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Nasal bone length throughout gestation: normal ranges based on 3537 fetal ultrasound measurements

J. D. SONEK*†, D. McKENNA†, D. WEBB‡, C. CROOM† and K. NICOLAIDES¶

**Department of Obstetrics and Gynecology, Ohio State University, Columbus, OH, †Department of Obstetrics and Gynecology, Wright State University, Dayton, OH, ‡Miami Valley Hospital, Dayton, OH, USA and ¶Harris Birthright Research Centre for Fetal Medicine, King's College Hospital Medical School, London, UK*

KEYWORDS: fetal biometry; nasal bone; normal ranges; ultrasound

ABSTRACT

Objective *To establish normal ranges for nasal bone length measurements throughout gestation and to compare measurements in two subsets of patients of different race (African-American vs. Caucasian) to determine whether a different normal range should be used in these populations.*

Method *Normal nasal bone length reference ranges were generated using prenatal measurements by a standardized technique in 3537 fetuses.*

Results *The nasal bone lengths were found to correlate positively with advancing gestation ($R^2 = 0.77$, second-order polynomial). No statistical difference was found between African-American and Caucasian subjects.*

Conclusion *These reference ranges may prove to be useful in prenatal screening and diagnosis of syndromes known to be associated with nasal hypoplasia. Different normal ranges for African-American and Caucasian women are not required. Copyright © 2003 ISUOG. Published by John Wiley & Sons, Ltd.*

INTRODUCTION

Genetic sonography has become a very important part of prenatal fetal evaluation. It is used as both a diagnostic and a screening tool. The first report of the association between the ultrasonographic absence of the fetal nasal bone and Down syndrome has recently been reported[1]. The presence or absence of the fetal nasal bone on prenatal ultrasound has been shown to be useful in screening for Down syndrome and other aneuploidies during the 11–14-week gestational period[2]. It is possible that the fetal nasal bone length may also prove to be a useful screening and diagnostic tool.

We set out to establish the normal ranges for nasal bone length measurements throughout gestation. This was initially attempted by Guis *et al.*[3] in 1995. However, this study included a relatively small number of subjects (376 patients), making the normal ranges of limited use. Our study included a total of 3537 subjects. We also compared a subset of patients of the same gestational ages based on race (African-American vs. Caucasian) to determine whether different normal ranges should be used in these populations.

MATERIALS AND METHODS

Unselected pregnant subjects who were examined at the Diagnostic Ultrasound and Antenatal Services Department at Miami Valley Hospital, Dayton, OH during the period 2001–2002 had the bony part of the fetal nasal bridge measured in a standardized fashion using real-time ultrasound. Each of the patients signed an informed consent form that was approved by the Institutional Review Board. The method was as described previously[1]. In brief, the fetal profile was viewed in the mid-sagittal plane. The fetal nasal bone was identified and measured at the level of the synostosis (Figure 1). Care was taken to keep the angle of insonation close to 45° or 135° (Figure 2). The ultrasound equipment used included the Acuson XP128 (Acuson, Mountain View, CA, USA), the Aspen (Acuson) and the Sequoia (Acuson). A permanent record of the image was retained on thermal print paper for future review. Each of the images was reviewed for adequacy of the technique by the principal investigator (J.S.). Only those images that met the strict criteria defined at the outset of the study were used to generate the normal curves. The personnel taking the measurements were all experienced sonographers certified by the American Registry

Correspondence to: Dr J. D. Sonek, Perinatal Ultrasound, One Wyoming Street, Berry Building, Dayton, OH 45409-2793, USA (e-mail: JDSonek@mvh.org)

