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ORIGINAL ARTICLE

Mid-second Trimester Measurement of Nasal Bone Length in the Indian Population

Narayani Bandeppa H. · Radhakrishnan Prathima

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Abstract

Objective The purpose of this study was to establish an Indian reference for normal fetal nasal bone length at 16–26 weeks of gestation.

Methods The fetal nasal bone was measured by ultrasound in 2,962 pregnant women at 16–26 weeks of gestation from 2004 to 2009 by a single operator, who performed three measurements for each woman when the fetus was in the midsagittal plane and the nasal bone was between a 45 and 135° angle to the ultrasound beam. All neonates were examined after delivery to confirm the absence of congenital abnormalities.

Results The median nasal bone length increased with gestational age from 3.3 mm at 16 weeks to 6.65 mm at 26 weeks in a linear relationship. The fifth percentile nasal bone lengths were 2.37, 2.4, 2.8, 3.5, 3.6, 3.9, 4.3, 4.6, 4.68, 4.54, and 4.91 mm at 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, and 26 weeks, respectively.

Conclusions We have established the nasal bone length in South Indian fetuses at 16–26 weeks of gestation and there is progressive increase in the fifth percentile of nasal bone length with advancing gestational age. Hence, gestational age should be considered while defining hypoplasia of the nasal bone.

Narayani B. H. (✉), Assistant Professor
OBG, Anapoya Medical College, Mangalore, India
e-mail: bandi_dd@yahoo.com

Radhakrishnan P., Consultant
Fetal Medicine, BFMC, Bangalore, India

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Introduction

Down syndrome is the most common chromosomal abnormality in neonates [1]. Invasive prenatal diagnosis has been proposed for populations at risk (mainly women >35 years or who have had a previous child with Down syndrome), but this strategy only detects 20–25 % of fetuses with Down syndrome [2]. Many new tests have been reported to improve the sensitivity of screening, such as maternal serum biochemical studies and sonographic markers.

Flattening of the facial profile and a small nose are common in neonates with Down syndrome. The absence or hypoplasia of the fetal nasal bone in children with Down syndrome has been detected by first and second trimester sonography [3, 4]. In the second trimester, using the fifth percentile of fetal nasal bone length as a cutoff value resulted in a Down syndrome detection rate of 77.7 % and a false-positive rate of only 0.7 % [5].

Normal fetal nasal bone length values have been established in white, African American, and South American populations [6–8]. Using first trimester sonography, Prefumo et al. [9] showed a trend of a higher incidence of an absent nasal bone in fetuses of healthy Asian mothers. Another study by Cicero et al. [10] reported that the incidence of an absent nasal bone at 11–14 weeks' gestation was substantially higher in African Caribbean (10.4 %) and Asian (6.8 %) fetuses than in white fetuses (2.8 %).

Mid-second trimester fetal nasal bone measurement in the Chinese population has also been studied, with the finding that the fetal nasal bone length in the healthy Chinese population was shorter than that in white and black populations. Thus, it appears likely that race and ethnicity have an impact on fetal nasal bone length. This study aimed to provide a reference range for second trimester nasal bone length in healthy Indian fetuses and compare our findings with other reports.

Materials and Method

This is a record-based retrospective study conducted in the Bangalore Fetal Medicine Center at Bangalore in southern India from 2004 to 2009. In this study, 2,962 Indian pregnant women at 16–26 weeks' gestation undergoing indicated sonographic examinations or amniocentesis were recruited. The following criteria were used for exclusion: abnormal karyotypes, fetal anomalies, fetal death in utero, an absent nasal bone, and structural anomalies in neonates.

Measurement of the fetal nasal bone was performed by a single operator via a midsagittal view of the fetal head, identifying the nasal bone, lips, maxilla, and mandible with an angle between the insonation beam and nasal bone axis close to 45 or 135°, following the method described by Sonek et al. [8] (Fig. 1). The maximum length was measured in millimeters. Three independent images were obtained, and 1 measurement per image was done for each patient. The fetal growth parameters (biparietal diameter, head circumference, abdominal circumference, and femoral length) were assessed for each fetus. The ultrasound machines used were Voluson 730 Expert (GE Healthcare, Vienna, Austria).

Fig. 1 Measurement of the fetal nasal bone following the method described by Sonek et al. [8]

Gestational age was calculated by the last menstrual period in women with certain and regular periods or by a first or early second trimester biometric scan. In cases in which the discrepancy between the last menstrual period and sonographic dating was greater than 7 days, the gestational age was redefined by sonographic assessment.

