

# Normative values of fetal nasal bone lengths of Turkish singleton pregnancies in the first trimester

## *Türk tekil gebeliklerdeki fetal nazal kemik uzunluklarının birinci trimester normal değerleri*

Murat Yayla<sup>1</sup>, Rahime Nida Ergin<sup>2</sup>, Gökhan Göynümer<sup>3</sup>

<sup>1</sup>Department of Gynecology and Obstetrics, International Hospital, İstanbul, Turkey

<sup>2</sup>Department of Gynecology and Obstetrics, Bayındır Hospital İçerenköy, İstanbul, Turkey

<sup>3</sup>Department of Gynecology and Obstetrics, Göztepe Education and Research Hospital, İstanbul, Turkey

### Abstract

**Objective:** Evaluation of nasal bone improves the performance of first-trimester screening for trisomy 21. In this retrospective study we aimed to determine normative values related to the measurement of nasal bone length of the Turkish population during the first trimester ultrasonographic fetal screening.

**Material and Methods:** Medical records of singleton pregnancies, whose first trimester fetal screening was performed between 2004 and 2010, were evaluated retrospectively. Pregnancies with any detected/suspicious anatomical or genetic fetal anomalies, biochemical abnormalities, increased nuchal translucency measurements, and pregnancies of artificial reproduction techniques were excluded from data analyses. Mean±standard deviation, median and percentile values of the length of nasal bone were calculated separately for 11<sup>0-6</sup>, 12<sup>0-6</sup> and 13<sup>0-6</sup> gestational weeks

**Results:** Nasal bone could be visualized in 99.6% of the included 1762 singleton pregnancies. In 16.5% of the cases nasal bones were only noted as present or absent. Mean maternal age was 29.67±4.50 years and mean gestational age was 12.54±0.61 weeks. Median values of nasal bone lengths were 1.7, 1.9, and 2.2 mm for 11<sup>0-6</sup>, 12<sup>0-6</sup> and 13<sup>0-6</sup> gestational weeks respectively. Nasal bone length (NBL) increased linearly with advancing gestational age and CRL.  $NBL (mm)=[0.298 \times \text{Gestational Age (week)}]-1.779$ ,  $R^2=0.318$ ;  $p<0.001$ ;  $NBL (mm)=[0.023 \times \text{CRL (mm)}]+0.520$ ,  $R^2=0.331$ ;  $p<0.001$

**Conclusion:** The present study presents normative values of nasal bone in the first trimester screening of normal singleton pregnancies of Turkish population. Nasal bone length increases with advancing gestational age and CRL. (J Turkish-German Gynecol Assoc 2011; 12: 225-8)

**Key words:** Screening, nasal bone, pregnancy, ultrasonography, fetus

**Received:** 11 August, 2011

**Accepted:** 26 September, 2011

### Özet

**Amaç:** Birinci trimester trizomi 21 taramasında nazal kemik değerlendirmesi performansı arttırmaktadır. Bu retrospektif çalışmada Türk popülasyonundaki tekil gebeliklerde birinci trimester fetal nazal kemik ölçümlerinin gebelik haftalarına göre persentil dağılımlarının saptanması amaçlandı.

**Gereç ve Yöntemler:** Retrospektif olarak 2004 ve 2010 tarihleri arasında taraması yapılmış olan anatomik anomali, biyokimyasal değer anormalliği, aile öyküsünde genetik hastalığı olmayan, nokal kalınlığı normal olan spontan tekil gebelikler değerlendirmeye alındı. 11<sup>0-6</sup>, 12<sup>0-6</sup> and 13<sup>0-6</sup> gebelik haftaları için fetal nazal kemik ölçümlerinin ortalama±standart sapma, medyan ve persentil değerleri saptandı.

