Smyrna Tıp Dergisi ***Araştırma Makalesi***

Determination of Fetal Nasal Bone Length Nomogram in the Second Trimester
İkinci Trimesterde Fetal Nasal Kemik Uzunluk Nomogramının Belirlenmesi

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Summary
Objective: It was aimed to measure the nasal bone length of fetuses in the 18th to 24th week of pregnancy, to determine the normal value interval for the Turkish population and to determine correlations of nasal bone length with week of pregnancy, maternal age, maternal body mass index and fetal parameters.
Material and Methods: The study included 1236 healthy fetuses in the 18th-24th gestational week of cases aged from 19 to 40 years. The nasal bone length, bi-parietal diameter, femur length and abdominal circumference of the fetuses were measured. Additionally, groups were divided according to maternal age and according to body mass index.
Results: The nasal bone length of fetuses from 18 to 24 weeks gestation was identified to vary from 6.25±0.84 - 7.81±0.75 mm. Additionally, the mean and standard deviation of nasal bone length and fetal parameters were determined according to gestational week, maternal age and maternal body mass index. Later, the correlations between nasal bone length with pregnancy week, maternal age, maternal body mass index and fetal parameters were examined. Nasal bone length was correlated with pregnancy week and fetal parameters ($p<0.01$) but was not correlated with maternal age ($p>0.01$). Nasal bone length and fetal parameters were determined to show negative correlation with maternal body mass index ($p<0.01$).
Conclusion: Maternal age and maternal body mass index are significant factors affecting fetal development. Data related to the nasal bone obtained at the end of the study will be beneficial for assessment of fetal development and identification of fetal anomalies.
Key words: Pregnancy, ultrasonography, nasal bone

Özet
Amaç: Gebeliğin 18.-24. haftaları arasındaki fetüslere ait nasal kemik uzunluğunu ölçerek Türk toplumu için normal değer aralığını belirlemeyi ve nasal kemik uzunluğunun gebelik haftası, anne yaşı, anne vücut kitle oranı ve fetal parametreler ile olan ilişkisininin belirlemesi amaçlanmıştır.
Gereç ve Yöntem: Çalışmaya yaşları 19-40 arasında değişen,18.-24. gebelik haftaları arasında 1236 sağlıklı fetüs dahil edildi. Fetüslere ait nasal kemik uzunluğu, bi-parietal çap, femur uzunluğu ve karın çevresi ölçüldü. Ayrıca gebeler yaşlarına ve vücut kitle oranlarına göre gruplara ayrıldı.
Bulgular: Gebeliğin 18.-24. haftaları arasındaki fetüslere ait nasal kemik uzunluğunun 6.25±0.84 - 7.81±0.75 mm arasında değiştiği tespit edildi. Ayrıca nasal kemik uzunluğunun ve fetal parametrelerin gebelik haftasına, anne yaşına ve anne vücut kitle oranına göre ortalamaları ve standart sapmaları belirlendi. Daha sonra nasal kemik uzunluğunun gebelik haftası, anne yaşı, anne vücut kitle oranı ve fetal parametreler ile olan korelasyon ilişkisine bakıldı. Nasal kemik uzunluğunun gebelik haftası ve fetal parametreler ile korelasyon gösterdiği

(p<0.01), anne yaşı ile korelasyon göstermediği (p>0.01) tespit edildi. Ayrıca nasal kemik uzunluğunun ve fetal parametrelerin anne vücut kitle oranı ile negatif korelasyon gösterdiği belirlendi (p<0.01).
Sonuç: Anne yaşı ve anne vücut kitle oranı fetal gelişimi etkileyen önemli faktörlerdendir. Nazal kemik ile ilgili verilerin fetal gelişimin değerlendirilmesinde ve fetal anomalilerin saptanmasında faydalı olacağı düşünülmektedir.
Anahtar kelimeler: Gebelik, ultrasonografi, nasal kemik

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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 anomalies like trisomy 21 and trisomy 18 are mentioned (1,2,3,4). The most commonly observed chromosomal anomaly is Down syndrome (DS), with increases expressed for some other chromosomal anomalies (2). Studies have stated that ultrasonographic absence or hypoplasia of the nasal bone in the 1st and 2nd trimester is associated with DS (2,4). In the second trimester, nasal bone hypoplasia is 77.7% sensitive for DS and provides 0.9% false positive results (4).

