

Analysis of the distribution and the mean values of nuchal translucency in singleton pregnancies

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Abstract

Objective: In this study, we aimed to evaluate the distribution and mean values of fetal nuchal translucency (NT) in singleton pregnancies with low risk in Manisa city. It was also aimed to evaluate relationship between NT values and week of gestation, crown-rump length (CRL), parity and maternal weight.

Methods: A total of 351 singleton pregnancy cases who admitted to our perinatology clinic in between March 2013 and May 2014 for screening at 11-14 weeks of gestation were included in the study. Fetal NT, CRL measurements, week of gestation, maternal weight and parity were evaluated. Three hundred and fifty-one cases that were included in the study were separated into four groups according to their CRL measurements: Those with CRL between 45 and 54 mm were determined as Group 1 (n=62), those with CRL between 55 and 64 mm were determined as Group 2 (n=133), those with CRL between 65 and 74 mm were determined as Group 3 (n=115), and those with CRL between 75 and 84 mm were determined as Group 4 (n=41). The groups were compared in terms of maternal age and mean NT value.

Results: Mean age of the cases was 28.76 ± 5.51 , mean week of gestation was 12.29 ± 0.69 , mean CRL value was 63.69 ± 9.07 mm, and mean NT value was 1.23 ± 0.48 mm. No significant difference was observed among the groups in terms of maternal age and NT measurement ($p=0.817$ and 0.072 , respectively). In the correlation analysis, it was seen that NT value was significantly correlated with CRL ($r=0.232$; $p=0.001$) and week of gestation ($r=0.203$; $p=0.001$) statistically. No relationship was found between NT and gravida, parity and maternal age.

Conclusion: First trimester screening is a method becoming more common in terms of prenatal diagnosis. Fetal NT is a part of this screening procedure. Fetal NT measurement should be carried out in accordance with the standards and pregnancy management should be planned according to the algorithms.

Keywords: Nuchal translucency, crown-rump length, first trimester screening.

Özet: Tekil gebeliklerde ense kalınlığı değerlerinin dağılımı ve ortalamalarının saptanması

Amaç: Bu çalışmada, Manisa ilindeki düşük riskli tekil gebeliklerde fetal ense kalınlığı (NT) değerlerinin dağılımı, ortalama ölçümlerinin değerlendirilmesi amaçlanmıştır. Ayrıca NT değerleri ile gebelik haftası, baş-popo mesafesi (CRL), parite ve maternal kilo arasındaki ilişkinin değerlendirilmesi amaçlanmıştır.

Yöntem: Mart 2013 - Haziran 2014 tarihleri arasında, 11-14. gestasyonel hafta taraması amacı ile perinatoloji polikliniğine başvuran 351 tekil gebelik çalışmaya alındı. Fetal NT, CRL ölçümleri, gebelik haftası, maternal kilo, parite özellikleri değerlendirildi. Çalışmaya dahil edilen 351 olgu, CRL ölçümüne göre 4 gruba ayrıldı: CRL 45-54 mm arasında olanlar Grup 1 (n=62), CRL 55-64 mm arasında olanlar Grup 2 (n=133), CRL 65-74 mm arasında olanlar Grup 3 (n=115) ve CRL 75-84 mm olanlar Grup 4 (n=41) olarak belirlendi. Gruplar arasında maternal yaş ve NT ortalaması açısından karşılaştırılma yapıldı.

Bulgular: Olguların ortalama yaşı 28.76 ± 5.51 , ortalama gebelik haftası 12.29 ± 0.69 , ortalama CRL değeri 63.69 ± 9.07 mm, ortalama NT değeri ise 1.23 ± 0.48 mm olarak tespit edildi. Gruplar arasında maternal yaş ve NT ölçümü açısından anlamlı fark izlenmedi (sırası ile $p=0.817$ ve 0.072). Korelasyon analizinde, NT değerinin CRL ($r=0.232$; $p=0.001$) ve gebelik haftası ($r=0.203$; $p=0.001$) ile istatistiksel olarak anlamlı derecede ilişkili olduğu izlendi. Gravida, parite ve maternal kilo ile NT arasında ilişki bulunmadı.

