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MEASUREMENT OF FETAL NASAL BONE LENGTH, PRENASAL THICKNESS AND CORPUS CALLOSUM LENGTH OF FETUSES IN THRACE REGION OF TURKEY

Türkiye'nin Trakya Bölgesi'nde Fetal Nazal Kemik Uzunluk, Prenazal Kalınlık ve Korpus Kallozum Ölçümü

Cem YENER, Füsun VAROL, Havva SÜTCÜ, Esra ALTAN, Sinan ATEŞ, Cenk SAYIN

Trakya University Faculty of Medicine, Department of Obstetrics and Gynecology, Division of Perinatology, Edirne, TURKEY.

Abstract

Aim: The nasal bone can be imaged with ultrasonography from the 10th week of pregnancy. In situations where the nasal bone is aplastic or hypoplastic, the risk of chromosomal anomalies increases. Thickening of the prenasal soft tissue is also apparent in the vast majority of second-trimester fetuses with Down syndrome. In addition to these, corpus callosum is an another fetal structure that can be visualized from 18th weeks of the gestation by ultrasound. Agenesis or dysgenesis of it is related with neuro-disabilities. In this study our objective was to provide reference charts for fetal nasal bone length, prenasal thickness and corpus callosum length obtained by prenatal sonography between 19th and 23rd weeks of pregnancy.

Materials and Methods: The medical records of pregnant women who were followed-up in Trakya University School of Medicine, Department of Obstetrics & Gynecology, Division of Perinatology during the time period of 1st of January 2018 to 31st of December 2019 were reviewed retrospectively. We studied 167 patients in between 19th and 23rd weeks of pregnancy.

Results: Nasal bone length, prenasal thickness and corpus callosum length increased as the gestation proceeded. Mean±SD for nasal bone length, prenasal thickness and corpus callosum length (mm) between 19th and 23rd weeks were 6.65±0.7, 4±0.5, 20.1±1.4 respectively.

Conclusion: Ultrasound measurements of nasal bone length, prenasal thickness and corpus callosum can be performed within the second-trimester anomaly scan, and these measurements appear to be highly necessary because these measurement sensitive for prenatal diagnosis of chromosomal abnormalities and genetic syndromes.

Keywords: Corpus callosum, nasal bone, prenasal thickness.

Öz

Amaç: Nazal kemik fetüste onuncu haftadan itibaren ultrason ile tespit edilebilir. Nazal kemik aplazisi ya da hipoplazisi durumunda kromozomal anomali riski artar. Prenazal kalınlık artışı da Down sendromlu fetüslerde ikinci trimester sırasında sıklıkla gözlenir. Bunlara ek olarak, korpus kallozum da on sekizinci haftadan itibaren fetüslerde ultrason ile tespit edilebilir. Bu yapının agenezisi ya da disgenezisi nöral bozukluklara sebep olur. Bu çalışmada on dokuz ile yirmi üçüncü hafta arasındaki fetüslerde nazal kemik uzunluğu, prenazal kalınlık ve korpus kallozum uzunluğu için nomogram hazırlamayı amaçladık.

Materyal ve Metot: 1 Aralık 2018 ile 31 Aralık 2019 tarihleri arasında Trakya Üniversitesi Tıp Fakültesi Kadın Hastalıkları ve Doğum Kliniği Perinatoloji Polikliniğinde tarafımızca takip edilen gebelerin dosyaları incelendi. Çalışmaya 19 ile 23 gebelik hafta arasındaki 167 hasta alındı.

Bulgular: Nazal kemik uzunluğu, prenazal kalınlık ve korpus kallozum uzunluğu gebelik haftası ilerledikçe artmış gözlendi. Nazal kemik uzunluğu, prenazal kalınlık ve korpus kallozum (mm) uzunluğu için Mean±SD sırasıyla 6.65±0.7, 4±0.5, 20.1±1.4 bulundu.

Sonuç: İkinci trimester ultrason muayenesi sırasında nazal kemik uzunluğu, prenazal kalınlık ve korpus kallozum uzunluğu ölçülebilir. Bu ölçümler kromozomal anomaliler ve genetik hastalıkların prenatal tanısında önemlidir.

Anahtar Kelimeler: Korpus kallozum, nazal kemik, prenazal kalınlık.