Facial structure and nasal bone length are stated to display differences linked to genetic factors according to ethnic group and race (1,2,3,4). Previous studies have stated there are deviations in nasal bone measurement values in populations like Caucasian, African-American, Chinese, Korean and South Asian (4). The results of studies have emphasized that there are differences in nasal bone length values between ethnic groups and races and as a result, it is necessary to determine the normal value intervals for populations (5,6,7,8,9,10). Additionally, studies have stated the necessity for assessment of more fetuses in multi-center studies and comparison of normal fetuses with DS fetuses (2,4,9).

In this study, it was aimed to measure the nasal bone length in fetuses in the 18th to 24th week of gestation to determine the normal value interval for the Turkish population and the correlation of nasal bone length with gestational week, maternal age, maternal body mass index and fetal parameters and to assess our results in clinical terms.

Materials and Methods

The study was completed by retrospectively screening files recorded in Ankara Yıldırım Beyazıt University Ankara Atatürk Education and Research Hospital Radiology Clinic from 1.January.2017 to 31.December.2017. The study included 1236 healthy fetuses from 18 to 24 weeks gestation of pregnant cases aged from 18 to 40 years (mean: 28.70±5.26). Pregnant cases with any chronic or systemic disease and fetuses with chromosome anomalies or developmental retardation were not included in the study. Permission for the study was granted by Ankara Yıldırım Beyazıt University Yenimahalle Education and Research Hospital ethics committee (date: 25.12.2018, protocol no: 66).

Later the nasal bone length, bi-parietal diameter (BPD), femur length (FL) and abdominal circumference (AC) parameters of the fetuses were recorded. Additionally, pregnant cases were divided into five groups according to age; 20 years or younger (n:60), 21-25 years (n:327), 26-30 years (n:409), 31-35 years (n:304) and older than 35 years (n:136) and into five groups according to body mass index; 20 or less (n:475), 20-24,99 (n:406), 25-29,99 (n:234), 30-34,99 (n:57) and 35 or higher (n:10).

Using the SPSS 17.0 statistical program, mean and standard deviation of parameters according to gestational age and groups were determined. Statistical comparisons within and between groups used the t test. The correlations between parameters and gestational age and groups were determined with the Pearson correlation test. For statistical analyses, the significance level was taken as

p<0.05. P values obtained are given in the results section and under the relevant tables.

Results

The mean age of pregnant cases was found to be 28.70±5.26 (18-40) years. Nasal bone length and fetal parameters together with mean and standard deviations determined according to gestational week, maternal age and maternal body mass index groups (Tables 1,2,3). Comparison of nasal bone length and fetal parameters (apart from the AC parameter from the 19th and 20th weeks) according to gestational week showed differences between the weeks (p<0.05; Table 1). Comparisons of maternal age and maternal body mass index (apart from BPD and FL parameters in Group 1 and Group 3) groups, did not show any differences between the groups (p>0.05; Tables 2 and 3). Additionally; the correlations between nasal bone length with pregnancy week, fetal parameters, maternal age and maternal body mass index were examined. Nasal bone length was correlated with pregnancy week and fetal parameters (p<0.01, Table 4, Graphic 1) but not correlated with maternal age (p>0.01, Table 4, Graphic 2). Additionally, there were negative correlations determined between nasal bone length and fetal parameters with maternal body mass index (p<0.01, Table 4, Graphic 3).

Table 1: *Mean and standard deviation (mm) of nasal bone length and fetal parameters according to week of pregnancy.*

Gestational weeks	N	Nasal bone length	BPD	FL	AC
18	112	6.25±0.84	43.30±4.81	27.98±4.17	142.03±18.28
19	117	6.77±0.58	46.34±3.76	32.28±3.52	153.81±13.27
20	118	6.81±0.74	47.61±3.18	33.61±2.44	156.02±10.14
21	436	7.17±0.68	50.22±2.93	35.64±2.34	164.50±10.36
22	241	7.36±0.65	52.83±2.75	37.77±2.30	173.45±10.44
23	104	7.65±0.69	55.60±2.97	40.43±2.34	183.12±10.73
24	108	7.81±0.75	58.90±3.91	43.87±2.77	200.24±33.21
Total	1236	7.15±0.80	50.69±5.24	35.97±4.77	167.08±20.83

p<0.05: Difference between weeks for all parameters (apart from AC parameter between weeks 19 and 20).

