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Fetal nasal bone length at 11-28 weeks in Indian fetuses

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Abstract

Objective: To establish the reference range of fetal NBL for Indian population and study the ethnic variation in fetal Nasal Bone Length.

Methods: Prospective Observational Cohort Study was conducted at a North Indian tertiary care Hospital in fetuses at 11-28 weeks. Fetal Nasal Bone Length was measured in mid-sagittal section of the face using electronic callipers. Gestational age was calculated based on Last Menstrual Period (LMP) or first trimester scan when LMP was not known. A total of 250 fetuses were scanned followed by post-natal follow up clinical examination to rule out aneuploidies.

Results: The NBL values showed positive linear correlation with gestational age. The median NBL values increased from 1.9 mm at 11-12 weeks till 8.0mm at 27-28 weeks. The NBLs in Indian fetuses were significantly shorter as compared to Western populations.

Conclusion: An indigenous reference range for fetal NBLs at 11-28 weeks better suited to be used in Indian population.

Keywords: Nasal bone length, Indian normogram, ethnic variation

Introduction

Nasal bone is an important fetal structure to be evaluated during the first and second trimesters of pregnancy. It begins its development at around the 6th week of gestation and is first visualized histologically and on ultrasound at 11 weeks of gestation or 42mm of crown-rump length (CRL) [1, 2, 3].

Since the early half of last decade, normograms of nasal bone length (NBL) have been in use in obstetric ultrasound for ruling out a number of fetal chromosomal aneuploidies. A hypoplastic nose is a component of more than 40 genetic syndromes, including the Down syndrome, Edward syndrome, Apert syndrome and de Lange syndrome [4]. In such cases, the fetal nasal bone is either absent or hypoplastic. This relationship between the NBL and fetal chromosomal aneuploidy stands the strongest in the case of Down syndrome, which, in turn, is the most common chromosomal aneuploidy found amongst the live births [2]. The subjective impression of flat profile observed in Down syndrome can be objectively confirmed by assessment of fetal NBL.

Maternal age of 35 years or more had been suggested as the earliest risk factor for the fetus to have a chromosomal aneuploidy. A number of markers of fetal aneuploidy has been in use since nearly last two decades like increased fetal nuchal skin fold thickness (6mm or more), low measured to expected long bone lengths, pyelectasis, mild cerebellar ventriculomegaly, hypoplastic middle phalanx of fifth digit, sandal gap in toes, pericardial effusion, increased echogenicity of fetal bowel, echogenic intracardiac focus and choroid plexus cyst [2, 5, 6]. Apart from this, a number of maternal serum biomarkers, most important being β human chorionic gonadotropin (β hCG) and pregnancy associated plasma protein A (PAPP-A) are also being used in clinical practice to estimate the risk of aneuploidy to the fetus. It has been seen that the NBL is independent of the maternal age, maternal serum biomarkers and existing sono-markers of aneuploidy and that if it is combined with these existing markers of fetal aneuploidy, enhanced detection of aneuploid fetuses at fixed false positive rates can be achieved. Consequently, a significant decrease in rate of miscarriage from invasive testing and cost of invasive testing and analysis can be achieved.

The morphometrics of human splanchnocranium and nasal bone, in particular, differs with ethnicity [1, 7]. A normal reference range for fetal NBL has been established for the Caucasian, Afro-American and South American populations, but such data is, at best, scanty with reference to the subcontinent [1, 4, 8, 9, 10, 11]. As the facial symmetry varies widely with ethnicity, the existing reference NBLs for populations in other continents may induce misinterpretation of normal Indian fetuses as possible aneuploid causing unnecessary anxiety and agony to pregnant women and their families. Also, higher incidence of absent nasal bone has been found in the healthy fetuses of Asian mothers [12]. Therefore, if this marker has to be applied for routine screening in the subcontinent, it is critical that a normal NBL reference be established.

Materials and methods

This Prospective Observational Cohort Study was carried out between November 2015 and April 2017 over a period of one year and six months in the Department of Radiodiagnosis, Vardhman Mahavir Medical College and Safdarjung Hospital, New Delhi. This centre is a tertiary care centre and caters to a large urban and rural population from the neighbouring states.

A total of 318 pregnant women with 11-28 weeks of gestation were recruited in the study. However, the mid sagittal view of fetal face could not be obtained in 40, fetal structural malformations were detected in 6 fetuses and 22 were lost to follow up who were excluded from the study making the number of participants as 250. Gestational age was calculated based on the date of Last Menstrual Period (LMP) or on the basis of first trimester dating scan in cases where LMP was not known. All pregnant women with 11-28 weeks of singleton euploid structurally normal pregnancies were included in the study. Those affected with physical and mechanical conditions which limit a proper view of fetal nasal bone like maternal obesity, oligohydramnios and fetal presentations incompatible with obtaining a mid-sagittal view of the fetal face were excluded from the study.