**Bulgular:** Dahil edilen 1762 tekil gebeliğin %99.6'sında nazal kemik görüntülenmişti; bunların %16.5'inde nazal kemik sadece var ya da yok olarak not edilmiştir. Ortalama anne yaşı 29.67±4.50 yıl ve ortalama gebelik haftası 12.54±0.61 idi. Nazal kemik ölçümlerinin medyan değerleri 11<sup>0-6</sup>, 12<sup>0-6</sup> ve 13<sup>0-6</sup> gebelik haftaları için sırasıyla 1.7, 1.9, ve 2.2 mm olarak saptandı. Nazal kemik uzunluğu (NBL) ilerleyen gebelik haftası ve artan CRL ile artmaktaydı ( $NBL (mm)=[0.298 \times \text{Gebelik Haftası}]-1.779$ ,  $R^2=0.318$ ;  $p<0.001$  ve  $NBL (mm)=[0.023 \times \text{CRL (mm)}]+0.520$ ,  $R^2=0.331$ ;  $p<0.001$ )

**Sonuçlar:** Mevcut çalışmada Türk popülasyonundaki tekil gebeliklerde birinci trimester fetal nazal kemik ölçümlerinin gebelik haftalarına göre persentil dağılımları gösterilmektedir. Nazal kemik uzunluğu ilerleyen gebelik haftası ve CRL ile orantılı olarak artmaktadır.

(J Turkish-German Gynecol Assoc 2011; 12: 225-8)

**Anahtar kelimeler:** Tarama, nazal kemik, hamilelik, ultrason, fetus

**Geliş Tarihi:** 11 Ağustos 2011

**Kabul Tarihi:** 26 Eylül 2011

### Introduction

The nasal bones, which begin to develop as collections of neural crest cells, can be histologically demonstrated when the fetal crown-rump length is 42 mm (10.9 weeks) (1). Absence of nasal bone ossification is one of the key skeletal features of trisomy 21 (2). Thus, determination of absence or presence of nasal bone is being used in the fetal sonographic

screening for trisomy 21 (3-8). The evaluation of the nasal bone has been also shown to improve the performance of first-trimester screening for trisomy 21 (9). However, interobserver and intraobserver variability is a limitation for the measurement of length of the nasal bone and experience was shown to be important in the use of the nasal bones as an additional sonographic marker in first trimester screening (10-14).

**Address for Correspondence:** Rahime Nida Ergin, Teşvikiye Cad. Bayer Apt. No: 63/11 Kat: 4 Nişantaşı, İstanbul, Turkey

Phone: +90 505 373 71 33 e.mail: drnidaergin@gmail.com

©Copyright 2011 by the Turkish-German Gynecological Education and Research Foundation - Available online at www.jtggga.org

doi:10.5152/jtggga.2011.56

In this retrospective study we aimed to determine normative values related to the measurement of nasal bone length of the Turkish population during the first trimester ultrasonographic fetal screening.

### Materials and Methods

All medical records of singleton pregnancies, whose first trimester fetal screening was performed between January 2004 and December 2010, were evaluated retrospectively. Ultrasonographic fetal screening were performed by one of two sonographers using one of two ultrasound machines (Voluson 730 Pro (U.S.A) and Philips 4000 (U.S.A)). Pregnancies with any detected/suspicious anatomical or genetic fetal anomalies, biochemical abnormalities, increased nuchal translucency measurements, and pregnancies of artificial reproduction techniques were excluded from the data analyses. Ultrasonographic evaluation and measurement of fetal nasal bone had been performed mostly transabdominally (in case of inadequate fetal position transvaginally) in accordance with previously stated in the literature (5, 6).

Mean±standard deviation, median and percentile values of the length of nasal bone were calculated separately for 11<sup>0</sup>-11<sup>6</sup>, 12<sup>0</sup>-12<sup>6</sup>, and 13<sup>0</sup>-13<sup>6</sup> weeks of gestational age. The linear regression analyses were done between the length of nasal bone and gestational week and CRL. Statistical analyses were done with SPSS ver. 14.0.

### Results

In accordance with the inclusion and exclusion criteria, data of 1762 singleton pregnancies were analyzed. The nasal bone could be visualized in 99.6% of these 1762 singleton pregnancies. In 16.5% of the cases nasal bones were only noted as present or absent. Therefore demographics and ranges of nasal bones were studied in 1465 fetuses. The mean maternal age was 29.67±4.50 years and the mean gestational age was 12.54±0.61 weeks. The mean and percentiles of ultrasonographic measurements of nasal bone according to the gestational weeks are shown in Table 1. The mean and percentiles of ultrasonographic measurements of nasal bone according to the measurements of CRL are shown in Table 2.