Table 2. *Mean and standard deviation (mm) for nasal bone length and fetal parameters according to maternal age groups.*

Maternal age	N	Nasal bone length	BPD	FL	AC
Group 1 (≤20 years)	60	7.10±0.80	50.20±5.17	35.53±4.81	165.61±18.95
Group 2 (21-25 years)	327	7.12±1.00	50.60±5.42	35.81±4.66	166.93±19.95
Group 3 (26-30 years)	409	7.15±0.79	50.62±5.25	35.90±4.95	167.01±18.49
Group 4 (31-35 years)	304	7.17±0.84	50.79±5.19	36.06±4.84	167.28±24.33
Group 5 (>35 years)	136	7.21±0.69	51.02±5.03	36.41±4.40	167.83±16.11
Total	1236	7.15±0.80	50.69±5.24	35.97±4.77	167.08±20.83

p>0.05: No difference between groups for all parameters.

Table 3. *Mean and standard deviation (mm) for nasal bone length and fetal parameters according to maternal body mass index groups.*

Maternal BMI	N	Nasal bone length	BPD	FL	AC
Group 1 (< 20)	475	7.20±0.74	51.06±4.63	36.43±4.12	168.40±17.13
Group 2 (between 20-24,99)	460	7.15±0.85	50.84±5.46	36.14±5.55	166.87±19.00
Group 3 (between 25-29,99)	234	7.15±0.85	50.49±6.41	35.91±4.94	165.96±22.17
Group 4 (between 30-34,99)	57	7.03±0.79	49.82±5.46	35.21±5.24	165.45±28.92
Group 5 (≥ 35)	10	6.87±1.36	48.60±7.66	33.80±7.06	158.30±26.16
Total	1236	7.15±0.80	50.69±5.24	35.97±4.77	167.08±29.83

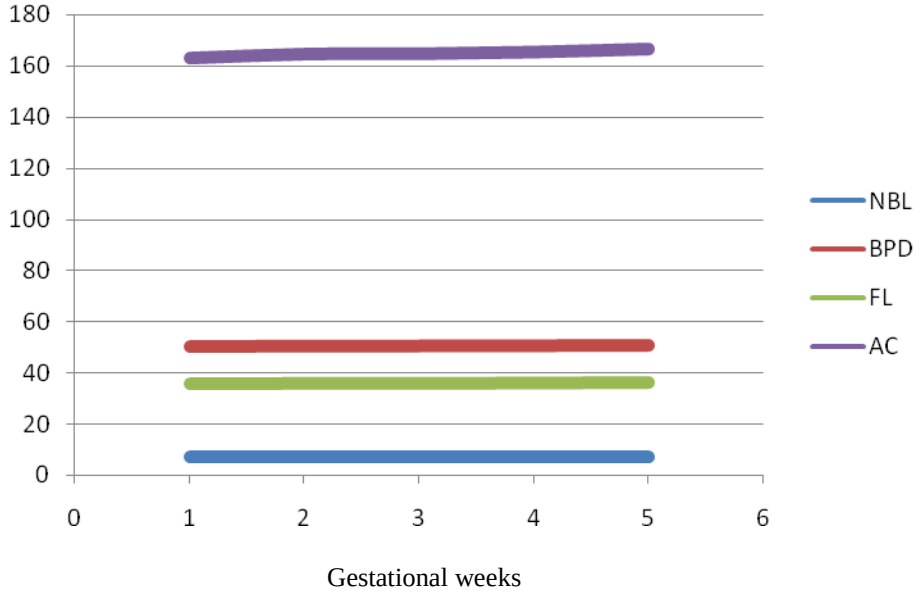
p>0.05: No difference between groups for all parameters (apart from BPD and FL parameters in group 1 and group 3).

