Normal fetal nasal bone length at 14 to 28 weeks of gestation

Shrestha A, Pradhan S, Tuladhar AS, Pradhan S, Yadav B, Acharya R, Pathak R, Thapa B

Department of Radiology, Nepal Medical College and Teaching Hospital, Jorpati, Kathmandu,Nepal

Corresponding Author: Dr. Amit Shrestha, Department of Radiology, Nepal Medical College and Teaching Hospital, Attarkhel, Jorpati, Nepal; e-mail: austrygypsy@gmail.com

ABSTRACT

The fetal nasal bone length (FNBL) is a recent sonographic marker included in second trimester genetic sonography which varies with race and ethnicity. The importance of measuring FNBL is in the prenatal diagnosis of Down's syndrome (DS), the most common chromosomal abnormality. Nasal bone hypoplasia or absence is one of the frequent features of DS. Different studies conducted in different parts of the world have established FNBL in different races. But, reference values for normal fetal nasal bone length are yet to be established for Nepalese population. So, the aim of this study was to determine normal FNBL in second trimester. Objective was to create normal reference values for fetal nasal bone in Nepalese population. A cross sectional study was carried out on 150 second trimester pregnancy cases referred for antenatal ultrasound to Department of Radiology at Nepal Medical College and Teaching Hospital between May 2014 and July 2014. Cases included all the clinically normal second trimester pregnancy in which fetal nasal bone could be visualized in midsagittal plane. Table demonstrating normal FNBL corresponding to weeks of gestation was generated using IBM SPSS Statistics Version 20.There was linear increase in mean FNBL with gestational age. Minimum mean FNBL was 2.93 mm at 14 weeks and maximum was 7.89 mm at 27 weeks. Age of patients ranged from 17 to 35 years. Normal FNBL values in Nepalese population corroborates with those published in Western literature but with variation. Hence, reference values for local population become more relevant for antenatal ultrasound practices in Nepal.

Keywords: Fetal nasal bone, Down's syndrome, ultrasound.

INTRODUCTION

The fetal nasal bone is a recent sonographic marker included in second trimester genetic sonography. [1]

The human body dimensions are affected by geographical, racial, gender, and age factors. Physical measurements can be worked out and used in differentiation of racial phenotypes. Basically, there are 3 types of race - Caucasoid, Negroid, and Mongoloid. There are 3 types of nose as classified by anthropologists - leptorrhine, mesorrhine, chamaerrhine. [2] Race and ethnicity significantly affect the mean regression line of expected nasal bone length (NBL) by biparietal diameter (BPD) among fetuses in the second trimester.[3] A study brought forth a striking ethnicity in the nasal index of fetuses of Manipuri population wherein the nose becomes chamaerrhine from 28 weeks of gestation onwards till term.[2] Genetic sonographic norms, therefore, appear to require race and ethnicity specific formulas for NBL.[4] b

Down syndrome (trisomy 21) is the most common trisomy and commonest genetic cause of mental retardation with numerous multi-system manifestations. World Health Organization (WHO) reports the estimated worldwide incidence as approximately 1 in 1,000 - 1,100 live births.[5] Risk of Down Syndrome (DS) significantly increases with maternal age, being 1 in 385 at 35 years to 1 in 11 at 49 years.[6] Several studies have shown strong correlation between absent or short FNBL with DS.[7-9]

Ever since , nasal bone length is used as soft marker for screening for Down's Syndrome in routine second trimester antenatal ultrasound (USG) scan, in conjunction with other tests like triple marker maternal serum test and karyotyping by USG guided amniocentesis or cordocentesis.

Reference values for normal fetal nasal bone length are yet to be established for Nepalese population. Hence, this study aims to provide base for further large scale studies evaluating normal FNBL in Nepalese population so that it may help in establishing antenatal diagnosis of Down's syndrome at the earliest.