INTRODUCTION

The nasal bone can be imaged with ultrasonography (USG) from the 10th week of pregnancy[1]. In recent years, measurement of the nasal bone has become a parameter for assessment of chromosomal anomalies. In situations where the nasal bone is aplastic or hypoplastic, karyotype

Corresponding Author / Sorumlu Yazar:

Cem YENER
Adres: Trakya University Faculty of Medicine, Department of Obstetrics and Gynecology, Division of Perinatology, Edirne/ TURKEY.
E-posta: cemyener@trakya.edu.tr

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anomalies like trisomy 21 and trisomy 18 are mentioned[2]. The most commonly observed chromosomal anomaly which is associated with nasal bone hypoplasia is Trisomy 21. Measurement of nasal bone length (NBL) by USG showed that there are differences in NBL between euploid and Down syndrome fetuses[3]. In addition to that, while analyzing of the facial profile, it was observed that there is an increasing of prenasal thickness (PNT) in the majority of Trisomy 21 fetuses in the second trimester of pregnancy. PNT increases also in several conditions such as skeletal anomalies, hydrops fetalis and genetic syndromes like Pallister-Killian Syndrome[4,5]. On the other hand, the corpus callosum (CC) is the main cerebral commissure connecting the two cerebral hemispheres. Its role is indispensable in the development and conservation of hemispheric specialization, comprising language in left hemisphere, or face processing, emotion and spatial attention in the right hemisphere. Therefore, agenesis or dysgenesis of this structure is related with neuro-disabilities. Normally, CC can be observed at the onset of the 18th week of gestation by USG[6]. CC starts to develop during the 8th week and it takes its final shape by 18 to 20 weeks, while some thickening continues[7]. Although direct visualization and measurement of the CC is not an integral part of the routine anomaly scan (because direct visualization of it needs expert sonographer), when indirect signs of CC anomalies such as colpocephaly and ventriculomegaly are detected, it is compulsory for a more detailed evaluation of its structure[8].

In this retrospective study our objective was to provide reliable reference charts for fetal NBL, PNT, CC length acquired by prenatal sonography between 19th and 23rd weeks of pregnancy.

MATERIAL AND METHOD

The medical records of pregnant women who were followed-up in Trakya University School of Medicine, Department of Obstetrics&Gynecology, Division of Perinatology during the time period of 1st of January 2018 to 31st of December 2019 were reviewed retrospectively. Ethical approval was obtained from Trakya University Human Ethics Committee (No: 2020/17). We studied 40 patients in between 19 weeks and 19 weeks 6 days, 41 patients between 20 weeks and 20 weeks 6 days, 43 patients between 21 weeks and 21 weeks 6 days and 43 patients between 22 weeks and 22 weeks 6 days. All pregnancies were singleton and accurately dated by first-trimester sonography, and the fetuses were free of structural and chromosomal abnormalities. We excluded patients with abnormal first and second trimester screening tests or cell-free DNA test. We also excluded patients that developed abnormal signs on ultrasonography in late weeks of pregnancy or pregnancies complicated by fetal growth restriction, oligohydramnios and polyhydramnios.

For measuring the NBL, a sagittal section of the fetal profile was obtained with the ultrasound transducer at an angle between 45° and 135° to the facial plane. The image was magnified so that the fetal head and upper thorax were present on 75% of the screen. The nasal bone and nasofrontal synostosis, which appear as an anechoic area on the glabellar region, were identified, besides other two linear, parallel and echogenic images corresponding to the skin interface right above the nasal bone. The caliper position was adjusted in such a way that each movement corresponded to a 0.1 mm-displacement. Once the appropriate plane was identified measurement of the nasal bone was

performed. In this plane the PNT was determined as the shortest distance between the anterior edge of the lowest segment of the frontal bone and frontal skin (Figure 1).

