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Investigation of the Distribution of Fetal Nasal Bone Percentile Values in First-Trimester Fetal Anomaly Screening

Birinci Trimester Fetal Anomali Taramasında Nazal Kemik Persantil Değerlerinin Dağılımının Araştırılması

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Abstract

Introduction: We aim to determine the fetal nasal bone length (NBL) percentile values that can be used in the prediction of the fetal anomaly at 11-14 weeks of gestation in a low-risk population.

Materials and Methods: Our prospective and cross-sectional study included four hundred and eighty-six singleton pregnancies who applied for the first-trimester aneuploidy screening test at 11-14 weeks of gestation. We excluded pregnant women with fetal structural or chromosomal anomaly, nuchal translucency >3 mm, an absent nasal bone, and in utero fetal death. Reference and percentile values of the NBL were calculated separately for 11-11^{6}, 12-12^{6}, 13-13^{6}, and 14-14^{2} gestational weeks.

Results: Standard NBL measurements were performed in 486 pregnancies according to inclusion and exclusion criteria. Median NBL values were computed for each gestational age (GA), for 11-11^{6} ,12-12^{6}, 13-13^{6} and 14-14^{2} weeks of gestation was found 1.6 mm (range=1.1-2.5), 1.8 mm (range=1.1-3.0), 2.0 mm (range=1.4-3.1), and 2.2 mm (range=1.7-2.8), respectively. A positive significant correlation was found between NBL and the crown-rump length (CRL) (NBL (mm) = [0.02xCRL(mm)] + 0.73). The 5th percentile of NBL for GA was calculated, for 11-11^{6} ,12-12^{6}, 13-13^{6}, and 14-14^{2} weeks of gestation was found 1.2 mm,1.4 mm,1.5 mm, and 1.7 mm respectively.

Conclusion: We revealed the reference value of NBL for each gestational week in the first trimester of the low-risk population. The data obtained in our study can be used in the screening of genetic syndromes, especially Down syndrome, associated with nasal bone hypoplasia. Our reference value of NBL for the first trimester in singleton pregnancy varies from both previous racial and ethnic groups studies, and other Turkish studies.

Keywords: First trimester; fetal anomaly; nasal bone length; percentile; ultrasonography.

Özet

Amaç: Düşük riskli populasyonunda 11-14. gebelik haftalarında fetal anomali öngörüsünde kullanılabilecek fetal nazal kemik (NK) persantil değerlerini belirlemeye çalıştık.

Gereç ve Yöntem: Prospektif ve kesitsel çalışmamız 11-14. gebelik haftalarında birinci trimester anöploidi tarama testi için başvuran dört yüz seksen altı tekil gebeden oluşmaktadır. Fetal yapısal veya kromozomal anomali, ense saydamlığı >3 mm, nazal aplazi ve in utero ex saptanan gebeler çalışma dışı bırakıldı. NK referans ve persantil değerleri 11-11^{6}, 12-12^{6}, 13-13^{6} ve 14-14^{2} gebelik haftaları için ayrı olarak hesaplandı.

Bulgular: Dahil etme ve hariç tutma kriterlerine göre 486 gebede standart NK ölçümleri yapıldı. Medyan NK değerleri 11-11^{6}, 12-12^{6}, 13-13^{6} ve 14-14^{2} gebelik haftaları için sırasıyla 1,6 mm (aralık=1,1-2,5), 1,8 mm (aralık=1,1-3,0), 2 mm (aralık=1,4-3,1) ve 2,2 mm (aralık=1.7-2.8) olarak hesaplandı. NK ve baş-popo mesafesi (CRL) arasında pozitif korelasyon saptandı (NK (mm) = [0.02xCRL(mm)] + 0.73). 5. persantil NK değerleri 11-11^{6}, 12-12^{6}, 13-13^{6} ve 14-14^{2} gebelik haftaları için sırasıyla 1.2 mm, 1.4 mm, 1.5 mm ve 1.7 mm bulundu.

Sonuç: Düşük riskli populasyonda, ilk trimesterde ortaya çıkardığımız NK referans değerleri; Down sendromu başta olmak üzere nazal kemik hipoplazi ile seyreden birçok genetik hastalığın taramasında kullanılabilir. Tekil gebelikte ilk trimester için NK referans değerimiz hem önceki ırksal ve etnik grup çalışmalarından hem de diğer Türk çalışmalarından farklılık göstermektedir.