MATERIALS AND METHODS

Cross sectional study was carried out on 150 cases of clinically normal pregnancy, between 14 to 28 weeks of gestation, referred for routine obstetrics scans to Department of Radiology, Nepal Medical College and Teaching Hospital, Attarkhel, Jorpati between May 2014 to July 2014 (for a period of 3 months). Ten random cases from each week of gestation were selected. Measurements of FNBL along with routine antenatal scan were carried out in each case. Three radiologists with minimum experience of 2 years in obstetric sonography carried out the scans. Two

ultrasound machines; Toshiba Nemio 17 and Toshiba Nemio XG were used. Transabdominal approach was employed in all cases using mutlifrequency probes (3 – 6 MHz). Ultrasound evaluation of the fetal nasal bone was conducted following already established criteria.[10] The criteria are as follows (Figure 1):

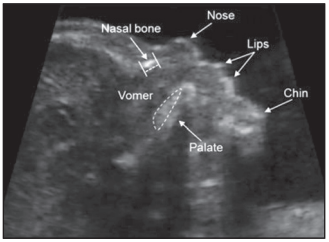

Fig. 1 Ultrasound image of a fetus at 20 weeks' gestation showing the exact mid-sagittal plane of the face with its sonographic landmarks and measurement of nasal-bone length.

- Fetus in midsagittal plane
- Tip of nose clearly seen on profile view
- 3rd and 4th ventricles visualized
- Ribs, stomach and heart not visualized
- Image zoomed so that head, neck and upper thorax occupy more than 50% of width and length of image
- Angle of insonation 45 degree to fetal profile, perpendicular to nasal bone
- Brightness of nasal bone same as overlying skin or brighter, appearing as "=" sign

Onscreen linear calipers were used to measure the nasal bone length only after all the above sonographic criteria were met. Cases were excluded from the study if one or more of the above technical specifications were not met. Exclusion criteria were: previous babies with Down syndrome, presence of other congenital malformations on USG scan, oligohydroamnios, atypical facies in mother and maternal age more than 35 years.

Mean values and range of FNBL for each week of gestation was tabulated and graph was generated using IBM SPSS Statistics Version 20.

RESULTS

A hundred and fifty patients with age range from 17 to 35 years were recruited for this prospective cross sectional study. Ten random cases from each week of gestation starting from 14 weeks to 28 weeks were selected. Mean examination time for measurement of FNBL alone was 4 minutes. FNBL showed linear increase with the weeks of gestation (Figure 2).

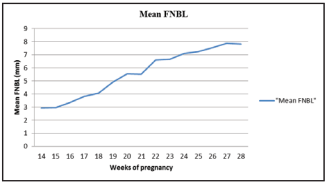

Fig. 2 Line plot graph showing linear progression of mean FNBL with gestational age

Shortest FNBL was 2.2 mm at 14 weeks and longest was 8.5 mm at 28 weeks .Minimum mean FNBL value of 2.93 mm was observed at 14 weeks and maximum of 7.89 mm at 27 weeks. Fastest growth in nasal bone occurred between 21 and 22 weeks where there was increase of about 1.08 mm.

Following accepted international standardized norm, anomaly scans are usually carried out between 18 and 22 weeks of gestation. The mean FNBL for 18th, 19th, 20th, 21st and 22nd weeks were 4.08, 4.89, 5.53, 5.51 and 6.59 mm respectively. Maximum standard deviation of 0.66 was observed at 28 weeks and minimum of 0.33 at 16 weeks. (Table 1) Lower limit of 95% confidence interval at 14 weeks was 2.58 and upper limit at 28 weeks was 8.29. (Table 1)

DISCUSSION

The fetal nasal bone can be seen by USG starting approximately at 11 weeks of gestation.[9] Only pregnancies beyond 14 weeks were taken into consideration because the reproducibility of ultrasound measurement of FNBL was inadequate between 11 to 13 weeks.[11]

Variation is seen in the FNBL values as compared to studies in American, European and other Asian countries; our FNBL values being smaller than those of Caucasian followed by Negroids. Studies have established normal FNBL for Brazilian and Thai population.[12,13] Studies establishing normal FNBL in midsecond trimester in China, 11 to 14 weeks in Italy and Netherland, 15 to 20 weeks in USA and 16 to 24 weeks in England and Spain have been conducted. J.D Sonek et al carried out nasal bone length measurements on 3537 fetuses throughout gestation between 2001-2002.[14-18] These are the largest study regarding FNBL till date. Thai study by Suchin et al and Chinese study by Chen et al proved normal nasal bones are shorter in Asians than those in Caucasian

Table 1: Weeks of gestation with corresponding FNBL values.