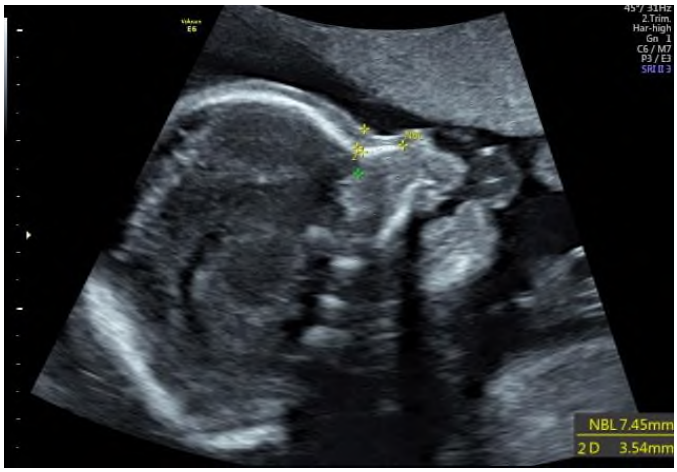

Figure 1. Measurement of nasal bone length and prenasal thickness.

The CC was visualized in a midsagittal plane as an anechoic structure delimited by two echogenic lines. The length was measured from the most anterior aspect of the genu to the most posterior aspect of the splenium, by using a straight rostro caudal length (Figure 2).

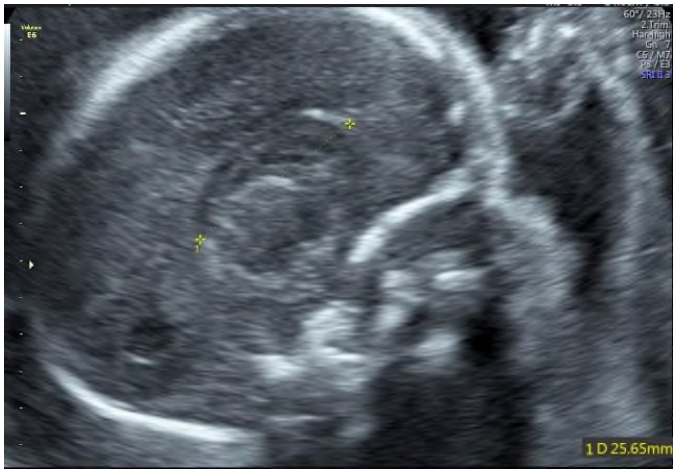

Figure 2. Measurement of corpus callosum length.

All measurements were performed by 1 of 2 different obstetric sonographers (C.Y, H.S). In all cases, Voluson E6 ultrasound systems (GE Healthcare, Milwaukee, WI) with a 2D (4.5–16.5 MHz) transabdominal probe were used. When visualization of the corpus callosum was difficult (high maternal body mass index or vertex presentation of the fetus), the examination was performed with a 2D (5–9 MHz) transvaginal probe.

The statistical analysis was performed using the SPSS Statics v25. Mean±standart deviation (SD) and percentile values of NBL and PNT were calculated for appropriate gestational weeks. Mean±SD and the 95% confidence limit were calculated in order to define the normal range of CC length.

RESULTS

The study group included 167 pregnant at gestational ages between 19 weeks (w) and 22 w+6 days (d). Mean±SD and 5th, 50th, 95th percentile of NBL between 19 w and 19 w+6 d (n=40) were 5.9±0.7

mm, 5 mm, 6 mm, 7.4 mm. Between 20 w and 20 w+6 d (n=41) were 6.3±0.6 mm, 5.2 mm, 6.3 mm, 7.6 mm. Between 21 w and 21 w+6 d (n=43) were 7.1±0.8 mm, 5.6 mm, 7.2 mm, 8.4 mm. Between 22 w and 22 w+6 d (n=43) were 7.3±0.7 mm, 6 mm, 7.4 mm, 8.5 mm respectively (Figure 3). PNT mean±SD levels for between 19 w and 19 w+6 d, 20 w and 20 w+6 d, 21w and 21 w + 6 d, 22 w and 22 w+6 d were 3.7±0.5, 3.8±0.5, 4.2±0.5, 4.3±0.7 respectively. 5th, 50th, 95th percentiles of PNT according to the weeks in increasing order were (3, 3.8, 4.6), (3.1, 4, 4.8), (3.4, 4.3, 5), (3.6, 4.3, 5.6) respectively. CC length mean±SD and confidence interval (CI) levels between 19 w and 19 w+6 d was 16.7±1.12 mm, (15.50-18.25) mm. Between 20 w and 20 w+6 d was 19.15±1.42, (18.43-20.88). Between 21w and 21 w+6 d was 20.88±1.44, (19.64-22.74). Between 22 w and 22 w+6 d was 23.85±1.66 and (21.66-25.82) respectively (Table 1, 2, 3).