Anahtar kelimeler: İlk trimester; fetal anomaly; nazal kemik uzunluğu; persantil; ultrasonografi.

Introduction

The nasal bone is a wedge-shaped bone ventral to the nasal septum and it is evaluated in the sagittal plane (1). Deficiencies in bone calcification cause the nasal bone hypoplasia or aplasia. Hypoplasia

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or agenesis of the nasal bone is one of the second trimester soft ultrasound markers for Down syndrome (2). In a meta-analysis, the likelihood ratio of the absence or hypoplasia of nasal bone during second-trimester ultrasound screening in prediction for Down syndrome was found to be 5.6 (3). Fetal nasal bone was started to be used in the first trimester of trisomy 21 screening in 2001 by Cicero et al (4). It is added to the parameters as present or absent in the current first-trimester screening test. But in the second-trimester ultrasonography, nasal bone hypoplasia or aplasia is considered a soft marker for Down syndrome (DS) (3). A significant correlation is known between the first and second-trimester nasal bone length in normal euploid fetuses (5). Nasal bone length should also be evaluated in first-trimester screening tests. The nasal bone is a structure that develops with gestational age (6). Therefore, nasal hypoplasia should be evaluated with nasal bone percentiles for each gestational age (GA). The nomograms and development of the fetal nasal bone differ between ethnic populations (7) . When we review the literature, it is seen that there are different reference values among the studies revealing the first-trimester nasal bone percentiles in the Turkish population (8-10). We aimed to create a new first-trimester nasal bone nomogram from singleton pregnant women who applied to our clinic without any fetal chromosomal and structural anomalies.

Materials and Methods

Our study is a prospective and cross-sectional study. Pregnant women who applied to the Ankara University Medical Faculty Obstetrics and Gynaecology Polyclinic between April 2022- July 2022 for the first-trimester aneuploidy screening test at 11-14 weeks of gestation were included in our study. Written informed consent was obtained from all participants. Our study was approved by the University Ethical Committee. The GA was calculated from the last menstrual period's first day and validated by the crown-rump length (CRL) measurement. The fetuses with CRL measurements between 45 and 84 mm were counted in the study. In the midsagittal view, the image is enlarged until the fetal head and thorax fill the whole monitor, and the fetal profile, nasal bone, and its covering skin, diencephalon, nuchal translucency, and zygomatic bone were visualized. The probe was slowly tilted from one side of the fetal face to the other to allow proper examination of the nasal bone. Three distinct lines were seen: two proximal lines, known as the 'equals sign', showing the more echogenic nasal bone (underline) and the skin overlying it (top line), and the distal line showing the skin arriving at the end of the nose. Each increase in the distance among the calipers was 0.1 mm. The NBL was calculated by accommodating the calipers in the out-to-out position (Figure 1).

Figure 1. Ultrasound imaging measurement of NBL with calipers in the out-to-out position.

Two measurements were performed and their average was calculated. Ultrasonographic assessment and measurement of fetal nasal bone had been performed generally transabdominal, in case of the inadequate fetal position, however, was made transvaginally. All ultrasonographic examinations and measurements were assessed by five practitioners with at least 10 years of experience, and the Voluson E8 Expert (GE Healthcare Austria GmbH & Co OG) color Doppler ultrasonography device was used.Turkish pregnant women who were admitted to our outpatient clinic between April 2022 and July 2022 for first-trimester screening between 11^{0}-14^{2}th weeks of pregnancy were included in the study. Since the 84 mm CRL measurement corresponds to 14 weeks and 2 days, the outcome week for the study was determined as 14^{2} weeks of gestation.
Our included criteria were that the first-trimester screening test was performed in our clinic and the parents were Turkish. The study excluded pregnant women with fetal structural or chromosomal anomalies, nuchal translucency >3 mm, an absent nasal bone, and in utero fetal death. In addition, cases in which appropriate