NBL increased linearly with advancing gestational age and was described by the following equation;  $NBL (mm) = [0.298 x$

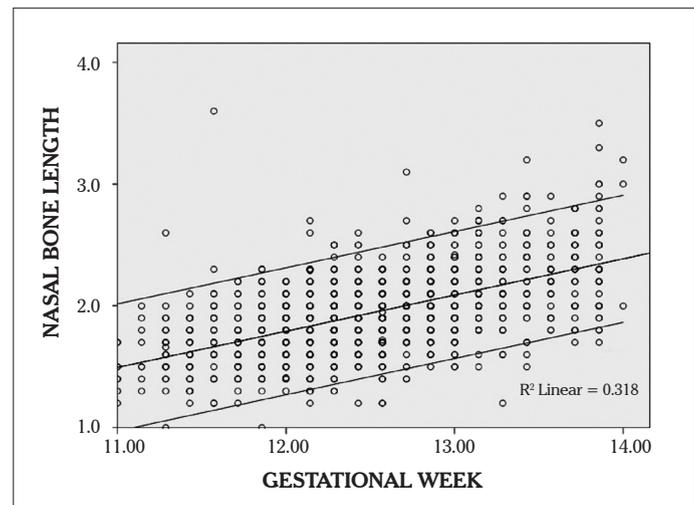
Gestational Age (week)]-1.779,  $R^2=0.318$ ;  $p<0.001$ . Again, a linear relationship was present between NBL and CRL and that was described by the following equation;  $NBL (mm) = [0.023x CRL (mm)] + 0.520$ ,  $R^2=0.331$ ;  $p<0.001$  (Figure 1 and Figure 2).

### Discussion

Genetic sonography is an important tool in prenatal fetal evaluation. Evaluation of the nasal bone has been suggested to improve the performance of first-trimester screening for trisomy 21 (3-9). Experience has been shown to be an important factor for the use of the nasal bone as an additional sonographic marker in first trimester screening (10-14). In most of the previous studies determining the presence of nasal bone for screen-

**Table 2. Nasal Bone Length Measurements (mm) according to CRL**

| CRL      | Percentiles     |                  |                  |
|----------|-----------------|------------------|------------------|
|          | 5 <sup>th</sup> | 50 <sup>th</sup> | 95 <sup>th</sup> |
| 45-54 mm | 1.3             | 1.7              | 2.1              |
| 55-64 mm | 1.5             | 1.9              | 2.3              |
| 65-74 mm | 1.6             | 2.1              | 2.6              |
| 75-84 mm | 1.8             | 2.3              | 3                |



**Figure 1. Nasal bone lengths according to gestational age (Lines indicating 95<sup>th</sup>, 50<sup>th</sup>, 5<sup>th</sup> percentiles above to bottom respectively)**

**Table 1. Nasal Bone Length Measurements (mm) according to gestational weeks**

| Gestational Age                               | Mean (mm) | Standard Deviation (mm) | Percentiles     |                  |                           |                  |                  |
|---|-----------|-------------------------|-----------------|------------------|---------------------------|------------------|------------------|
|   |           |                         | 5 <sup>th</sup> | 25 <sup>th</sup> | 50 <sup>th</sup> (Median) | 75 <sup>th</sup> | 95 <sup>th</sup> |
| 11 <sup>0</sup> -11 <sup>6</sup> week (N=330) | 1.73      | 0.27                    | 1.30            | 1.50             | 1.70                      | 1.90             | 2.15             |
| 12 <sup>0</sup> -12 <sup>6</sup> week (N=855) | 1.95      | 0.26                    | 1.50            | 1.80             | 1.90                      | 2.10             | 2.40             |
| 13 <sup>0</sup> -13 <sup>6</sup> week (N=280) | 2.23      | 0.34                    | 1.80            | 2.00             | 2.20                      | 2.40             | 2.80             |

ing of trisomy 21 the ratio of successful examination varied between 83.2% to 100% (4, 8, 14-18). However, in these studies the determination ratio of trisomy 21 varied between 60% to 80% (4, 8, 14-18).