Table 1. Length and percentiles of the nasal bone according to the gestational age.

		Percentiles (mm)		
	Mean (mm) ±SD	**5th**	**50th**	**95th**
19 w-19 w+6 d (n=40)	5.9±0.7	5	6	7.4
20 w-20 w+6 d (n=41)	6.3±0.6	5.2	6.3	7.6
21 w-21 w+6 d (n=43)	7.1±0.8	5.6	7.2	8.4
22 w-22 w+6 d (n=43)	7.3±0.7	6	7.4	8.5

w: weeks d: days SD: standart deviation n: number

Table 2. Length and percentiles of the prenasal thickness according to the gestational age.

		Percentiles (mm)		
	Mean (mm) ±SD	**5th**	**50th**	**95th**
19 w-19 w+6 d (n=40)	3.7±0.5	3	3.8	4.6
20 w-20 w+6 d (n=41)	3.8+0.5	3.1	4	4.8
21 w-21 w+6 d (n=43)	4.2±0.5	3.4	4.2	5
22 w-22 w+6 d (n=43)	4.3±0.7	3.6	4.3	5.6

w: weeks d: days SD: standard deviation n: number

Table 3. Length of the corpus callosum according to the gestational age.

Gestational Age	**Lower Bound (mm) (%95 CI)**	**Mean (mm) ±SD**	**Upper Bound (mm) (%95 CI)**
19 w-19 w+6 d (n=40)	15.50	16.7±1.12	18.25
20 w-20 w+6 d (n=41)	18.43	19.15±1.42	20.88
21 w-21 w+6 d (n=43)	19.64	20.88±1.44	22.74
22 w-22w+6 d (n=43)	21.66	23.85±1.66	25.82

w: weeks d: days SD: standard deviation CI: confidence interval n:number

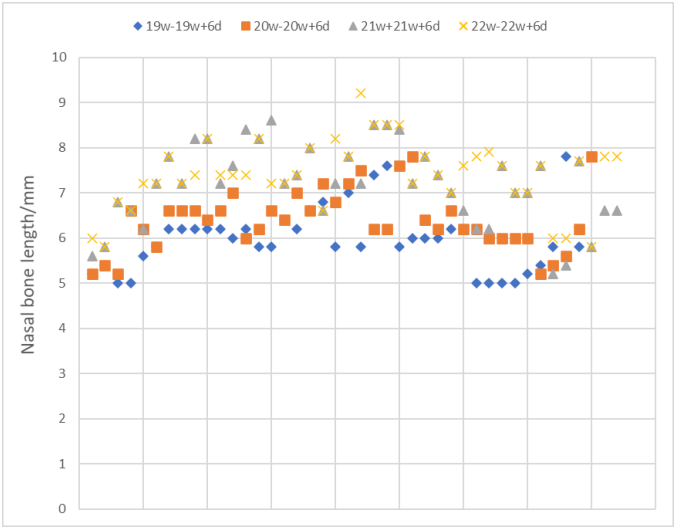

Figure 3. Nasal bone length according to the gestational weeks. w: week d: days

DISCUSSION

Between 19th and 23rd weeks of the pregnancy, during sonographic screening we evaluate all of the systems of the fetus and we perform fetal echocardiography and neurosonography. Because of the absence or hypoplasia of the nasal bone is associated with various congenital anomalies, nasal bone assessment is crucial parameter for target USG. In our study the NBL varied from 6.2 mm to 7.6 mm between 19 and 23 weeks of the pregnancy. In literature there are studies from various geographies. For Indian population between 19 and 22 weeks of the pregnancy, NBL varied from 4.6 mm to 6.1 mm[9]. Another research that studied Japanese population, NBL measurement varied from 5. 2 mm to 5.8 mm between 19 and 22 weeks of the pregnancy[10]. Yang et al.[11] studied 102 fetuses during the mid-trimester in Taiwanese women and concluded that NBL changed from 3.9 mm to 5.1 mm. There are some studies from Turkish population in literature for measurement of the fetal NBL. In one study NBL were measured in 1236 healthy fetuses in the 18th to 24th of the pregnancy and it was concluded that NBL changed from 6.25 mm to 7.81 mm[12]. In another study made by Goynumer et al.[13] stated that between 19 and 23 weeks of the pregnancy, mean NBL showed variety between 5.62 mm to 7.27 mm. There were subtle differences between our study and the researches that comprised Turkish population. Therefore, we concluded that nasal bone measurement varies according to race and ethnicity. While we measure NBL, it is necessary to consider our population nomograms. In addition to that, in present study we found out that NBL increased as the gestational week progressed and this result showed us that nasal bone continues to develop during fetal period.