Table 1: NBL, CRL, maternal age, and BMİ median values according to GA

GA (weeks)	Maternal age (years) Median (min-max)	Maternal BMİ (kg/m^2) median (min-max)	CRL (mm) median (min-max)	NBL (mm) median (min-max)
$11\text{-}11^6$ (n=56)	28 (range=19-39)	26.2 (range=16.3-48.7)	49.5 (range=45.0-52.2)	1.6 (range=1.1-2.5)
$12\text{-}12^6$ (n=207)	27 (range=18-43)	24.8 (range=15.3-49.9)	60.0 (range=52.4-66.2)	1.8 (range=1.1-3.0)
$13\text{-}13^6$ (n=201)	28 (range=18-41)	25.0 (range=14.7-41.6)	72.0 (range=66.3-79.2)	2.0 (range=1.4-3.1)
$14\text{-}14^2$ (n=22)	28 (range=18-38)	24.3 (range=17.6-34.5)	80.8 (range=79.4-84.0)	2.2 (range=1.7-2.8)

(GA, gestational age; BMİ, body mass index; CRL, crown-rump length; NBL, nasal bone length)

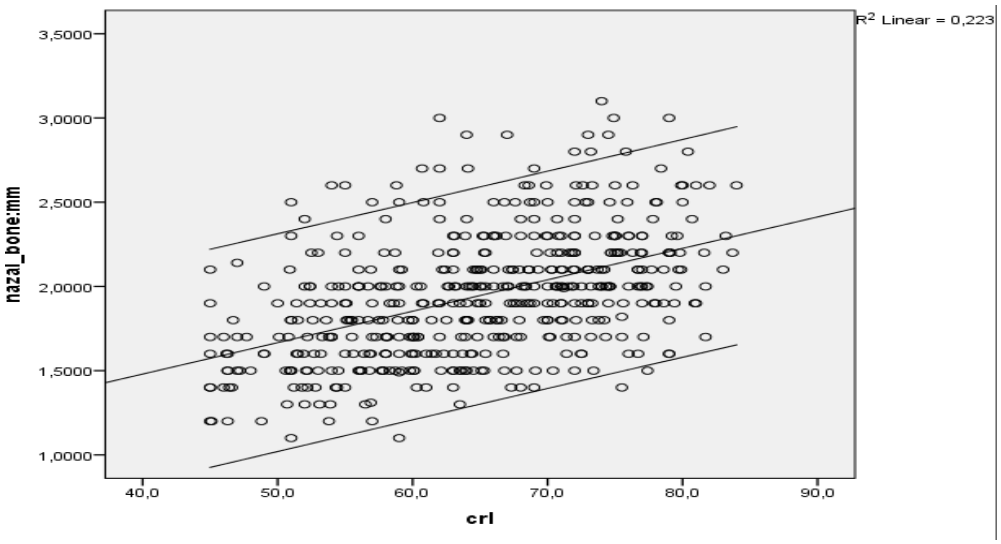

Figure 2. Scatter plot of nasal bone length and CRL (Lines indicating 5th and 95th percentiles)

nasal bone measurement could not be performed due to maternal or fetal reasons were also excluded from the study.

Statistical analysis: BM SPSS version 20 was used for all statistical analyses. For detecting normal distribution, the Kolmogorov-Smirnov test and histograms were used. As descriptive statistics, mean ± standard deviation was used for distributed normally continuous variables, while the median (min-max) was used for not normally distributed values. Categorical variables were given as n (%). The reference values of median and percentiles of 5^{th}, 10^{th}, 25^{th}, 50^{th}, 75^{th}, and 95^{th} were calculated for each gestational age and CRL range. Spearman's test was used for correlation analysis. P-value is accepted as significant under 0.05.

Ethical approval: In our study, written consent was obtained from all the cases participating in our study, in accordance with the Declaration of Helsinki. Ethics Committee permission was obtained from Ankara University Medical Faculty Clinical Research Ethics Committee with the decision dated 21.04.2022 and numbered I04-201-22.

Results

A total of 526 pregnant women applied to Medical Faculty Obstetrics and Gynaecology outpatient clinic for the first-trimester screening test between April 22-July 22. Twelve pregnant women with twin pregnancies, seven fetuses with structural or chromosomal anomalies (three with cystic hygroma, one with down syndrome, one with megacystis, one with omphalocele, and one with

Table 2: Percentiles of NBL according to GA

		Percentiles						
	GA	5	10	25	50	75	90	95
NBL	11-11^6	1.2	1.3	1.4	1.6	1.8	2.1	2.3
(mm)	12-12^6	1.4	1.5	1.6	1.8	2.0	2.3	2.5
	13-13^6	1.5	1.7	1.9	2.0	2.2	2.6	2.7
	14-14^2	1.7	1.9	2.0	2.2	2.6	2.6	2.8

(GA, gestational age; NBL, nasal bone length)