The ossification of the vomeral bone begins with two bilateral ossification centers before ossification of the nasal bone and then these two bilateral ossification centers fuse caudally below the cartilaginous nasal septum, changing into a U-shaped bone when observed in the coronal plane (1). The gap between these structures may sometimes be misinterpreted as absence of nasal bone (19).

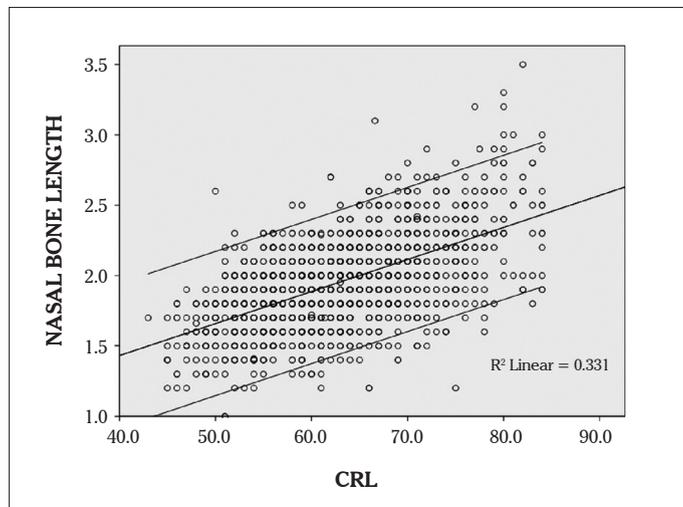
In the literature, there are many studies indicating the normative values related to the length of nasal bone in different geographical parts of the world (12, 20-24). The median values

of these nasal bone measurements vary from one study to another. In the present study, the sample size is larger and our results of nasal bone measurements were between the values of two other studies with a large sample size (20, 23). The values related to various previous studies indicating nasal bone measurements including the ones above mentioned are shown in Table 3. In all of these studies the reference values have different ranges. The examinations were commonly performed as transabdominal in the previous studies and as well our study (12, 20, 24). However, our mean NBL findings differ negatively at the 11<sup>th</sup>, 12<sup>th</sup> and 13<sup>rd</sup> gestational weeks from some of these studies (12, 22, 23) and positively from some others (19, 23). This difference might be due to ethnical difference (25) as well as interobserver and intraobserver variability in the measurement of length of the nasal bone (11, 13, 14). Variations may also be due to the quality of the machine as well, however it seems to be difficult to compare all these previous studies in this sense as most had different brand types of sonographic devices (12, 20-24). As a result, it seems to be impossible to clarify whether these differences are solely due to ethnical difference, interobserver/intraobserver variability or systematic differences in these studies.

The nasal bone length has been already found to increase linearly with advancing gestational week or CRL in the first trimester (13, 20, 22-24). In this study NBL of Turkish singleton pregnancies is also found to increase linearly with advancing gestational week and CRL in accordance with these previous studies in the literature.

### Conclusion

This study presents normative values of nasal bone in the first trimester screening of normal singleton pregnancies of the Turkish population. In accordance with previous reports, nasal



**Figure 2.** Nasal bone lengths according to CRL. (Lines indicating 95<sup>th</sup>, 50<sup>th</sup>, 5<sup>th</sup> percentiles above to bottom respectively)

