obtain reproducible results improves with training; good results are achieved after 50 scans (3). Appropriate training, high motivation and adherence to a standard technique for the measurement of nuchal translucency are essential prerequisities for good clinical practice. Monni et al reported that, after modifying their technique of measuring nuchal translucency by following the guidelines established by The Fetal Medicine Foundation, their defection rate of trisomy 21 improved from 30% to 84% (4).

Fetal nuchal translucency increases with crown-rump length, and therefore it is essential to take gestation into account when determining whether a given translucency thickness has increased. In a study involving more than 100.000 pregnancies, the median increased from 1.2 mm at 11 weeks to 1.9 mm at 13 weeks (5).

The heterogeneity of conditions of increased nuchal translucency suggests that there may not be a single underlying mechanism for the collection of fluid in the skin of the fetal neck. Possible mechanisms include:

1. Cardiac failure in association with abnormalities of the heart and great arteries.

2. Venous congestion in the heart and neck, due to constriction of the fetal body in amnion rupture sequence or superior mediastinal compression found in diaphragmatic hernia.

3. Altered composition of the extracellular matrix.

4. Abnormal or delayed development of the lymphatic system.

5. Failure of lymphatic drainage.

6. Fetal anemia or hypoproteinemia.

7. Congenital infection (5).

Increased nuchal translucency thickness is present in about 40% of fetuses with diaphragmatic hernia (6). It is possible that, in the cases with increased nuchal translucency at 11-14 weeks, there is indeed intrathoracic herniation of the abdominal viscera during this stage of gestation and the increased nuchal translucency

may be the result of venous congestion due to mediastrial compression. In the cases where diaphragmatic hernia is associated with a good prognosis, the intrathoracic herniation of viscera may be delayed until the second or third trimesters of pregnancy (7). In the literature, some authors suggest that, in pregnancies with increased nuchal translucency, the prevalence of maternal infection with the TORCH group of organism is not higher than in the normal population (8).

In The Fetal Medicine Foundation Multicenter Project of screening for trisomy 21 by a combination of maternal age and fetal nuchal translucency thickness at 10-14 weeks, 325 cases of chromosomal abnormalities other than trisomy 21 were identified (5). In 229 (70.5%) of these, the fetal nuchal translucency was above the 95th centile of the normal range for crown-rump length.

In trisomy 21, the median nuchal translucency thickness is about 2,0 mm above the normal median for crown-rump length. The corresponding values for trisomies 18 and 13, triploidy and Turner syndrome are 4.0 mm, 2.5 mm, 1.5 mm and 7 mm respectively. In addition to increased nuchal translucency, there are other characteristic sonographic findings in these fetuses (Table I), (9,10-12).

In trisomy 21 during the first trimester of pregnancy, the maternal serum concentration of free β-hCG is higher than in chromosomally normal fetuses, whereas PAPP-A is lower. Maternal serum free β-HCG normally decreases with gestation after 10 weeks. In trisomy 21 pregnancies, the levels are increased and the difference between those of normal pregnancies increases with advancing gestation (13,14). Maternal serum PAPP-A normally increases with gestation. In trisomy 21 pregnancies, the levels are lower but the difference between 21 and normal pregnancies decreases with advancing gestation. In trisomy 21 pregnancies, the levels are lower but the difference between trisomy 21 and normal pregnancies decreases with advancing gestation (9,13,14).

There is no significant association between fetal nuchal translucency and maternal serum free β-hCG or PAPP-A in either trisomy 21 or chromosomally normal pregnancies. The estimated detection rate for trisomy 21 by a combination of maternal age, nuchal translucency, maternal serum PAPP-A and free β-hCG is about 90% for a screen-positive rate of 5% (2,15-18).

Table I. Ultrasound findings in chromosomally abnormal fetuses at 10-14 weeks of gestation

Fetal karyotype	Ultrasound findings
Trisomy 18	growth restriction, bradycardia, exomphalos
Trisomy 13	growth restriction, tachycardia, holoprosencephaly, exomphalos
Turner syndrome	growth restriction, tachycardia, large nuchal translucency
Triploidy	growth restriction, bradycardia, holoprosencephaly, exomphalos, molar placenta

In our antenatal clinic, we have started to measure nuchal translucency in all pregnancies since last August. We have got the software program from the King's College Harris Birthright Research Center. In the near future, we hope to publish our results according to the same program.

Nuchal translucency followed by second trimester ultrasonography

Ultrasound studies have demonstrated that major chromosomal defects are often associated with multiple fetal abnormalities. It is therefore recommended that, when an abnormality is detected at routine USG examination, we should look for other features of the chromosomal abnormalities known to be associated with that marker.

The overall risk for chromosomal abnormalities increases with the total number of defects that are identified. Trisomy 18 is associated with choroid plexus cysts, strawberry-shaped head, absent corpus callosum, Dandy-Walker Complex, facial cleft, nuchal edema, myelomeningocele, growth restriction, overlapping fingers and talipes. Trisomy 21 is associated with a tendency towards brachicephaly, mild ventriculomegaly, nuchal

edema, sandal gap, echogenic bowel duedonal atresia clinodactyly. In trisomy 13, common defects include holoprosencephaly and associated facial abnormalities, microcephaly, cardiac and renal abnormalities, examphalos, postaxial polydactyly. Triploidy, where the extra set of chromosomes is paternally derived, is associated with a molar placenta and the pregnancy rarely persists beyond 20 weeks. The placenta is of normal consistency and the fetus demonstrates severe asymmetrical growth retardation. Commonly, there is mild ventriculomegaly micrognathia, cardiac abnormalities, myelomeningocele, syndactyly. The lethal type of Turner syndrome presents with large nuchal cystic hygromata, generalized edema, mild pleural effusions and ascites and cardiac abnormalities (19,20).

Consequently, ultrasound examination should be offered routinely to all pregnant women. The scan, which is usually performed at 18-23 weeks of pregnancy, should be carried out to a high standard and should include systematic examination of the fetus for the detection of both major and minor defects. If the 20 weeks scan shows no abnormalities, the adjusted risk of trisomy 21 is three times decreased compared to the first trimester nuchal translucency adjusted risk (19).

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