Table 3: Percentiles of NBL according to CRL

		Percentiles						
	CRL (mm)	5	10	25	50	75	90	95
NBL	45-54	1.2	1.3	1.4	1.6	1.9	2.1	2.3
(mm)	55-64	1.4	1.5	1.6	1.8	2.0	2.3	2.5
	65-74	1.5	1.7	1.8	2.0	2.3	2.5	2.6
	75-84	1.6	1.7	1.9	2.2	2.3	2.6	2.7

(CRL, crown-rump length; NBL, nasal bone length)

vertebral anomaly), six fetuses with NT measurements >3 mm and three in utero ex fetuses were excluded from the study. In addition, 12 fetuses who could not have standard nasal bone measurements were excluded from the study. The data of the remaining 486 Turkish pregnant women were included in the statistical analysis. Measurements were usually made transabdominal, only 5.7% (28/486) were measured transvaginal.

The median maternal age and body mass index (BMİ) were 28 years (range: 18–43) and 25.0 kg/m^2 (range: 14.7–49.9), respectively. The median gestational age (GA), CRL and nasal bone length (NBL) were 12.4 weeks (range: 11.2–14.2), 65.5 mm (range:45.0-84.0), 1.9 mm (range:1.1-3.1), respectively (Table-1). A positive significant correlation was found between NBL and CRL (NBL (mm) = [0.02xCRL(mm)] + 0.73, r= 0.483; p<0.001) (Figure 2). Median NBL values were calculated according to CRLs measurements 45-54 mm, 55-64 mm, 65-74 mm, and 75-84 mm. They were calculated 1,6 mm (range=1.1-2.6), 1,8 mm (range=1.1-3.0), 2.0 mm (range=1.4-3.1) and 2.2 mm (range=1.4-3.0) respectively. In addition, a positive significant correlation was found between NBL and GA (r= 0.456; p<0.001). Median NBL values were computed for each GA, for 11-11^6 ,12-12^6, 13-13^6 and 14-14^2 weeks of gestation was found 1.6 mm (range=1.1-2.5), 1.8 mm (range=1.1-3.0), 2.0 mm (range=1.4-3.1), 2.2 mm (range=1.7-2.8), respectively. The 5th, 10th, 25th, 50th, 75th, 90th and 95th percentile of NBL for CRL and GA were calculated (Table2, Table3).

Discussion

Down syndrome (DS) is the most widespread chromosomal abnormality within liveborn infants. Prenatal diagnosis of DS has both medical and medicolegal importance for obstetricians in practice. There are various screening tools for DS, such as first-trimester sonography and maternal biochemical markers, cell-free DNA, and soft marker in the second-trimester ultrasound screening(11). The absence or hypoplasia of the nasal bone is one of the phenotypic features of DS (2). Therefore, it is advised to add the second-trimester ultrasound scan (12). There was found a significant correlation between the first and second-trimester absence or hypoplasia of the nasal bone (5). First-trimester nasal bone evaluation has great value for DS screening and is detected more valuable than the second trimester for aneuploidy screening in a study (13). The absence or hypoplasia of the nasal bone is not only associated with trisomy 21 but also associated with many genetic syndromes (14, 15). In a previous study, absent nasal bone was reported to be present in euploid, trisomy 21, trisomy 13, and trisomy 18 fetuses at percentiles of 2.5, 60, 45, and 53 % respectively (16). Even in isolated cases, chromosomal microarray analysis (CMA) and whole exome sequencing (WES) should be studied in addition to karyotype analysis (17). The ethnic origin of the Parents affects the normal range of fetal NBL (7, 18). NBL values of Latin America, Germany, China, USA+UK, Korea, Brazilian, and the Netherlands were revealed in the literature