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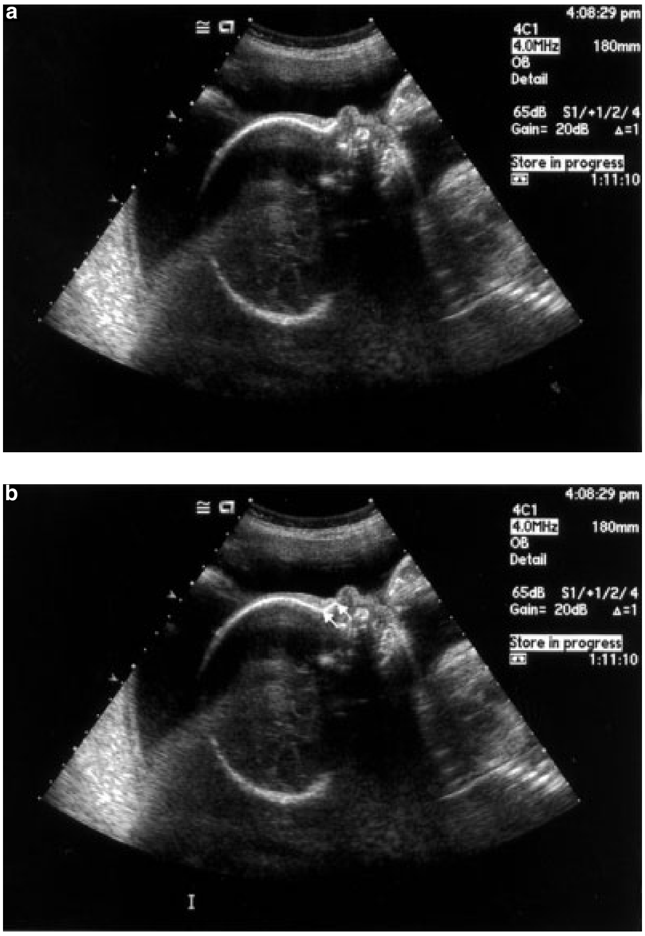

Figure 1 A mid-sagittal view of the face with the nasal bones appearing as a linear echogenic structure (a). The appropriate caliper placement for nasal bone length measurement (b).

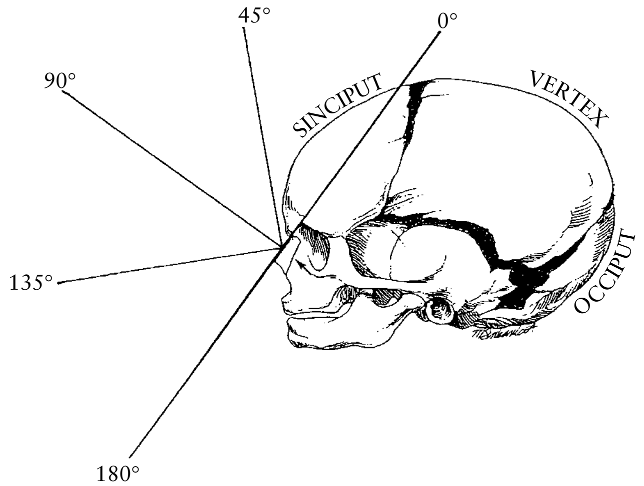

Figure 2 A diagrammatic representation of the fetal skull. The ideal angle of insonation for the measurement of the upper edge of the nasal bone approaches 45° or 135°. Figure reprinted with permission from O'Brien W, Cefalo R, Labor and delivery, in *Obstetrics: Normal and Problem Pregnancies* (3rd edn), Gabbe S, Niebyl J, Simpson J (eds), New York, NY: Churchill Livingstone, 1996; 393.

of Diagnostic Medical Sonographers and had undergone training in the technique.

Statistical analyses were performed using JMP 4.0 (SAS Institute, Cary, NC, USA) and GraphPad Prism 3.00 (GraphPad Software, San Diego, CA, USA). A *P*-value < 0.05 was considered significant.

RESULTS

The nasal bone measurements of 234 African-American women were compared with those of 1223 Caucasian women (Figure 3). Linear regression was performed and the R^2 values were 0.74 and 0.79 for the African-American and Caucasian women, respectively ($P = 0.001$). The slopes and intercepts of the two lines were compared by analysis of covariance with $P = 0.53$ and 0.85 showing no statistical difference.

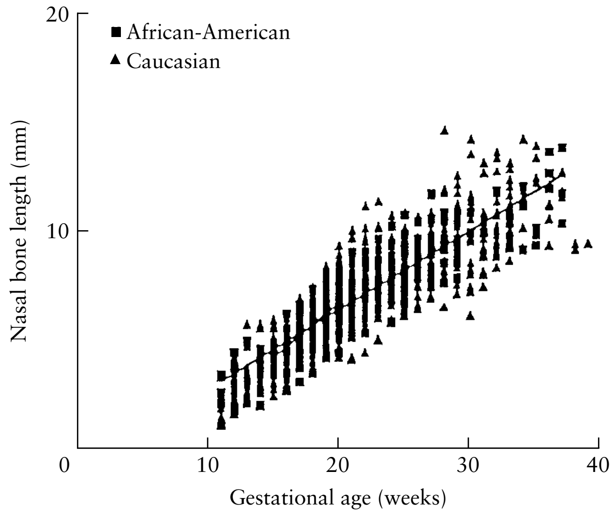

Figure 3 A comparison of nasal bone measurements between 234 African-American and 1223 Caucasian subjects (11–38 weeks' gestation). There was no statistical difference in either the slopes or intercepts ($P = 0.53$ and 0.85, respectively).