Table 4. *Correlation between nasal bone length and other parameters.*

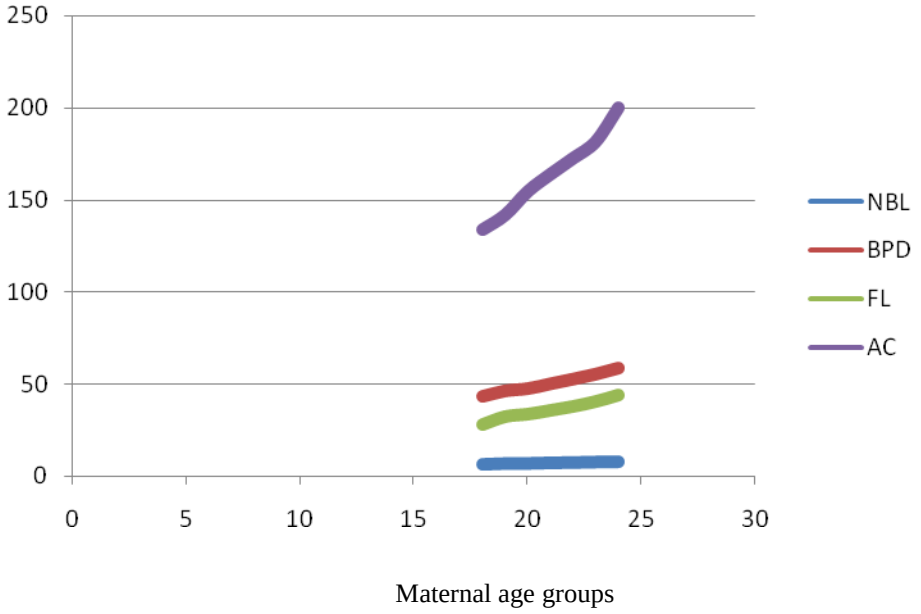
	Age	BMI	Week	BPD	FL	AC	Nasal bone length
Age	1						
BMI	0,116**	1					
Week	0,014	-0,073*	1				
BPD	0,021	-0,079**	0,771**	1			
FL	0,033	-0,083**	0,814**	0,876**	1		
AC	0,018	-0,060	0,685**	0,805**	0,798**	1	
Nasal bone length	0,040	-0,068*	0,495**	0,587**	0,617**	0,523**	1

***: p<0.01, *: p<0.05*

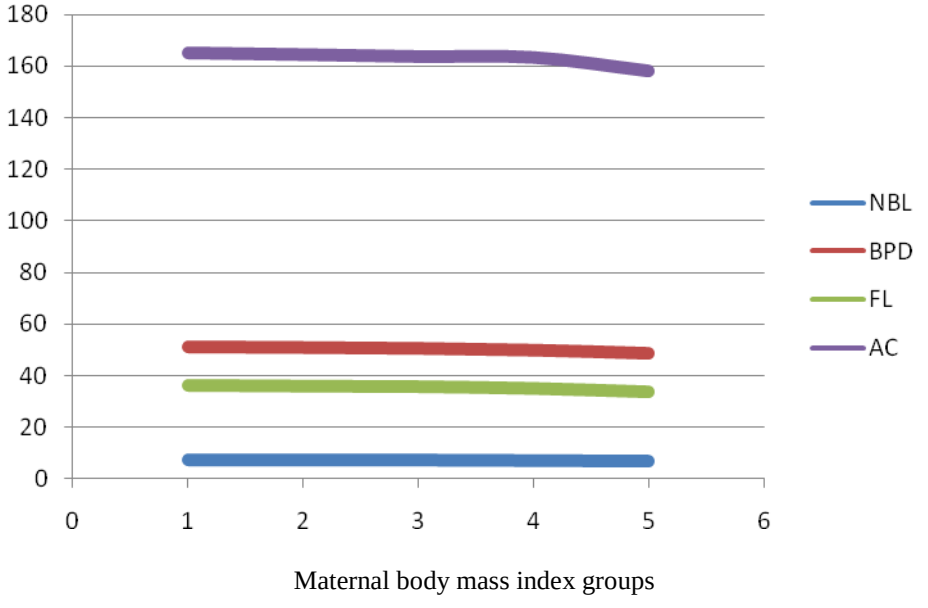
Graphic 1. *Correlation between nasal bone length (NBL) and fetal parameters in gestational weeks.*



Graphic 2. *Correlation between nasal bone length (NBL) and fetal parameters in maternal age groups.*



Graphic 3. *Correlation between nasal bone length (NBL) and fetal parameters in maternal body mass index groups.*



Discussion

From the 10th week of pregnancy, the nasal bone can be imaged with USG. In recent years, nasal bone measurement has become a parameter included in assessment of chromosome anomalies. A range of differentiating points have been determined

during obstetric USG investigation to reveal chromosomal anomalies. One of these differentiating points is nasal bone hypoplasia or absence which was shown to be associated with DS in radiological studies (2,4).