Weeks of pregnancy	Age range	FNBL range (mm)Q	Mean FNBL	SD	95% Confidence Interval of the Difference	
					Lower	Upper
14	20-31	2.2-3.6	2.93	0.47621	2.5893	3.2707
15	18-34	2.4-3.7	2.95	0.47434	2.6107	3.2893
16	18-37	2.9-3.9	3.34	0.33400	3.1011	3.5789
17	17-30	3.0-4.3	3.81	0.46774	3.4754	4.1446
18	19-32	3.2-4.8	4.08	0.54324	3.6914	4.4686
19	22-33	4.2-5.5	4.89	0.53009	4.5108	5.2692
20	19-30	4.7-6.1	5.53	0.52504	5.1544	5.9056
21	17-35	4.9-6.4	5.51	0.53009	5.1308	5.8892
22	20-35	5.5-7.1	6.59	0.51088	6.2245	6.9555
23	18-32	5.9-7.5	6.66	0.56999	6.2523	7.0677
24	19-33	6.5-7.6	7.09	0.37845	6.8193	7.3607
25	19-35	6.5-7.9	7.25	0.49497	6.8959	7.6041
26	17-30	6.8-8.2	7.55	0.52334	7.1756	7.9244
27	18-32	7.1-8.4	7.89.	0.44335	7.5728	8.2072
28	19-31	6.3-8.5	7.82	0.66299	7.3457	8.2943

races.[13,14] Cicero et al in 2001 showed higher prevalence of nasal bone hypoplasia in African Caribbean than in White population.[19] These studies prove that there should be specific normal reference range for fetal nasal bone length for each racial population set. However the values are closer and comparable to Asian studies (particularly Thai population) than studies on other races. Table 2 shows the comparison between FNBL values from Thai, Chinese and our population. [13,14]

Although Nepalese population FNBL values are closer to the Asians than from Western literatures, our FNBL values were smaller compared with that of Thai and Chinese population. Study has shown that the mean nasal bone length increased linearly with gestation from 6.2 mm at 19 weeks to 6.8 mm at 22 weeks.[20] Thai study showed this to be from 3.58 mm at 15 weeks to 7.32 mm at 23 weeks.[13]

This may be largely due to racial similarities we share with the South Eastern population. Fastest growth in nasal bone was noted between 21 and 22 weeks where there was increase of about 1.08 mm in FNBL. This peculiar phenomenon is subjected to debate and can only be verified by large population based studies. Mean FNBL was lesser at 28 weeks (7.82 mm) than at 27

Table 2: Comparison of mean FNBL(mm) in different ethnic groups. ND indicates not determined

Weeks of pregnancy	Mean FNBL (mm)			SD (mm)
	Chen M et al. [14]	Sutthibenjakul et al. [13]	This study	
14	ND	ND	2.93	0.47621
15	3.5	3.58	2.95	0.47434
16	4.1	3.9	3.34	0.334
17	4.6	4.33	3.81	0.46774
18	5	4.81	4.08	0.54324
19	5.6	5.53	4.89	0.53009
20	5.8	6.15	5.53	0.52504
21	6.2	6.39	5.51	0.53009
22	6.7	7.05	6.59	0.51088
23	ND	7.32	6.66	0.56999
24	ND	ND	7.09	0.37845
25	ND	ND	7.25	0.49497
26	ND	ND	7.55	0.52334
27	ND	ND	7.89.	0.44335
28	ND	ND	7.82	0.66299

weeks (7.89 mm), which is probably a data aberration rather than actual representation. Maximum standard deviation of 0.66 was observed at 28 weeks, which again is intriguing given that visibility and henceforth reproducibility of fetal nasal bone and its measurement should increase by increase in period of gestation. This, again, can be a result of small sample size.

Short FNBL or absent nasal bone are one of the frequent features of DS and several studies have established strong correlation between the two.[7-9] In a study by Keeling et al, malformation or agenesis of the nasal bone was present in 19 of 31 fetuses with DS.[8] Cicero et al, in their study concluded that nasal hypoplasia is likely to be the single most sensitive and specific second-trimester marker of DS.[19]

Despite the preliminary nature of the study, it proves that local population based reference values of FNBL has become mandatory. This study provides a base for further large scale studies evaluating normal FNBL in Nepalese population so that it may help in establishing antenatal diagnosis of DS at the earliest. Larger population based studies are required to further establish concrete reference values for Nepalese population.