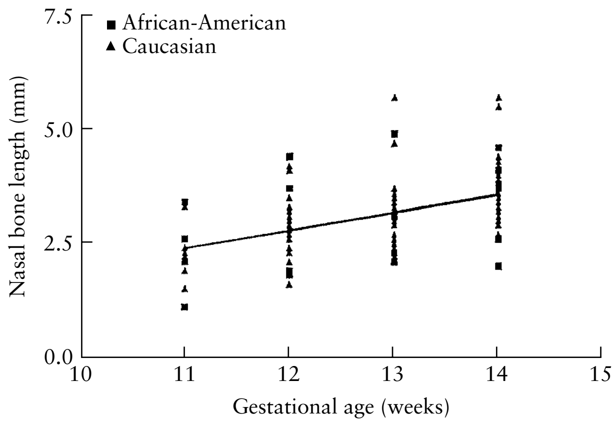

Figure 4 A comparison of nasal bone measurements between 19 African-American and 96 Caucasian subjects (11–14 weeks' gestation). There was no statistical difference in either the slopes or intercepts ($P = 0.97$ and 0.92, respectively).

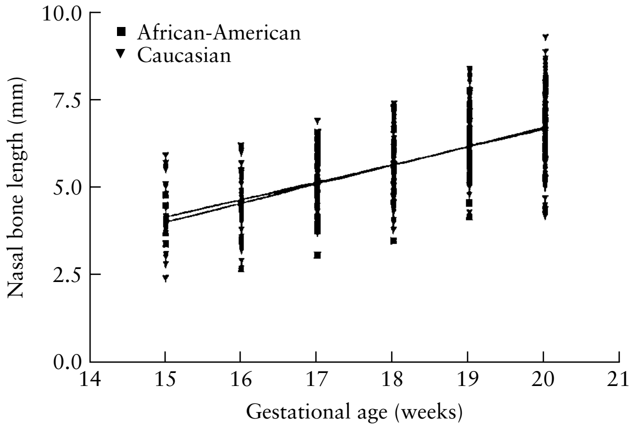

Figure 5 A comparison of nasal bone measurements between 95 African-American and 555 Caucasian subjects (15–20 weeks' gestation). There was no statistical difference in either the slopes or intercepts ($P = 0.53$ and 0.85, respectively).

The nasal bone measurements at 11–14 weeks (Figure 4) and 15–20 weeks (Figure 5) were then stratified by race and compared. The linear regression revealed R^2 values of 0.18 and 0.24 for the African-American ($n = 19$) and Caucasian ($n = 96$) women at 11–14 weeks ($P = 0.07$ and < 0.001, respectively). The slopes and intercepts were not significantly different ($P = 0.97$ and 0.92). The R^2 values were 0.48 and 0.43 for the African-American ($n = 95$) and Caucasian women ($n = 555$), $P < 0.001$ for both groups at 15–20 weeks and the slopes and intercepts were not significantly different ($P = 0.53$ and 0.85).

The nasal bone measurements of all racial groups were pooled and 3537 subjects were included in the study. The best-fit polynomial line was constructed for the nasal bone measurements compared to gestational age (Figure 6). The second-order polynomial yielded an $R^2 = 0.77$, $P < 0.001$, and there was no improvement in fit with higher-order polynomials.

The rate of increase of the nasal bone length decelerates as the pregnancy progresses. The average nasal bone length increases by 4.4 mm (300%) between 11 and 20 weeks' gestation. The increase in average nasal bone length was only 2.9 mm (30%) between 21 and 30 weeks' and 1.5 mm (18%) between 31 and 40 weeks' gestation.

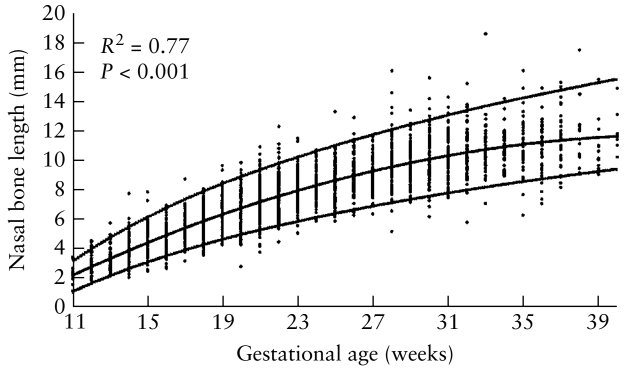

Figure 6 A second-degree polynomial curve based on data from 3537 nasal bone measurements at 11–40 weeks' gestation ($R^2 = 0.77$, $P = 0.001$).