This study firstly determined the mean and standard deviation for nasal bone length in 1236 fetuses from the 18th to 24th week of gestation. The results of the study identified the nasal bone length varied from 6.25±0.84 - 7.81±0.75 mm (mean: 7.15±0.80 mm) (Table 1). When previous studies are examined; Yalınkaya A et al., (1) in a study of 607 fetuses in the 11th-40th week of pregnancy, stated nasal bone length varied from 1.30±0.1 - 10.80 mm. Dizen P et al., (2) in a study of 250 fetuses from the 16th to 22nd week of gestation stated that nasal bone length varied from 3.8±0.52 - 6.4±0.50 mm (mean: 5.4±0.87 mm). Yayla M et al., (3) in a study of 540 fetuses from 11-38 weeks gestation sated that nasal bone length varied from 2.29±0.39 - 13.48±0.44 mm. A study by Yang PY. et al. (4) in 2012 on 102 fetuses in the 15th to 22nd weeks of pregnancy stated the nasal bone length varied from 3.99±0.69 - 5.13±1.09 mm. A study of 3011 fetuses from the 15th to 28th week of gestation found the nasal bone length varied from 3.9±0.72 - 9.9±0.66 mm according to Rahimi-Sharbaf F. et al. (5). A study of 2432 fetuses from the 19th-26th week of pregnancy in 2016 found the nasal bone length varied from 6.07±0.68 - 7.71±1.03 mm (mean: 6.75±0.82 mm) (7). Ozer A et al., (8) in a study of 415 fetuses from the 11th to 14th weeks of pregnancy stated the nasal bone length varied from 2.4±0.4 - 3.4±0.5 mm. A study to determine the normal value interval for nasal bone length in the Korean population examined 3019 fetuses from the 16th-28th week of pregnancy in 2007 and stated the nasal bone length varied from 2.9±0.39 - 8.3±0.94 mm (9). A study of 1467 fetuses with low birth risk from the 16th to 23rd weeks of gestation stated that nasal bone length varied from 3.72±0.3 - 6.24±0.4 mm (10). Other study results identified that nasal bone length increases as the gestational week progresses, similar to the performed study. This result is interpreted as showing that the nasal bone continues to develop during the weeks of pregnancy and development continues after birth to complete development in later periods. In the performed study; differences in nasal bone length values were detected according to gestational week compared to nasal bone length values obtained in other studies. However, the data were compared with the study results for the 18th to 14th weeks in other studies, no significant difference was detected ($p>0.05$). The difference in nasal bone length values in the study is interpreted as being due to differences in gestational week, populations measured and case numbers, lack of focus on a certain week in cases, and due to the person measuring or the device used. The data obtained in the study were compared with other study results in table 5.

Also, mean and standard deviation for nasal bone length according to maternal age and maternal body mass index groups were obtained (table 2,3). Any such parameters in other studies related to nasal bone length were not encountered. The results of the study showed that; as maternal age increased, the nasal bone lengths increased by low rates (table 2); while as maternal body mass index increased, nasal bone lengths reduced (table 3). Additionally, no statistical difference was identified between nasal bone length, maternal age and maternal body mass index groups ($p>0.05$, tables 2 and 3).

Later in the study, the mean and standard deviations for fetal parameters like BPD, FL and AC according to gestational week, maternal age and maternal body mass index groups were determined (tables 1-3). Fetal parameters increased during the weeks of gestation and a statistical difference between the weeks was detected (apart from 19th and 20th weeks for AC parameter) ($p<0.05$, table 1, graphic 1). In maternal age groups, fetal parameters had a low rate of increase and no difference was identified when the groups ($p>0.05$, table 2, graphic 2). In maternal body mass index groups; there was a reduction in fetal parameters and no difference was observed between the groups (apart from BPD and FL parameters in group 1 and group 3) ($p>0.05$, table 3, graphic 3). The data obtained from the study showed that pregnancy week and maternal age positively affect fetal parameters while maternal body mass index affects them negatively.

It was seen that in the previous studies, the correlation between nasal bone length with BPD and FL were examined (2,3,4,7,10). In the performed study, different to other studies, the correlation of nasal bone length with AC was examined. In other studies, nasal bone length was correlated with BPD and FL. In the performed study, a positive correlation between nasal bone length with BPD, FL and AC was determined (Table 4). This result showes that; as fetal development continues, fetal parameters and nasal bone length increase continues in a related way.