An informed written consent was taken of all participants who fit into the inclusion criteria. In each participant, a detailed clinical history and serial sonogram findings were recorded using a pre-designed proforma. The compliance of PC-PNDT act was strictly adhered. The Ultrasound scan was performed using a 1-5 MHz curvilinear transducer (Philips iU22). Ultrasound was performed with the pregnant mother lying supine. Trans-abdominal sonogram was performed by placing the transducer over the gravid uterus. Measurement of the fetal nasal bone was performed via a mid-sagittal view of the fetal head (Fig. 1) which is characterized by nasal bones' synostosis, fetal lips and aligned maxilla and mandible. An anechoic cartilaginous area between the midline of the frontal bone and nasal bones can be recognized and identifies the nasal bridge.[4] The image including fetal head, neck and mid thorax is magnified significantly to approximately 70% of the screen area until two echogenic lines are visible in the region of fetal nose. The nasal bone has the appearance of a thin, echogenic line. It is measured at the level of the synostosis. When these criteria are satisfied, three distinct lines are seen at the level of the fetal nose. The first two, which are proximal to the forehead, are horizontal and parallel to each other, resembling an 'equals sign'. The top line represents

the skin and the bottom one, usually thicker and more echogenic than the overlying skin, represents the nasal bone which becomes more echolucent at its distal end. A third line, almost in continuity with the skin, but at a higher level, represents the tip of the nose [9, 13]. The angle of insonation between the transducer and nasal bone was kept at 45° or close to 135° and the maximum length was measured in millimetres using electronic callipers up to one decimal point.

The scans were used to evaluate the length of the fetal nasal bone in millimeters and each participant was followed up till delivery and the neonate was examined clinically for any syndrome or abnormality.

Percentiles of fetal NBL were calculated for different gestational weeks.

Pearson's correlation coefficient analysis and Spearman's rank correlation analysis were used to correlate the NBL with gestational age. A p value of <0.05 was considered statistically significant.

Regression analysis of the obtained data taking NBL as the dependable variable and GA as independent variable was done using Statistical Package for Social Sciences (SPSS) version 21.0 which is licensed with the Department of Community Medicine, Vardhman Mahavir Medical College and Safdarjung Hospital.



Fig 1: NBL measurement in mid-sagittal view of face in a 25 weeks old fetus

Results, Discussion and Conclusion

The age of the pregnant mothers in the study group was in the range of 19 to 37 years with a mean maternal age of 24.90 years. The fetal NBL and maternal age was correlated using Pearson's correlation coefficient analysis and Spearman's rank correlation analysis. The fetal NBL showed weakly negative to weakly positive correlation coefficient values with maternal age which was statistically insignificant ($p = 0.10$). Hence, there was no relationship between maternal age and fetal NBL. Though being a risk factor for fetal chromosomal aneuploidies, the maternal age did not show any correlation with the NBL. This finding is in agreement with most of the other studies conducted worldwide.

Out of 318 pregnant mothers scanned, nasal bone was successfully assessed in 272 patients taking the success rate of ultrasound examination to 85.5%.

Pearson's correlation coefficient analysis and Spearman's rank correlation analysis were also utilised to correlate fetal NBL with gestational age. It showed positive correlation coefficients with gestational age and hence statistically significant ($p < 0.05$). The NBL showed a positive linear relationship with GA and was given by equation:

$NBL = 0.356GA - 1.871$

$R^2 = 0.788$

Scatter plot was drawn to establish the relationship between NBL and gestational age show a linear increase in NBL with advancing gestational age (Fig. 2).

Of the fetuses scanned, none showed an absent nasal bone which was seen in significant number of healthy fetuses of Asian mothers as compared to other populations [1]. The participants also underwent fetal structural anomaly scan during the course of the study and fetal structural anomaly was detected by ultrasound in six of the cases who were subsequently excluded from the study.

The normogram of the fetal Nasal Bone Length from 11 till 28 weeks of gestation was obtained in present study and provided in Table 1. The median NBL values increased from 1.9 mm at 11-12 weeks till 8.0mm at 27-28 weeks.

Comparison with normograms of NBL from different ethnic origins reveal the NBL values in current study were significantly lower than in Caucasian populations.[4, 8, 10] The median NBL values were slightly greater than the values in the study conducted by Narayani and colleagues in southern Indian population in 2013 [14]. The values were also higher than NBL values in Korean population [7]. The present study had median NBL values comparable with Japanese and Chinese populations [15, 16]. A comparative analysis of median NBL values in different studies is given in Table 2. Thus, an indigenous NBL normogram is imperative to diagnose fetal nasal bone hypoplasia in Indian fetuses. Using Western normogram in Indian population may give rise to false positive result resulting in parental anxiety and further increased risk of pregnancy failure due to invasive as well as expensive prenatal tests.