Sonuç: İlk trimester taraması prenatal tanı açısından giderek daha yaygınlaşan bir yöntemdir. Fetal NT, bu taramanın bir parçasıdır. Fetal NT ölçümü standartlara uygun bir şekilde yapılmalı ve algoritmalara göre gebeliğin yönetimi planlanmalıdır.

Anahtar sözcükler: Ense kalınlığı, baş popo mesafesi, ilk trimester tarama.

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Introduction

Nuchal translucency (NT) is the subcutaneous fluid collection accumulated in the area between fetal skin and cervical spines between 11 and 14 weeks of gestation.^[1] It has become a routine for the early diagnosis of chromosomal anomalies and other malformations in the screening at 11-14 weeks.^[2] Its size is more significant than its appearance (with or without septa etc.) in terms of chromosomal anomalies. Fetal NT increase applies to the cases where it is above 95th percentile (p) according to the week of gestation. However, no matter what week of gestation it is, NT values which are 3.5 mm and above are over 99 p.^[3] Fetal NT measurement should be carried out ideally between 11 and 14 weeks of gestation and when fetal crown-rump length is between 45 and 84 mm.^[2] During the measurement, appropriate magnification should be done as fetal head and upper thorax cover at least 75% of the screen and fetus should be on neutral position; fetal head should not be on flexion (it causes the measurement to be 0.4 mm less) and hyperextension (it causes the measurement to be 0.6 mm much).^[4] During the measurement, the umbilical cord is around the neck in 5% of the cases, and this may lead to false high results. In such cases, the cord must be measured from the lower and upper parts, and their mean values should be taken.^[5]

The etiology of fetal NT increase is heterogeneous; however, every NT increase should not be interpreted as an anomaly.^[4] For instance, 100 fetuses with NT between 3.5 and 4.4 mm, chromosome anomaly would be observed in 20 (20%) of them. Two (2.5%) of remaining 80 fetuses with normal chromosomal structure would be lost in following weeks (fetal death); minor structural anomalies would be found in 8 of them (10%). Remaining 79 fetuses would be resulted in health live births.^[6]

In this study, we aimed to evaluate the distribution and mean values of fetal nuchal translucency in singleton pregnancies with low risk in Manisa city. It was also aimed to evaluate relationship between NT values and week of gestation, crown-rump length (CRL), parity and maternal weight.

Methods

A total of 351 singleton pregnancy cases who admitted to our perinatology clinic in between March 2013 and May 2014 for screening at 11-14 weeks of gestation were included in the study. The inclusion criteria were determined as (1) singleton pregnancy, (2) normal fetal kary-

otyping (12 pregnant women who had 1/250 risk of first trimester screening test and found to have normal karyotype by chorionic villus sampling), (3) having no structural anomaly, and (5) CRL measurement between 45 and 84 mm. All measurements were done by using Voluson 730 (GE Medical Systems, Milwaukee, WI, USA) 3.5 MHz abdominal probe. The measurements were carried out by 2 operators (B.A.Ü. or H.G.P.) who had professional competency certificate for NT measurement granted by Fetal Maternal Foundation (FMF). Fetal NT measurement was carried out at sagittal section and when fetal head was on neutral position, and by providing magnification as fetal head and upper thorax cover 2/3 of the screen. The distinction between fetal skin and amnion was paid attention. Fetal NT measurement was done by measuring from the thickest area and interiorly. The study was approved by the local ethical committee of our university.

Three hundred and fifty-one cases that were included in the study were separated into four groups according to their CRL measurements: Those with CRL between 45 and 54 mm were determined as Group 1 (n=62), those with CRL between 55 and 64 mm were determined as Group 2 (n=133), those with CRL between 65 and 74 mm were determined as Group 3 (n=115), and those with CRL between 75 and 84 mm were determined as Group 4 (n=41). The groups were compared in terms of maternal age and mean NT value.

The results were evaluated by SPSS v.20 (SPSS Inc., Chicago, IL, USA). The data obtained were expressed as mean \pm standard deviation. The general characteristics of the patients included in the study were evaluated by definitive statistics and their mean, median and lower-upper limit values were determined. The data analyzed in 4 different groups according to CRL measurement were evaluated by multiple variance ANOVA test. Correlation analysis was used to determine the relationship between NT and other parameters. The value $p < 0.05$ was considered statistically significant.