**Table 3.** Different studies indicating nasal bone measurements in the first trimester of pregnancy

| Gestational Age        | Percentile | Present Study   | Casasbuena et al. (20) | Staboulidou et al. (21) | Chen et al. (22) | Sonek et al. (23) | Moon et al. (24) | Bekker et al. (12) |
|------------------------|------------|-----------------|------------------------|-------------------------|------------------|-------------------|------------------|--------------------|
|                        |            | Turkey (N=1465) | Latin America (N=1040) | Germany (N=122)         | China (N=2169)   | USA + UK (N=3537) | Korea (N=982)    | Netherlands (N=90) |
| 11 <sup>0-6</sup> week | 5          | 1,3             | 1                      | **                      | **               | 1.4               | 1,2              | **                 |
|                        | 50         | 1.7             | 1.5                    | 1.73                    | **               | 2.3               | 1.5              | 2.3                |
|                        | 95         | 2.2             | 1.8                    | **                      | **               | 3.3               | 1.9              | **                 |
| 12 <sup>0-6</sup> week | 5          | 1.5             | 1.2                    | **                      | 1.7              | 1.7               | 1.4              | **                 |
|                        | 50         | 1.9             | 1.7                    | 2.25                    | 2.2              | 2.8               | 1.7              | 2.6                |
|                        | 95         | 2.4             | 2.2                    | **                      | 2.8              | 4.2               | 2.1              | **                 |
| 13 <sup>0-6</sup> week | 5          | 1.8             | 1.4                    | **                      | 2.0              | 2.3               | 1.6              | **                 |
|                        | 50         | 2.2             | 1.9                    | **                      | 2.5              | 3.1               | 1.9              | 2.9                |
|                        | 95         | 2.8             | 2.4                    | **                      | 3.2              | 4.6               | 2.3              | **                 |
| 14 <sup>0-6</sup> week | 5          | **              | **                     | **                      | 2.2              | 2.5               | 1.7              | **                 |
|                        | 50         | **              | **                     | **                      | 2.9              | 3.8               | 2.1              | **                 |
|                        | 95         | **              | **                     | **                      | 3.5              | 5.3               | 2.6              | **                 |

\*\* : data not given

bone length increases linearly with advancing gestational age and CRL. The values show variance similar to previous studies, which might be a consequence of ethnical difference or interobserver/intraobserver variability.

#### Acknowledgements

No financial or commercial interests from any drug company or others were involved and there is no relationship of authors that may pose a conflict of interest.

#### Conflict of interest

No conflict of interest was declared by the authors.

