ORIGINAL RESEARCH

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Second Trimester Fetal Nasal Bone Length Measurement: A Single Center Study and National Data Review

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ABSTRACT Objective: To evaluate second trimester fetal nasal length measurement results in healthy singleton pregnancies in Turkey. **Material and Methods:** We analyzed the nasal bone lengths within 19-24 weeks in 661 pregnancies in our hospital. All pregnant women with a single healthy fetus who applied to our perinatology outpatient clinic for detailed obstetric ultrasonography were included in the study. All measurements were performed by the same clinician during routine mid-trimester ultrasound scan. Only the patients who were considered healthy by the examining pediatrician were included in the study. The parents of all fetuses are of Turkish ethnicity. Pearson correlation, regression analysis and P value were calculated between gestational week and nasal bone length. **Results:** Mean nasal length measurement was 6,21 ± 0,08; 6,66 ± 0,05; 6,88 ±0,05; 7,13 ± 0,08; 7,77 ± 0,11 and 8,33 ± 0,25 mm from 19 to 24 week of pregnancy, respectively. A significant positive correlation was observed between gestational week and nasal bone length. Normal values of nasal bone length measuremens are identified for each gestational weeks acoording to our data and previous 5 studies. **Conclusion:** In this study, we presented the data of our own center and the results obtained from other studies conducted in our country show significant differences. We are of the opinion that studies conducted by different researchers in different regions remain insufficient to reflect the nomogram of Turkish ethnic origin. For this purpose, multicenter studies are needed to cover the whole society.

Keywords: Gestational weeks; nasal bone length

Ultrasonography is widely used for the healthy delivery of fetuses throughout the pregnancy process. In addition, ultrasonography is also used to evaluate such factors as fetal growth pattern, amniotic fluid volume, cervical length measurement, a valuable predictive of preterm birth, and early diagnosis of complications specific to multiple pregnancies.[1] In addition to these, one of the aims of ultrasonography is to detect fetal anomaly markers one of which is hypoplasia of nasal bone or its absence. Studies have shown that nasal bone hypoplasia is highly associated with various chromosomal anomalies, especially Down syndrome, and is a marker for these anomalies.[2,3]

In many countries, it is recommended that all pregnant women undergo fetal anomaly screening between 18 and 22 weeks of gestation. Similarly, Turkish Ministry of Health recommends that all pregnant women have second trimester organ screening.[4]

Routine measurement of the nasal bone is recommended during the second trimester. However, some factors may have an effect on optimum nasal bone measurement. The quality of the ultrasonography device used the evaluating clinician's experience, oligohydramnios, fetal position, and gestational week (GW) are the factors limiting the evaluation of nasal bone measurement.[5]

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It is known that hypoplasia or absence of the nasal bone is closely related to chromosomal anomalies. Nasal bone measurement is one of the markers used to detect trisomy 21 in pregnancy in the first trimester.[6] A strong association of nasal bone measurement in the first and second trimesters in euploid fetuses has been demonstrated in a study. Some of the fetuses evaluated as nasal bone aplasia in the first trimester ultrasonography can be considered as nasal bone hypoplasia cases in the second trimester ultrasonography.[7] For this reason, while it is recommended to evaluate the presence of nasal bone in the first trimester in all pregnant women, nasal bone measurement is recommended in the second trimester ultrasonography. Invasive procedures are also recommended for definitive diagnosis of chromosomal abnormalities in the absence or hypoplasia of nasal bone. In addition, even when the most common trisomy 21, 18, 13 are excluded, it has been recommended to perform chromosomal microarray analysis when hypoplasia of nasal bone is encountered.[8]

Facial structure and therefore nasal bone structures may differ based on ethnic group, race, and genetic factors. For the diagnosis of nasal bone shortness, the normal nasal bone length (NBL) values of each population should initially be determined. We aimed to determine the normal range of NBL in healthy fetuses between 19-24 weeks of gestation in the Turkish population. For this purpose, we aimed to compile the results of all other studies conducted in Türkiye for the first time in the literature by presenting our own data.