Neonatal outcomes were recorded in all cases, and karyotypes were obtained from amniocentesis results in high-risk cases.

After data collection, statistical analysis was performed. Scatter plots for nasal bone length as a function of gestational age and biparietal diameter were constructed. The 5th and 50th percentile values were calculated for each gestational week.

Results

Two thousand nine hundred sixty two pregnant women were recruited. The median maternal age was 29 years (range, 15–46 years) and showed no correlation with the nasal bone length (Table 1).

The nasal bone length increased significantly with gestational age ($P < 0.001$). The mean nasal bone length was 5.51 mm with an overall SD of 1.23 mm. The correlation of nasal bone length and gestational age was described by the following equation, nasal bone length (millimeters) = 0.351 × gestational age (weeks) − 2.07 ($R^2 = 0.405$), as shown in Fig. 2. The linear model was preferred because higher-order polynomial coefficients of the equation were not significantly different from 0.

The 5th and 50th percentile nasal bone lengths for each gestational age are shown in Table 2. The medians were 3.30–4.20 mm from 16 to 18 weeks, 4.60 to 5.70 mm from 19 to 22 weeks, and 6.00 to 6.65 mm from 23 to 26 weeks. The nasal bone lengths were significantly shorter than in the white population [6] ($P < 0.001$), but were close to the median values in Chinese [11] and Japanese [12] populations, as shown in Table 3. This trend was also shown in another Southeast Asian study, as shown in Table 4. The distribution of nasal bone lengths and biparietal diameters was also a linear correlation, as shown in Fig. 3.

Table 1 Age distribution

Mother age (years)	$N = 2{,}962$
Mean	28.87
Median	29.0000
Standard deviation	4.40713
Range	31.00
Minimum	15.00
Maximum	46.00

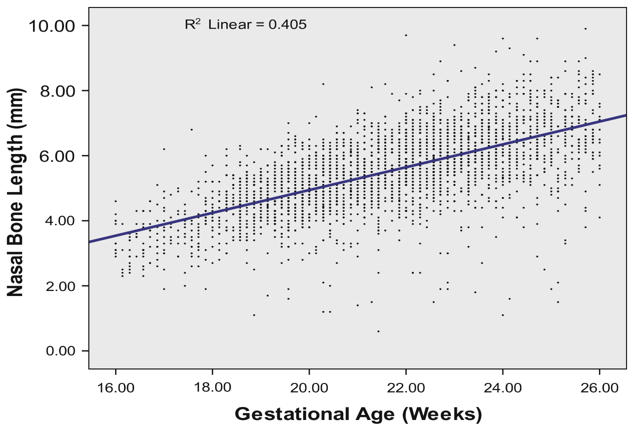

Fig. 2 Scatter plot between nasal bone length and gestational age

Discussion

Second trimester sonographic screening for Down syndrome is based on multiple morphologic and biometric parameters, such as major structural anomalies, nuchal fold thickening, a hyper echoic bowel, pyelectasis, a short humerus, and a short femur. A recent study by Cicero et al. [3] found that an absent nasal bone or one shorter than expected for gestational age was observed in fetuses with Down syndrome.

A study by Sonek [13] showed that the assessment of the fetal nasal bone was a useful screening tool for Down syndrome in both the first and second trimesters of pregnancy. Previous reports of sonographic examinations [4–6]

Table 2 Nasal bone percentiles

Gestational age (week)	Cases	Percentiles (nasal bone)						
		5	10	25	50 (median)	75	90	95
16.00	34	2.3750	2.4500	2.9000	3.3000	3.6750	4.1000	4.3750
17.00	80	2.4050	2.6100	3.1000	3.7000	4.1750	4.6000	4.9000
18.00	133	2.8700	3.1000	3.6500	4.2000	4.7500	5.3600	5.5600
19.00	304	3.5000	3.7000	4.1000	4.6000	5.2000	5.5000	5.7750
20.00	424	3.6250	4.0000	4.4000	4.9000	5.6000	6.0000	6.3000
21.00	427	3.9000	4.4000	4.7000	5.3000	5.9000	6.4000	6.8000
22.00	440	4.3000	4.6000	5.2000	5.7000	6.4000	6.8000	7.2000
23.00	462	4.6000	4.9000	5.5000	6.0000	6.6000	7.1000	7.5000
24.00	335	4.6800	5.2000	5.8000	6.4000	7.0000	7.7000	8.0000
25.00	223	4.5400	5.1000	5.9000	6.6000	7.3000	7.9000	8.2800
26.00	100	4.9100	5.6100	6.2000	6.6500	7.6750	8.4000	8.5950