The nasal bone can be imaged with USG from the 10th week of pregnancy and is a structure composed to two different bones. In parallel with development of other bones in the body, the nasal bone shows linear increase. For assessment of the nasal bone, investigation with the correct technique and angle is important. Additionally; factors affecting nasal bone assessment include the quality of the measurement device, experience of the performing person, position of the fetus, oligohydramnios, obesity and week of gestation (11,12,13).

Nasal bone measurement can be performed in the 1st trimester. In this period, the nasal bone has not fully ossified and has very small size; so nasal bone assessment may be erroneous linked to position. Additionally, it is stated that the nasal bone may not be imaged from the 11th-14th week and in the black race. As a result, 2nd trimester measurements are stated to be accurate (14,15). Ultrasonographic absence or shortness of the nasal bone has been accepted as a marker for diagnosis of DS in fetuses in the 2nd trimester in studies and these studies have identified false positive rates and sensitivity (14,15,16,17). The false positivity rates in these studies are 0-3.7%, with sensitivity from 34.6-57% (16,17). Studies of fetuses with trisomy 21 have identified absence or hypoplasia of the nasal bone (18,19). The researchers stated that apart from identifying the presence of the nasal bone, the addition of nasal bone length to screening programs will reduce false positivity rates and prevent unnecessary invasive procedures being performed (17,18). However, it is necessary to know the normal nasal bone measurement interval to assess nasal bone hypoplasia.

In conclusion; the results of studies show a correlation between the nasal bone with DS. Especially; in the 1st trimester, the absence of the nasal bone and in the 2nd trimester hypoplasia gains importance. As the structure of the population is different linked to race and ethnic factors; nasal bone measurement intervals in the fetal period will be different.

As a result, it is necessary to identify the nasal bone measurement interval for every ethnicity and race. In conclusion, it is necessary to assess more fetuses in multicenter studies and that comparing normal fetuses with DS fetuses will provide more reliable and accurate results.

Conflicts of interest

There is no conflict of interest in the performed study.

Table 5: *Comparison between study results and other studies.*

	Performed study		Yalınkaya A. et al. (1)		Dizen P. et al. (2)		Yayla M. et al. (3)		Yang PY. et al.(4)		Rahimi-Sharbaf F. et al. (5)		Tomai XH. et al. (7)		Jung E. et al. (9)		Yanik FF. et al.(10)	
Week	N	Mean	N	Mean	N	Mean	N	Mean	N	Mean	N	Mean	N	Mean	N	Mean	N	Mean
15	-	-	-	-	-	-	21	3.81	-	-	20	3.9	-	-	-	-	-	-
16	-	-	38	4.14	9	3.8			14	3.99	74	4.4	-	-	5	2.9	30	3.7
17	-	-	70	4.59	27	4.4	48	4.82	37	4.25	100	4.8	-	-	9	3.6	195	4.0
18	112	6.25	68	5.00	46	4.9			14	4.32	261	5.5	-	-	22	4.0	355	4.3
19	117	6.77	40	5.37	53	5.4	44	5.62	16	4.48	515	6.0	58	6.07	56	4.7	386	4.8
20	118	6.81	23	5.86	49	5.6			10	5.39	648	6.4	416	6.36	254	5.4	278	5.1
21	436	7.17	33	6.41	45	6.1	35	6.39	7	5.33	546	6.9	843	6.62	1038	5.7	104	5.5
22	241	7.36	30	6.63	21	6.4			4	5.13	292	7.3	619	6.79	785	6.0	73	5.9
23	104	7.65	19	7.01	-	-	26	7.27	-	-	184	7.7	257	7.14	272	6.3	46	6.2
24	108	7.81	17	7.36	-	-			-	-	105	8.3	121	7.41	126	6.9	-	-
25	-	-	27	7.48	-	-	14	8.03	-	-	89	8.6	58	7.72	111	7.2	-	-
26	-	-	16	8.13	-	-			-	-	62	8.9	60	7.71	88	7.7	-	-
27	-	-	17	9.21	-	-	9	9.16	-	-	57	9.3	-	-	33	7.7	-	-
28	-	-	16	9.00	-	-			-	-	5	9.9	-	-	34	8.3	-	-

p>0.05: no significant difference between mean nasal bone length between 18-24 weeks.

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