Results

Mean age of the cases was 28.76 ± 5.51 , mean week of gestation was 12.29 ± 0.69 , mean CRL value was 63.69 ± 9.07 mm, and mean NT value was 1.23 ± 0.48 mm (Table 1). The mean maternal age and NT value were as follow: 28.37 ± 5.29 and 1.06 ± 0.43 mm for the cases in Group 1 (n=62); 28.49 ± 5.94 and 1.15 ± 0.53 mm for the cases in Group 2 (n=133); 28.50 ± 5.63 and 1.33 ± 0.42 mm

Table 1. Definitive statistical data of the patients who undergone screening at 11-14 weeks of gestation.

	Mean±SD	Median	Lower-upper limit
Maternal age	28.76±5.51	29	16.0-43.0
Gravida	2.32±1.12	2	0-6
Parity	0.87±0.87	1	0-4
Abortion	0.46±0.79	0	0-4
CRL (mm)	63.69±9.07	63.5	46.6-83.8
NT (mm)	1.23±0.48	1.15	0.20-5.01
Week of gestation	12.29±0.69	12	11-14
Maternal weight (kg)	66.44±12.35	64	45.0-116.0

CRL: crown-rump length; NT: nuchal translucency; SD: standard deviation.

for the cases in Group 3 (n=115); 29.71±4.61 and 1.40±0.40 mm for the cases in Group 4 (n=41), respectively. No significant difference was observed among the groups in terms of maternal age and NT measurement (p=0.817 and 0.072, respectively) (Table 2, Fig. 1). In the correlation analysis, it was seen that NT value was significantly correlated with CRL (r=0.232; p=0.001) and week of gestation (r=0.203; p=0.001) statistically. No relationship was found between NT and gravida, parity and maternal age (Table 3).

Discussion

The physiopathological mechanisms causing fetal NT increase are heterogeneous.^[3,7] When all genetically normal fetuses are taken into consideration, it is found that NT increase is %5.^[7] In 1% of all pregnancies, NT is above 99 p (>3.5 mm). In our study, NT was over 99 p in

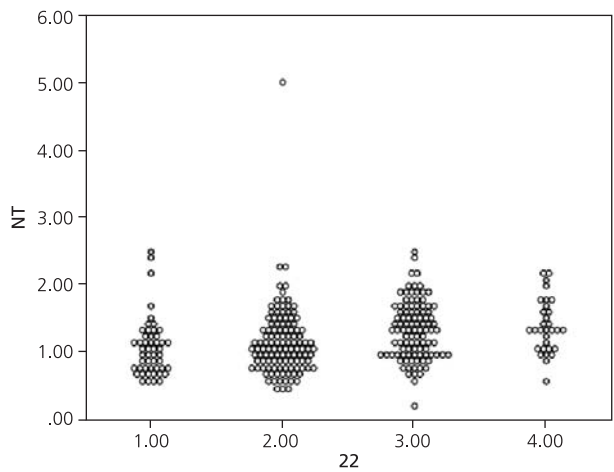


Fig. 1. NT distribution according to CRL groups (1= 45-54 mm; 2= 55-64 mm; 3= 65-74 mm; 4= 75-84 mm). CRL: crown-rump length; NT: nuchal translucency.

Table 2. Mean maternal age and NT values according to CRL groups.

CRL range (mm)	Maternal age (mean±SD)	CRL (mean±SD)	NT (mean±SD)
45-54 (Group 1)	28.37±5.29	51.56±2.71	1.06±0.43
55-64 (Group 2)	28.49±5.94	60.44±2.56	1.15±0.53
65-74 (Group 3)	28.50±5.63	70.21±2.64	1.33±0.42
75-84 (Group 4)	29.71±4.61	78.52±2.04	1.40±0.40

CRL: crown-rump length; NT: nuchal translucency; SD: standard deviation.

0.85% (n=3) of the cases. In all three cases, karyotype analysis, detailed ultrasound and fetal echocardiography results were normal. All three cases were resulted in live birth.