Nasal bone absence or hypoplasia is a marker for Trisomy 21 in the first and second trimester. Bromley et al.[14] evaluated 239 fetuses in which 16 fetuses (%7) had down syndrome and 6 (%37) of 16 have nasal bone hypoplasia, compared with 1 (0.5%) of euploid fetuses. In another prospective, cross-sectional study it was found out that nasal bone hypoplasia was observed in all fetuses with fetal trisomy (6 of 6 cases of fetal trisomy) in the second trimester[15].

Maymon et al.[16] stated that PNT increased in fetuses with Trisomy 21 syndrome in the second trimester. In another study by Persico et al.[4] it was shown that PNT alone could prove a very sensitive method of second-trimester screening for Down syndrome. It has been also highlighted that the PNT/NBL ratio is a good marker for sonographic screening for Down syndrome in low-risk populations[17]. Szabo et al.[18] also mentioned that the ratio has high sensitivity and specificity. In various studies, it was presented that the PNT/NBL ratio was stable during pregnancy and mean level for PNT/NBL ratio was 0.61 mm in healthy fetuses[16,17]. These results are in line with our study. In present study, we found that PNT/NBL ratio was <0.65 mm in all fetuses.

In this study, we established a normogram for fetal CC length in fetuses between 19th and 23rd weeks of the pregnancy. CC consists of four parts: rostrum, genu, body and splenium[19]. Determining the appropriate growth pattern of the fetal CC is significant, as it can be an indicator of normal brain development and maturation. Abnormal developing of the CC leads to agenesis (completed or partial) or dysgenesis. Agenesis of the CC is a rare brain defect. It can be detected in both the prenatal and neonatal periods, and its exact incidence is not easy to detect, ranging from %0.05 to %3, according to the investigated populations.[20] Agenesis of the CC can be related to both CNS and extra-CNS

malformations, chromosomal disorders, and genetic syndromes such as Aicardi Syndrome[21,22]. Neurobehavioral disorders, such as difficulties in emotional, social communication or hyperactivity can appear in later life in pathologies of the CC[23]. In addition, some disabilities such as slow processing speed appear progressively at school-age. Early diagnosis of this anomaly is important because early interferences such as special medical needs or educational support needed. Therefore, measurement of the CC during second-trimester is important. Even though, direct visualization of the CC needs experienced sonographer, there are indirect signs of agenesis of corpus callosum which are: colpocephaly, absent cavum septum pellucidum and ventriculomegaly, and these findings can be detected by non-experienced sonographer also[24].

In literature there are some reference charts for the length of CC[7,25,26]. We tried to make a reference chart in Thrace Region of Turkey. Similar to these studies, our data showed that CC length increased as the gestational age proceeded.

In our practice, when we detect dysgenesis or agenesis of CC, we look for another anomaly in fetuses. We offer diagnostic test (amniocentesis or cordocentesis) for chromosomal analysis. We inform the parents about uncertain neurological outcomes of the current situation. We offer termination of pregnancy when agenesis/dysgenesis of CC is associated with other major structural anomalies, chromosomal anomalies and infectious diseases such as maternal rubella and congenital toxoplasmosis.

In conclusion, measurements of NBL and PT can be performed during the second-trimester anomaly scan, and these measurements seem to be sensitive for diagnosing of the fetuses with chromosomal abnormalities. Direct visualization of CC can be difficult but indirect signs of agenesis of CC can be detected on ultrasound easily. Because of the absence of the CC seems to diminish the quantity and effectiveness of inter-hemispheric interactions, causing of complications in integrating the most complex tasks, comprising verbal and visuospatial activities in later life, prenatal diagnosis of CC pathologies is crucial.

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