MATERIAL AND METHODS

In our retrospective study, a total of 661 fetuses between 19-24 weeks of gestation presenting between April 01, 2021 and September 15, 2022 were included. GWs determined according to the last menstrual date were confirmed with first trimester crown-rump length. The study was planned in accordance with the principles of the Helsinki Declaration and the ethical committee approval was obtained from the Local Ethics Committee of Selçuk University (Ethics Committee number: 2022/401) before starting the study.

All singleton pregnancies who applied to our perinatology outpatient clinic for a detailed ultrasonography were included in the study. Our study is retrospective and all patients who gave birth in our hospital, birth reports and newborn examinations in the system were scanned retrospectively in the electronic system. Only the patients who were considered healthy by the examining pediatrician were included in the study. Patients whose information could not be accessed in the electronic system or who had abnormal examination findings were excluded from the study. 124 fetuses with major anomalies, 26 twin pregnancies, 5 early-onset intrauterine growth retardation (absent end diastolic flow in the umbilical artery or reverse wave, reversed a-wave in ductus venosus), 16 fetuses with minor anomalies at birth, and 110 patients whose information we could not access from the electronic system were excluded from the study. Biometric measurements were evaluated for intrauterine growth restriction. Fetuses with abnormal Doppler parameters accompanying the diagnosis of growth retardation were excluded from the study.

Fetuses with increased nuchal translucency, structural fetal anomaly or abnormal doppler ultrasonography findings in the first trimester ultrasonography were not included. Fetuses with abnormal structural findings in the second trimester organ screening were also excluded from the study. The parents of all fetuses were of Turkish ethnicity.

All measurements of fetuses applying for organ screening were performed by a single clinician specialized in perinatology. Ultrasonography examination was first started with biometric measurements. For this purpose, biparietal diameter, head circumference, femur length, humeral length, and abdomen circumference were measured in accordance with the rules specified in the literature. Then, fetal structures were examined in detail as directed in the guidelines.[1]

Optimal fetal position was obtained. The skin above the nose, nasal bone, and nasal tip were visualized in the midsagittal plane, covering 75% of the fetal head and chest screen. Nasal bone was measured from the outside to the outside using calibrated calipers every 0.1 millimeter and recorded in mil-

FIGURE 1: The figure shows the fetal nasal bone length measurement technic by ultrasonography.

FIGURE 2: Nasal hypoplasia (Down syndrome was confirmed after birth).

limeters (mm). All fetuses were evaluated transabdominally using the Voluson E6 (GE Medical Systems, Milwaukee, WI) convex probe. Figure 1 shows the fetal nasal length measurement technic by ultrasonography. A short nasal length in a fetus with Down syndrome has also been shown by Figure 2.

SPSS version 21 (IBM SPSS Statistics, IBM Corporation, Armonk, NY, USA) was used for all statistical calculations. Using descriptive statistics; such variables as mean, standard deviation, median, minimum, maximum, percentile, and confidence interval distribution were calculated. Correlation analysis of fetal parameters according to GW was performed using the Spearman test. Scatter/dot graph and regression analysis were used to understand the relationship between NBL and GW.

RESULTS

A total of 661 fetuses were included in the study. Mean week of gestation during NBL measurement was 20.86±1.22 weeks. Distribution of fetuses by GW was determined as follows: 77 (19-19 weeks 6 days), 206 (20-2 weeks 6 days), 199 (21-21 weeks 6 days), 106 (22-22 weeks 6 days), 55 (23-23 weeks 6 days), and 18 (24-24 weeks 6 days).

While 53.9% of the fetuses were male (n=356), 46.1% were female (n=305). The mean maternal age of the pregnant women included in the study was 28.60±5.28 years.

Our data related to NBL percentile with 95% confidence interval according to GW are shown in Table 1. Mean values and standard deviations of NBL ranged from 6.21±0.08 mm to 8.33±0.25 mm between 19 and 24 weeks of gestation.

A significant positive correlation was observed between GW and NBL. (Pearson correlation value; R: 0.414; $p<0.001$). In the regression analysis, R square was found to be 0.221 and p: 0.001. It was shown that the most effective formula for estimating the GW was NBL=GWx0.612+16.938.