The normal ranges are listed in Table 1. The ranges (2.5th to 97.5th percentiles) for each gestational age are relatively narrow and increase with increasing gestation (2.1 to 3.6 mm from 11 to 20 weeks, 4.2 to 5.9 mm from 21 to 30 weeks, and up to 7.5 mm in the late third trimester). The relatively smaller number of subjects in the late third-trimester categories renders these normal ranges less reliable.

DISCUSSION

This study provides nasal bone length reference ranges throughout gestation based on a large number of subjects and using a standardized technique. A comparison of two subgroups (African-American and Caucasian) suggests that the nasal bone lengths *in utero* do not appear to vary significantly depending on race. However, in a study looking at nasal bones in a population at risk for aneuploidy, there did appear to be an increased incidence of nasal bone hypoplasia in the Afro-Caribbean population as compared to the Caucasians (8.8% vs. 5%)[4]. We did not examine enough subjects from other racial groups to make

Table 1 Normal ranges for nasal bone lengths (in millimeters) ($n = 3537$)

Gestational age (weeks)	*Subjects* (n)	*Percentile* 2.5%	5%	50%	95%	97.5%
11	16	1.3	1.4	2.3	3.3	3.4
12	54	1.7	1.8	2.8	4.2	4.3
13	59	2.2	2.3	3.1	4.6	4.8
14	82	2.2	2.5	3.8	5.3	5.7
15	103	2.8	3.0	4.3	5.7	6.0
16	134	3.2	3.4	4.7	6.2	6.2
17	203	3.7	4.0	5.3	6.6	6.9
18	252	4.0	4.3	5.7	7.0	7.3
19	388	4.6	5.0	6.3	7.9	8.2
20	440	5.0	5.2	6.7	8.3	8.6
21	322	5.1	5.6	7.1	9.0	9.3
22	208	5.6	5.8	7.5	9.3	10.2
23	157	6.0	6.4	7.9	9.6	9.9
24	121	6.6	6.8	8.3	10.0	10.3
25	123	6.3	6.5	8.5	10.7	10.8
26	96	6.8	7.4	8.9	10.9	11.3
27	80	7.0	7.5	9.2	11.3	11.6
28	103	7.2	7.6	9.8	12.1	13.4
29	95	7.2	7.7	9.8	11.8	12.3
30	104	7.3	7.9	10.0	12.6	13.2
31	92	7.9	8.2	10.4	12.6	13.2
32	66	8.1	8.6	10.5	13.6	13.7
33	54	8.6	8.7	10.8	12.8	13.0
34	41	9.0	9.1	10.9	12.8	13.5
35	37	7.5	8.5	11.0	14.1	15.0
36	40	7.3	7.8	10.8	12.8	13.6
37	36	8.4	8.7	11.4	14.5	15.0
38	13	9.2	9.3	11.7	15.7	16.6
39	12	9.1	9.2	10.9	14.0	14.8
40	6	10.3	10.4	12.1	14.5	14.7

a similar comparison. The interobserver and intraobserver variabilities were not formally evaluated in this study. They appear to vary depending on the gestational age and are currently being assessed in ongoing studies.

Facial dysmorphism is a recognized feature of many genetic syndromes. Because of their complex nature, standardized measurements of most bony facial structures are difficult to generate and much of the ultrasonographic evaluation of the fetal face remains subjective. The nasal bone is one of the few facial features that has distinctly identifiable borders and its length can be obtained in a standardized fashion.

In his initial description of the eponymous syndrome, Langdon Down described the nose as being small[5]. Therefore, it is reasonable to assume that this finding may translate into nasal bone hypoplasia on prenatal ultrasound. The ultrasonographic absence of the nasal bone was first described in association with trisomy 21[1]. It has also been noted in some cases of trisomy 18 and 13, and appears to be useful in screening for these syndromes during the 11–14-week gestational time period[2]. It is also possible that nasal bone length may inversely correlate with the risk of aneuploidy[1]. If this proves to be correct, a screening method for aneuploidy similar to the nuchal translucency (NT) measurement may become feasible. As is the case with the NT screening, a standardized approach, together with adequate training and audit, are essential.

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