Table 3 Nasal bone length in the second trimester in different ethnic groups

Gestational age (week)	50th percentile bone length (mm)				5th percentile bone length (mm)			
	Bunduki et al. [6]	Chen et al. [11]	Kanagawa et al. [12]	This study	Bunduki et al. [6]	Chen et al. [11]	Kanagawa et al. [12]	This study
15	ND	3.5	3.2	ND	ND	3.2	2.7	ND
16	5.9	4.1	3.5	3.3000	4.1	3.3	3.1	2.3750
17	6.2	4.6	4.5	3.7000	4.3	3.9	3.5	2.4050
18	6.5	5	4.9	4.2000	4.6	4.3	4.1	2.8700
19	6.8	5.6	5.2	4.6000	4.9	4.3	4.4	3.5000
20	7	5.8	5.8	4.9000	5.2	5.5	4.9	3.6250
21	7.3	6.2	5.7	5.3000	5.4	5	4.8	3.9000
22	7.6	6.7	6.6	5.7000	5.7	6.2	5.5	4.3000
23	7.8	ND	7.2	6.0000	6	ND	5.4	4.6000
24	ND	ND	ND	6.4000	ND	ND	ND	4.680
25	ND	ND	ND	6.6000	ND	ND	ND	4.5400
26	ND	ND	ND	6.6500	ND	ND	ND	4.9100

ND not determined

Table 4 Fifth percentile nasal bone length in the second trimester compared with another Southeast Asian study

Gestational age (week)	5th percentile bone length (mm)	
	This study	Naraphut et al. [15]
15	ND	2.59
16	2.3750	2.97
17	2.4050	3.36
18	2.8700	3.74
19	3.5000	4.13
20	3.6250	4.51
21	3.9000	4.9
22	4.3000	5.28
23	4.6000	5.67

ND not determined

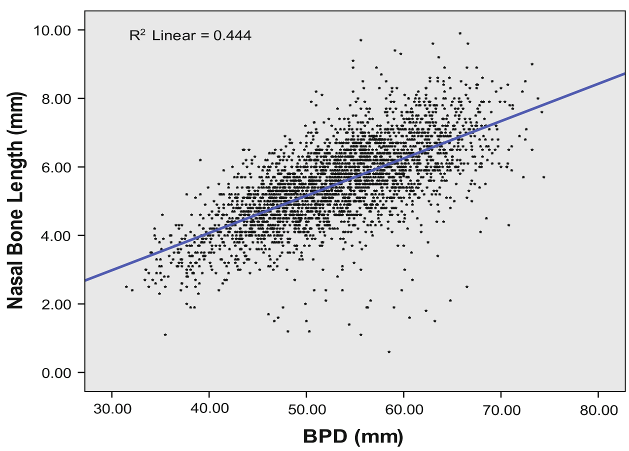

Fig. 3 Scatter plot between nasal bone length and biparietal diameter (BPD)

have shown that nasal bone length increases with gestational age, in accordance with our results.

Nasal bone length is an objective measurement and is considered useful in clinical practice. In this study, successful measurement was achieved in all cases.

In a previous report, the absence or hypoplasia (defined as <2.5 mm) of the fetal nasal bone was the single most sensitive and specific second trimester marker for Down syndrome, with a detection rate of 61.8 % and a false-positive rate of only 1.2 % [3]. Another study showed 59.1 % sensitivity, 5.1 % false-positive rate, and a likelihood ratio of 11.6 at the fifth percentile cutoff value for Down syndrome screening [6]. These detection rates were similar to those of second trimester maternal serum biochemical screening [14].

The mechanisms that result in delayed ossification of the nasal bone in Down syndrome are unclear. However, a delayed maturation mechanism has also been seen in different racial groups. Our study confirmed that there are significant differences in the median and fifth percentile nasal bone lengths between white, African American, and Thai populations and Japanese populations and our Indian population.

However, a large sample study in the Indian population to assess the sensitivity and specificity when using our normal reference range as cutoff values is required.

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