TABLE 1: Percentiles of nasal bone length by GW, at 95% confidence interval.

GW	Number of fetuses	2.5 p (%)	5 p (%)	50 p (%)	95 p (%)	95% Confidence interval (mm)
19	77	4.75	4.99	6.30	7.90	6.04-6.37
20	206	4.91	5.20	6.70	8.29	6.56-6.76
21	199	5.31	5.60	7.05	9.01	6.76-7.00
22	106	5.48	5.80	7.50	9.30	6.97-7.29
23	55	6.11	6.40	7.90	9.60	7.53-8.01
24	18	6.52	7.00	8.30	10.00	7.78-8.87

GW: Gestational week; p: Percentile.

TABLE 2: Average values, standard deviation and percentile values of nasal bone lengths in male and female fetuses according to GW.

	Female					Male				
GW	Number of fetuses n=305	Mean values	Standard deviation	Lower bound 5%	Upper bound 95%	Number of fetus n=356	Mean values	Standard deviation	Lower bound 5%	Upper bound 95%
19	35	6.00	0.11	5.77	6.22	42	6.40	0.12	6.16	6.63
20	86	6.72	0.08	6.56	6.88	120	6.62	0.07	6.48	6.76
21	93	6.87	0.08	6.70	7.03	106	7.00	0.10	6.73	7.07
22	57	7.04	0.11	6.82	7.25	49	7.24	0.13	7.00	7.50
23	27	7.74	0.15	7.43	8.04	28	7.81	0.20	7.42	8.20
24	7	8.01	0.45	6.81	9.01	11	8.60	0.30	8.00	9.27

GW: Gestational week.

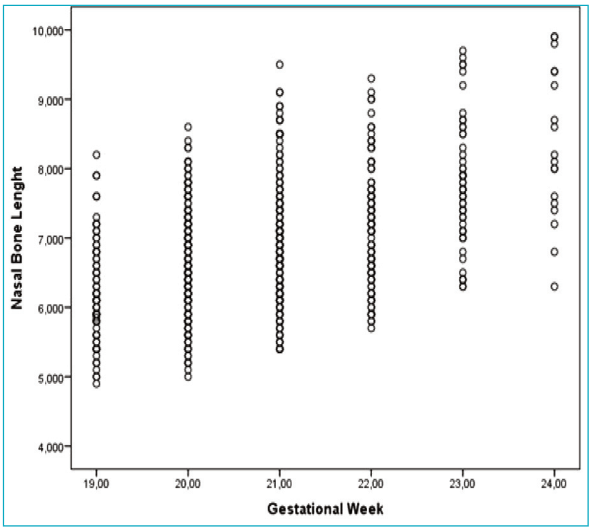

FIGURE 3: The figure shows the gestational week and fetal nasal bone length distribution of the patients in our study.

In Table 2, mean values, standard deviation, and percentile values of NBLs according to GW in male and female fetuses are shown separately.

Figure 3 shows the relationship between GW and fetal NBL. NBL increases linearly with increasing GW. In measurements made at earlier GWs, the distribution of NBL is narrower. As the GW progresses, the normal distribution of NBL also increases.

The relationship between GW and fetal NBL in male fetuses is shown in Figure 4. NBL increases linearly with increasing GW.

Figure 5 shows the relationship between GW and fetal NBL in female fetuses. NBL increases linearly with increasing GW.

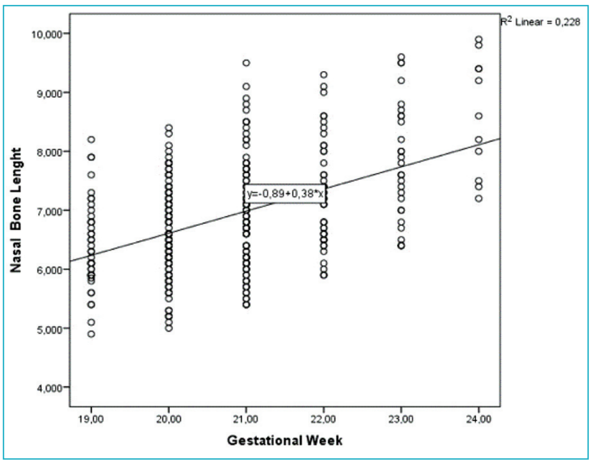

FIGURE 4: The figure shows the distribution between gestational week and fetal nasal bone length in male fetuses in our study.