(19-24). The median values of NBL in these studies were not only different from each other but also the values reported in our study. The median value of NBL for each GA in the current study is greater than the Korean and Latin American studies, but shorter than the China, US+UK, Brazilian, and Netherlands studies(19-24). These studies show that ethnicity and race have an unignorable impact on the NBL. All studies have shown that ethnic factors should also be taken into account when using NBL in the first trimester of trisomy 21 screening. However, since values are in millimetric diameters the differences might be affected by technical issues regarding measurements but also interobserver differences. these differences may also be due to observer differences or ultrasound quality. There are some Turkish studies about first-trimester NBL measurement in the literature (8-10). The 50th percentile of NBL in the study by Ozer et al were 2.5, 2.9, and 3.4 at 11,12 and 13 weeks of GA, respectively (9). On the other hand, In the study by Yayla et al, the 50th percentile of NBL was 1.7 mm, 1.9 mm, and 2.2 mm for 11, 12, and 13 weeks of GA, respectively (10). In the study of Cansu et al., mean NBL measurements for the 11th, 12th, and 13th GAs were calculated as 2.18 mm, 2.46 mm, and 2.91 mm, respectively (8). In our study, we found different median values from other Turkish studies (Table 4). We calculated the 50th percentile values of NBL at 11, 12, 13, and 14 weeks of GA as 1.6 mm, 1.8 mm, 2.0 mm, and 2.2 mm, respectively. The median values of NBL for each GA in our study were shorter than the other Turkish studies. The NBL has been found to increase in all studies linearly with advancing GA or CRL in the first trimester (19-24). A positive significant correlation was found between NBL and GA or CRL both in our study and in the other Turkish studies (8-10). In our study, which included low-risk pregnancies, Down syndrome was found in only one patient. the fetal NBL was in the 25th percentile compared to the 12th week of gestation. The NBL of this fetus was excluded from the study. The small number of patients with genetic anomalies and excluding these patients' data limit the study. The fetal NBL nomograms according to the gestational week in the pregnant population, including fetuses with structural and chromosomal anomalies, may be the subject of a separate study. Although our case is the first study to compare the first-trimester value of the NBL range in the Turkish population, the use of data obtained from pregnant women in only one province might be a significant limitation of our study. To eliminate this limitation, we have to make studies with larger samples covering various geographical regions of the country.

Table 4: Reference values for NBL in the First Trimester from different Turkish studies

GA (weeks)	Percentiles	This study N=486	Ozer et al N=415	Yayla et al N=1465	Cansu et al N=479
	5	1.2	1.8	1.3	-
NBL (mm) 11-11^{6}	50	1.6	2.5	1.7	2.18
	95	2.3	3.0	2.2	-
NBL (mm) 12-12^{6}	5	1.4	2.1	1.5	-
	50	1.8	2.9	1.9	2.46
	95	2.5	3.0	2.4	-
NBL (mm) 13-13^{6}	5	1.5	2.7	1.8	-
	50	2.0	3.4	2.2	2.91
	95	2.7	4.1	2.8	-
NBL (mm) 14-14^{2}	5	1.7	-	-	-
	50	2.2	-	-	-
	95	2.8	-	-	-

(GA, gestational age; NBL, nasal bone length)

Conclusion

We revealed the reference value of NBL for each gestational week in the first trimester of the low-risk population. The data obtained in our study can be used in the screening of genetic syndromes, especially Down syndrome, associated with nasal bone hypoplasia. Our reference value of NBL for the first trimester in singleton pregnancy varies from both previous racial and ethnic groups

studies, and other Turkish studies. First-trimester reference values of the NBL in the Turkish population can be determined by studies with larger samples covering various geographical regions of the country.

Study limitation: The small number of patients with genetic anomalies and excluding these patients' data limit the study.

Ethical approval: Ethics Committee permission was obtained from Ankara University Medical Faculty Clinical Research Ethics Committee with the decision number I04-201-22 on 21.04.2022.

Conflict of interest: The authors have no conflict of interest regarding this study.

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Author contributions: Concept (HS, GAY, EŞ, CÜ), Design (HS, MK, BV, AK), Data Collection and/or Processing (EŞ, CÜ, MK, BV), Analysis and/or Interpretation (HS, GAY, AK).