REFERENCES

1. Sonek JD, Nicolaides KH. Prenatal ultrasonographic diagnosis of nasal bone abnormalities in three fetuses with Down Syndrome. Am J Obstest Gynecol 2002; 186: 139-41.
2. Rajlakshmi C. Nasal index and age estimation from nasal dimensions of Manipuri fetuses. J Med Soc 2012; 26(3): 156-8.
3. Carolyn MZ, Kimberly B, Elizabeth M, Adam B. Variation of fetal nasal bone length in second trimester fetuses according to race and ethnicity. Am J Obstet Gynecol 2004; 191(6): 174.
4. Zelop CM, Milewski E, Brault K, Benn P, Borgida AF, Egan JFJ. Variation of fetal nasal bone length in second trimester fetuses according to race and ethnicity. J Ultrasound Med 2005; 24(11): 1487-9.
5. World Health Organization. Genes and Chromosomal diseases: Down syndrome (Internet). 2010 (cited May 2014). Available from: http://www.who.int/genomics/public/geneticdiseases/en/index1.html
6. David SN. Down Syndrome: Prenatal Risk Assessment and Diagnosis Am Fam Physician 2000; 62(4): 825-32.
7. Langdon JLH. Observation on an ethnic classification of idiots. Clinical Lecture and Reports, London Hospital 1866; 3: 259-62.
8. Keeling JW, Hansen BF, Kjaer I. Pattern of malformations in the axial skeleton in human trisomy 21 fetuses. Am J Med Genet 1997; 68(4): 466-71.
9. 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
10. The Fetal Medicine Foundation. Nasal Bone: Protocol for the assessment of fetal nasal bone (Internet). 2010 (cited May 2014). Available from: http://www.fetalmedicineusa.com/nasalbone.php
11. Bekker MN, Twisk JW, Van Vugt JM. Reproducibility of the fetal nasal bone length measurement. J Ultrasound Med 2004; 23(12): 1613-8.
12. Sérgio PC, Júnior EA, Bussamra LCDS, Filho HAG, 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. Radiol Bras 2008; 41: 155-8
13. Sutthibenjakul S, Suntharasaj T, Suwanrath C, Kor-anantakul O, Geater A. A Thai Reference for Normal Fetal Nasal Bone Length at 15 to 23 Weeks Gestation. J Ultraound Med 2009; 28(1): 49-53.
14. Chen M, Lee CP, Leung KY, Hui PW, Tang MH. Pilot study on the midsecond trimester examination of fetal nasal bone in the Chinese population. Prenat Diagn 2004; 24: 87-91.
15. Orlandi F, Bilardo CM, Campgrande M et al. Measurement of nasal bone length at 11-14 weeks of pregnancy and its potential role in Down Syndrome risk assessment. Ultrasound Obstet Gynecol 2003; 22(1): 36-9.
16. Bromely B, Lieberman E, Shipp DT, Benacerraf BR. Fetal Nasal Bone Length A Marker for Down Syndrome in the Second Trimester. J Ultrasound Med 2002; 21: 1387-94.
17. Persicoc N, Molina F, Borenstein M, Azumendi G, Nicolaides KH. Nasal-bone length in euploid fetuses at 16-24 weeks gestation by three-dimensional ultrasound. Ultrasound in Obstetr & Gynecol 2010; 36: 285-90.
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 in Obstetr & Gynecol 2003; 21(2): 152–5.
19. Cicero S, Sonek JD, McKenna DS, Croom C, Johnson L, Nocolaides K. Nasal bone hypoplasia in trisomy 21 at 15-22 weeks of gestation. Ultrasound Obstet Gynecol 2003; 21: 15-18.
20. Gámez F, Ferreiro P, Salmeán JM. Ultrasonographic measurement of fetal nasal bone in a low-risk population at 19-22 gestational weeks. Ultrasound Obstet Gynecol 2004; 23(2):152-3.