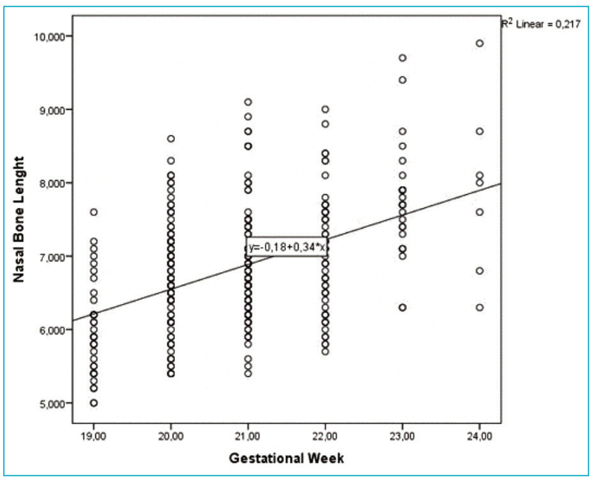

FIGURE 5: The figure shows the distribution between gestational week and fetal nasal bone length of female fetuses in our study.

TABLE 3: Table showing the average nasal bone length by GW in studies conducted in different Turkish populations.

GW	Our study X̄±SD (mm)	Küpeli et al.[9] X̄±SD (mm)	Goynumer et al.[10] X̄±SD (mm)	Asal et al.[11] X̄±SD (mm)	Yalınkaya et al.[12] X̄±SD (mm)	Kavak and Kavak[13] X̄±SD (mm)
19	6.21±0.83	6.2±0.67	4.37±0.64	5.41±0.58	5.37±0.85	6.04±0.82
20	6.66±0.05	6.6±0.74	4.94±0.70	5.74±0.59	5.86±0.74	6.20±0.89
21	6.88±0.05	7.0±0.72	5.32±0.68	6.04±0.69	6.41±0.73	7.46±0.93
22	7.13±0.08	7.3±0.70	5.62±0.69	6.49±0.72	6.63±1.15	7.59±0.74
23	7.77±0.11	7.8±0.76	5.85±0.75		7.01±0.92	8.27±1.24
24	8.33±0.25		6.26±0.77		7.36±0.84	

GW: Gestational week; SD: Standard deviation.

The results of 5 previous studies together with our findings are shown in Table 3. The data obtained from the studies for all weeks of gestation are analyzed for each GW.

DISCUSSION

It has been known for a long time that the presence of hypoplasia or the absence of nasal bone is closely related to chromosomal anomalies, and this makes the measurement of the nasal bone a very important obstetric ultrasonography examination method. Hypoplasia or the absence of nasal bone can be easily detected by second trimester ultrasonography. For this reason, all societies should have their own nomograms. We aimed to share the normal NBL values of healthy fetuses obtained within the course of this study, reflecting the Turkish population in line with the available literature.

It is possible to detect the nasal bone by ultrasonography starting from the 10th week of gestation. The nasal bone shows a linear growth pattern in parallel with the development of other bones in the body. Odibo et al. found in their study that the length of the nasal bone showed a linear increase according to the GW.[14] Similarly, in another study, it was shown that NBL increases linearly in both the second and third trimesters.[15] In our study, we showed that the NBL in healthy fetuses increased proportionally with the GW between 19th and 24th weeks of gestation.

In the first trimester ultrasonography, the presence or absence of the nasal bone is more important than the measurement of the NBL. In the measurements made during this period, the risk of incorrect measurements increases because the nasal bone ossification is not fully formed or the nasal bone is very small. In the second trimester, nasal bone imaging becomes easier in which more objective and more accurate measurements can be obtained. In our study, NBL was easily measured in all fetuses after the appropriate positioning was achieved.