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References

1. Sandikcioglu M, Mølsted K, Kjaer I. The prenatal development of the human nasal and vomeral bones. J Craniofac Genet Dev Biol 1994;14(2):124-34..
2. Moreno-Cid M, Rubio-Lorente A, Rodriguez M, Bueno-Pacheco G, Tenias J, Román-Ortiz C, et al. Systematic review and meta-analysis of performance of second-trimester nasal bone assessment in detection of fetuses with Down syndrome. Ultrasound Obstet Gynecol 2014;43(3):247-53..
3. Agathokleous M, Chaveeva P, Poon L, Kosinski P, Nicolaides K. Meta-analysis of second-trimester markers for trisomy 21. Ultrasound Obstet Gynecol 2013;41(3):247-61..
4. 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(9294):1665-7..
5. Bernardeco J, Cruz J, Rijo C, Cohen Á. Nasal bone in fetal aneuploidy risk assessment: are they independent markers in the first and second trimesters? J Perinat Med 2022;50(4):462-6.6.
6. S Sahota D, Leung T, Chan L, Law L, Fung T, Chan O, et al. First-trimester fetal nasal bone length in an ethnic Chinese population. Ultrasound Obstet Gynecol 2009;34(1):33-7.
7. Papasozomenou P, Athanasiadis AP, Zafrakas M, Panteris E, Loufopoulos A, Assimakopoulos E, et al. Fetal nasal bone length in the second trimester: comparison between population groups from different ethnic origins. J Perinat Med 2016;44(2):229-35.
8. Cansu A, Ozgur H, Guven S, Dinc G, Dinc H. Fetal nasal bone length at 11+ 0-13+ 6 weeks of gestation: an evaluation of 554 consecutive cases. Clin Exp Obstet Gynecol 2014;41(5):556-60.
9. Ozer A, Ozaksit G, Kanat-Pektas M, Ozer S. First trimester examination of fetal nasal bone in the Turkish population. J Obstet Gynaecol Res 2010;36(4):739-44.
10. Yayla M, Ergin RN, Göynümer G. Normative values of fetal nasal bone lengths of Turkish singleton pregnancies in the first trimester. J Turk Ger Gynecol Assoc 2011;12(4):225-8.
11. Prabhu M, Kuller JA, Biggio JR. Society for Maternal-Fetal Medicine Consult Series #57: Evaluation and management of isolated soft ultrasound markers for aneuploidy in the second trimester: (Replaces Consults #10, Single umbilical artery, October 2010; #16, Isolated echogenic bowel diagnosed on second-trimester ultrasound, August 2011; #17, Evaluation and management of isolated renal pelviectasis on second-trimester ultrasound, December 2011; #25, Isolated fetal choroid plexus cysts, April 2013; #27, Isolated echogenic intracardiac focus, August 2013). Am J Obstet Gynecol 2021;225(4):B2-b15.
12. Du Y, Ren Y, Yan Y, Cao L. Absent fetal nasal bone in the second trimester and risk of abnormal karyotype in a prescreened population of Chinese women. Acta Obstet Gynecol Scand 2018;97(2):180-6.
13. Shanks A, Odibo A. Nasal bone in prenatal trisomy 21 screening. Obstet Gynecol Surv 2010;65(1):46-52.
14. Huang H, Cai M, Ma W, Lin N, Xu L. Chromosomal Microarray Analysis for the Prenatal Diagnosis in Fetuses with Nasal Bone Hypoplasia: A Retrospective Cohort Study. Risk Manag Healthc Policy 2021;14:1533-40..
15. Moczulska H, Serafin M, Wojda K, Borowiec M, Sieroszewski P. Fetal Nasal Bone Hypoplasia in the Second Trimester as

a Marker of Multiple Genetic Syndromes. J Clin Med 2022;11(6):1513.
16. Nicolaides KH. Screening for fetal aneuploidies at 11 to 13 weeks. Prenat diagn 2011;31(1):7-15.
17. Zhang F, Long W, Zhou Q, Wang J, Shi Y, Liu J, et al. Is Prenatal Diagnosis Necessary for Fetal Isolated Nasal Bone Absence or Hypoplasia? Int J Gen Med 2021:4435-41.
18. 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(2):152-5.
19. Casasbuenas A, Wong AE, Sepulveda W. First-trimester nasal bone length in a normal Latin American population. Prenat diagn 2009;29(2):108-12.
20. 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(6):524-7.
21. 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(8):703-6.
22. Staboulidou I, Steinborn A, Schmidt P, Günter HH, Hillemanns P, Scharf A. [References values for the fetal nasal bone in the first trimenon of pregnancy in a normal collective. A prospective study]. , Z Geburtshilfe Neonatol 2006;210(5):173-8.
23. Bekker MN, Twisk JW, van Vugt JM. Reproducibility of the fetal nasal bone length measurement. J Ultrasound Med 2004;23(12):1613-8.
24. Cossi PS, Araujo Júnior E, Bussamra LCdS, Guimarães Filho HA, Nardozza LMM, Moron AF. Measurement of fetal nasal bone length in the period between 11 and 15 gestational weeks in a Brazilian population: a preliminary study. Radiologia Brasileira 2008;41:155-8.