Cardiovascular malformations which affect cardiac and major vessels, congestion at head-neck region, changes in the structure of extracellular matrix (ECM) and failure in lymphatic drainage are the mechanisms most commonly suggested for NT increase.^[8-11] Most of the proteins forming ECM structure are coded by 13th, 18th and 21st chromosomes. This explains the NT increase in fetuses with chromosomal anomalies.^[7] Also, the changes in ECM structure may be the reason of NT increase accompanying various genetic syndromes (i.e. achondrogenesis type II, achondroplasia, Zellweger syndrome). The failure of lymphatic drainage is the most common physiopathological mechanism. Turner syndrome, Noonan syndrome and congenital lymphedema are associated with increased NT together with hypoplastic lymphatic canal.^[7,12-14] In congenital neuromuscular diseases such as fetal akinesia deformation sequence, myotonic dystrophy and spinal muscular atrophia, the lymphatic drainage corrupted due to decreased fetal movements may cause increased NT.^[15] Apart from that, genetic fetal anemias [α thalassemia, Blackfan-Diamond anemia, Fanconi anemia etc.] may be presented by increased NT.^[7] The pathologies that cause fetal NT increase are given in Table 4.

Table 3. The relationship of NT measurement with CRL, week of gestation, maternal weight and parity (correlation analysis).

NT	CRL	WG	G	P	Maternal weight
r	0.232	0.203	0.036	0.060	0.018
p	0.001*	0.001*	0.512	0.275	0.763

*Statistically significant. CRL: crown-rump length; G: gravida; WG: week of gestation; NT: nuchal translucency; P: parity.

Table 4. Pathophysiological mechanisms in nuchal translucency increase.^[15]

Cardiac defect/dysfunction	
Venous congestion at head and neck	Superior mediastinal compression: diaphragmatic hernia, skeletal dysplasia
Altered ECM composition	Trisomies, change in collagen metabolism (achondrogenesis type II), change in fibroblast growth factor receptors (achondroplasia)
Problem in lymphatic drainage	Turner syndrome, Noonan syndrome, myotonic dystrophy, spinal muscular atrophy, fetal akinesia deformation sequence
Fetal hypoproteinemia	
Fetal infection	

ECM: extracellular matrix

In our study, the mean week for NT measurement was found as 12.29 ± 0.69 (median: 12) weeks. The first trimester screening should be done at 11-12 weeks ideally.^[7] As gestational age increases, the rate to detect trisomy decreases together with biochemical markers.^[7] On the other hand, evaluation of fetal anatomy becomes more successful as weeks pass; however, it becomes difficult to find fetus at a suitable position for NT measurement after 13 weeks.^[7] At 12-13 weeks, about 96-98% of the fetuses can be evaluated anatomically.^[4,16] By these data, 12 weeks are considered as the most appropriate week for the evaluation. We found mean NT value as 1.23 ± 0.48 mm (median: 1.15 mm). In a study carried out in Taiwan, mean NT was found as 1.56 mm.^[17] Fetal NT displays ethnical and racial difference except the week of gestation.

If fetal NT measurement is between 95 and 99 p (2.5 and 3.5 mm), the family should be informed about chromosomal anomaly risk and karyotype analysis should be done when requested. According to the result of double test, patient should be managed in terms of case karyotype analysis based on specific risk. Also, detailed ultrasonography should be planned between 11-14 weeks and 20-24 weeks. If NT measurement is above 99 p (3.5 mm), karyotype should certainly be recommended regardless of the result of double test. This is because the contribution of biochemical characteristics is minimal if NT is above 3.5 mm. Moreover, if NT is above 4 mm, double test has no additional contribution to the management of double test.^[18] If common edema and hydrops develop on further weeks in fetuses with normal karyotype analysis, such cases should be analyzed in terms of perinatal infection and genetic syndromes. The

family should be informed about perinatal risk which is 10%. Also, neurodevelopmental disorders can be seen in 3-5% of these babies.^[19]

Conclusion

In conclusion, first trimester screening is a method becoming more common in terms of prenatal diagnosis. Fetal NT is a part of this screening procedure. Fetal NT measurement should be carried out in accordance with the standards and pregnancy management should be planned according to the algorithms.

Conflicts of Interest: No conflicts declared.

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