The facial structure is different in each ethnic group and race, the reference range of NBL may differ, which might call for a preliminary information on normal NBL distribution of that particular population in order to diagnose nasal bone hypoplasia. Zelop et al. have revealed the effect of both ethnicity and race on the measurement of NBL.[16] Also, in a study conducted in Japan, it has been shown that the NBLs of Japanese fetuses are shorter compared to white and black races.[17] While another study reported that Chinese fetuses have longer nasal bones compared to Japanese fetuses and shorter nasal bones compared to Korean and Caucasian fetuses.[18]

Similar results were obtained in studies conducted in different countries in which second trimester NBL measurements of fetuses of different ethnic origins were investigated. Similarly, Gautier et al. have found in their study that Cubans of African descent have the NBL value varying between 4.3 mm and 6.5 mm for 20 weeks of gestation.[19] In another study conducted in Brazil in which healthy fetuses were evaluated, it was reported that the NBL varied between 3 mm and 11 mm for 20 and 21 weeks of gestation.[20]

Isolated nasal bone aplasia or hypoplasia increases the probability of trisomy 21 by 6,6-fold.[21] Maternal-Fetal Medicine Association recommends counseling and cell free DNA (cfDNA) to pregnant patients with isolated nasal bone aplasia or hypoplasia without previous aneuploidy screening. If cfDNA is not possible, quadruple screening test and amniocentesis can be recommended by talking to the patient in detail.[22] In our study, a 19 week and 3 days pregnant patient applied to us for routine second trimester ultrasonography scanning. Nasal bone hypoplasia and mild pyelectasis were found in the patient. Detailed genetic counseling was given to the patient. Non-invasive and invasive diagnostic tests options were presented to the patient. The patient did not accept any screening and diagnostic test. The fetus was diagnosed with Down syndrome postnatally.

In the literature, 5 studies have been encountered investigating second trimester NBL in Turkish population, and NBL values are seen to differ considerably between studies, regardless of the GW. In these studies, the shortest NBL was 4.94±0.70 mm for the 20^{th} GW, while the longest one was 6.66±0.05 mm. Similarly, the shortest NBL for the 21^{st} GW was 5.32±0.68 mm, while the longest was 7.46±0.93 mm.

Our study has some limitations. First of all, the number of patients may be insufficient to reflect the whole society. In addition, since all studies mentioned in this study were carried out in different centers, there may be problems in terms of standardization. The differences in the devices used as well as the differences in terms of the experience of the people performing the measurements, and the retrospective design of all studies may have affected the results.

CONCLUSION

As a result, fetal aneuploidy is one of the screening targets that can be detected antenatally. One of these screening methods is to detect fetal structural abnormalities early with sonography. Nasal bone measurement is associated with situations where the probability of aneuploidy is increased. In this study, we presented the data of our own center and the results obtained from other studies conducted in our country show significant differences. We are of the opinion that studies conducted by different researchers in different regions remain insufficient to reflect the nomogram of Turkish ethnic origin. For this purpose, multicenter studies are needed to cover the whole society.

Source of Finance

During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that provides or produces medical instruments and materials which may negatively affect the evaluation process of this study.

Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: *Nizamettin Bozbay, Gökçen Örgül;* ***Design:*** *Nizamettin Bozbay;* ***Control/Supervision:*** *Gökçen Örgül;* ***Data Collection and/or Processing:*** *Nizamettin Bozbay, Fazıl Avcı;* ***Analysis and/or Interpretation:*** *Nizamettin Bozbay, Fazıl Avcı, Gökçen Örgül;* ***Literature Review:*** *Nizamettin Bozbay;* ***Writing the Article:*** *Nizamettin Bozbay;* ***Critical Review:*** *Gökçen Örgül;* ***References and Fundings:*** *Gökçen Örgül;* ***Materials:*** *Nizamettin Bozbay, Fazıl Avcı, Gökçen Örgül.*

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