#### References

- Sandikcioglu M, Molsted K, Kjaer I. The prenatal development of the human nasal and vomeral bones. *J Craniofac Genet Dev Biol* 1994; 14: 124-34.
- Stempfle N, Hutten Y, Fredouille C, Brisse H, Nessmann C. Skeletal abnormalities in fetuses with Down's syndrome: a radiographic post-mortem study. *Pediatr Radiol* 1999; 29: 682-8. [\[CrossRef\]](#)
- Orlandi F, Bilardo CM, Campogrande M, Krantz D, Hallahan T, Rossi C, et al. Measurement of nasal bone length at 11-14 weeks of pregnancy and its potential role in Down syndrome risk assessment. *Ultrasound Obstet Gynecol* 2003; 22: 36-9. [\[CrossRef\]](#)
- Zoppi MA, Ibba RM, Axiana C, Floris M, Manca F, Monni G. Absence of fetal nasal bone and aneuploidies at first-trimester nuchal translucency screening in unselected pregnancies. *Prenat Diagn* 2003; 23: 496-500. [\[CrossRef\]](#)
- Cicero S, Curcio P, Papageorghiou A, Sonek J, Nicolaides K. Absence of nasal bone in fetuses with trisomy 21 at 11-14 weeks of gestation: an observational study. *Lancet* 2001; 358: 1665-7. [\[CrossRef\]](#)
- Pandya PP, Snijders RJM, Johnson SP, De Lourdes Brizot M, Nicolaides KH. Screening for fetal trisomies by maternal age and fetal nuchal translucency thickness at 10 to 14 weeks' gestation. *Br J Obstet Gynaecol* 1995; 102: 957-62. [\[CrossRef\]](#)
- Cicero S, Longo D, Rembouskos G, Sacchini C, Nicolaides KH. Absent nasal bone at 11-14 weeks of gestation and chromosomal defects. *Ultrasound Obstet Gynecol* 2003; 22: 31-5. [\[CrossRef\]](#)
- Cicero S, Rembouskos G, Vandecruys H, Hogg M, Nicolaides KH. Likelihood ratio for trisomy 21 in fetuses with absent nasal bone at the 11-14-week scan. *Ultrasound Obstet Gynecol* 2004; 23: 218-23. [\[CrossRef\]](#)
- Kagan KO, Cicero S, Staboulidou I, Wright D, Nicolaides KH. Fetal nasal bone in screening for trisomies 21, 18 and 13 and Turner syndrome at 11-13 weeks of gestation. *Ultrasound Obstet Gynecol* 2009; 33: 259-64. [\[CrossRef\]](#)
- Cicero S, Dezerega V, Andrade E, Scheier M, Nicolaides KH. Learning curve for sonographic examination of the fetal nasal bone at 11-14 weeks. *Ultrasound Obstet Gynecol* 2003; 22: 135-7. [\[CrossRef\]](#)
- Staboulidou I, Wüstemann M, Vaske B, Scharf A, Hillemanns P, Schmidt P. Interobserver variability of the measurement of fetal nasal bone length between 11+0 and 13+6 gestation weeks among experienced and inexperienced sonographers. *Ultraschall Med* 2009; 30: 42-6. [\[CrossRef\]](#)
- Bekker MN, Twisk JW, van Vugt JM. Reproducibility of the fetal nasal bone length measurement. *J Ultrasound Med* 2004; 23: 1613-8.
- Kanellopoulos V, Katsetos C, Economides DL. Examination of fetal nasal bone and repeatability of measurement in early pregnancy. *Ultrasound Obstet Gynecol* 2003; 22: 131-4. [\[CrossRef\]](#)
- Senat MV, Bernard JP, Bouvain M, Ville Y. Intra- and interoperator variability in fetal nasal bone assessment at 11-14 weeks of gestation. *Ultrasound Obstet Gynecol* 2003; 22: 138-41. [\[CrossRef\]](#)
- Otano L, Aiello H, Igarzabal L, Matayoshi T, Gadow EC. Association between first trimester absence of fetal nasal bone on ultrasound and Down's syndrome. *Prenat Diagn* 2002; 22: 930-2.
- Viora E, Masturzo B, Errante G, Sciarrone A, Bastonero S, Campogrande M. Ultrasound evaluation of fetal nasal bone at 11 to 14 weeks in a consecutive series of 1906 fetuses. *Prenat Diagn* 2003; 23: 784-7. [\[CrossRef\]](#)
- Wong SF, Choi H, Ho LC. Nasal bone hypoplasia: is it a common finding amongst chromosomally normal fetuses of southern Chinese women? *Gynecol Obstet Invest* 2003; 56: 99-101. [\[CrossRef\]](#)
- Orlandi F, Rossi C, Orlandi E, Jakil MC, Hallahan TW, Macri VJ, et al. First-trimester screening for trisomy-21 using a simplified method to assess the presence or absence of the fetal nasal bone. *Am J Obstet Gynecol* 2005; 192: 1107-11. [\[CrossRef\]](#)
- Peralta CF, Falcon O, Wegrzyn P, Faro C, Nicolaides KH. Assessment of the gap between the fetal nasal bones at 11 to 13 + 6 weeks of gestation by three-dimensional ultrasound. *Ultrasound Obstet Gynecol* 2005; 25: 464-7. [\[CrossRef\]](#)
- Casasbuenas A, Wong AE, Sepulveda W. First-trimester nasal bone length in a normal Latin American population. *Prenat Diagn* 2009; 29: 108-12. [\[CrossRef\]](#)
- Staboulidou I, Steinborn A, Schmidt P, Günter HH, Hillemanns P, Scharf A. Reference values for the fetal nasal bone in the first trimester of pregnancy in a normal collective. A prospective study. *Z Geburtshilfe Neonatol* 2006; 210: 173-8. [\[CrossRef\]](#)
- Chen M, Lee CP, Tang R, Chan B, Ou CQ, Tang MH. First-trimester examination of fetal nasal bone in the Chinese population. *Prenat Diagn* 2006; 26: 703-6. [\[CrossRef\]](#)
- Sonek JD, McKenna D, Webb D, Croom C, Nicolaides K. Nasal bone length throughout gestation: normal ranges based on 3537 fetal ultrasound measurements. *Ultrasound Obstet Gynecol* 2003; 21: 152-5. [\[CrossRef\]](#)
- Moon MH, Cho JY, Lee YM, Lee YH, Yang JH, Kim MY, et al. Nasal bone length at 11-14 weeks of pregnancy in the Korean population. *Prenat Diagn* 2006; 26: 524-7. [\[CrossRef\]](#)
- Collado F, Bombard A, Li V, Julliard K, Aptekar L, Weiner Z. Ethnic variation of fetal nasal bone length between 11-14 weeks' gestation. *Prenat Diagn* 2005; 25: 690-2. [\[CrossRef\]](#)