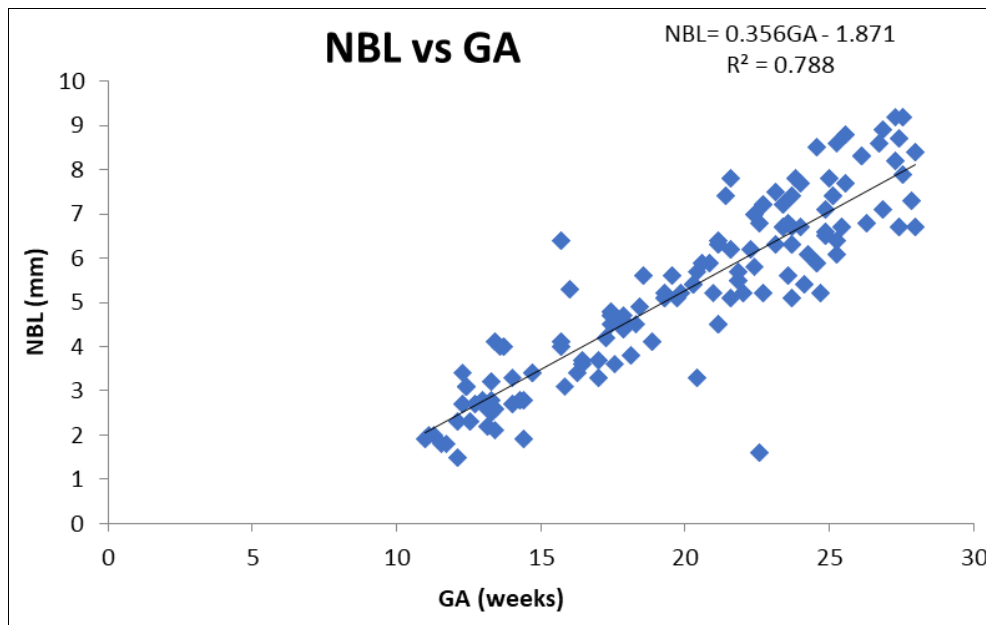


Fig 2: Scatter plot showing relationship between NBL and GA

Table 1: The normogram of the fetal Nasal Bone Length in millimeters obtained from the present study

Gestational Age (weeks)	N= 250	5 th centile	50 th centile	95 th centile
11-11 ⁺⁶	06	1.5	1.9	2.0
12-12 ⁺⁶	19	1.6	2.2	3.4
13-13 ⁺⁶	19	1.8	2.8	3.4
14-14 ⁺⁶	09	1.9	2.8	3.7
15-15 ⁺⁶	09	2.1	3.6	4.1
16-16 ⁺⁶	10	3.1	4.1	4.8
17-17 ⁺⁶	15	3.3	4.5	5.6
18-18 ⁺⁶	09	3.3	4.6	5.6
19-19 ⁺⁶	11	3.6	5.2	5.9
20-20 ⁺⁶	12	3.8	5.4	6.4
21-21 ⁺⁶	23	4.5	5.7	7.2
22-22 ⁺⁶	14	4.9	6.5	7.7
23-23 ⁺⁶	29	5.1	6.5	7.8
24-24 ⁺⁶	20	5.2	6.7	8.5
25-25 ⁺⁶	15	6.1	7.4	8.8
26-26 ⁺⁶	12	6.7	8.0	8.9
27-28	18	6.8	8.3	9.2

Table 2: Comparison of median NBL values in different studies

Gestation (weeks)	Sonek <i>et al.</i> (2003)	Bunduki <i>et al.</i> (2003)	Chen <i>et al.</i> (2004)	Kangawa <i>et al.</i> (2006)	Jung <i>et al.</i> (2007)	Narayani <i>et al.</i> (2013)	Present study
11-11 ⁺⁶	2.3	ND	ND	ND	ND	ND	1.9
12-12 ⁺⁶	2.8	ND	ND	ND	ND	ND	2.2
13-13 ⁺⁶	3.1	ND	ND	ND	ND	ND	2.8
14-14 ⁺⁶	3.8	ND	ND	ND	ND	ND	2.8
15-15 ⁺⁶	4.3	ND	3.5	3.2	ND	3.3	3.6
16-16 ⁺⁶	4.7	5.9	4.1	3.5	3.0	3.5	4.1
17-17 ⁺⁶	5.3	6.2	4.6	4.5	3.5	4.2	4.5
18-18 ⁺⁶	5.7	6.5	5.0	4.9	3.8	4.6	4.6
19-19 ⁺⁶	6.3	6.8	5.6	5.2	4.8	4.9	5.2
20-20 ⁺⁶	6.7	7.0	5.8	5.8	5.4	5.3	5.4
21-21 ⁺⁶	7.1	7.3	6.2	5.7	5.7	5.7	5.7
22-22 ⁺⁶	7.5	7.6	6.7	6.6	6.0	6.0	6.5
23-23 ⁺⁶	7.9	7.8	ND	7.2	6.3	6.4	6.5
24-24 ⁺⁶	8.3	8.0	ND	7.3	7.0	6.6	6.7
25-25 ⁺⁶	8.5	ND	ND	7.6	7.2	6.6	7.4
26-26 ⁺⁶	8.9	ND	ND	ND	7.7	ND	8.0
27-28	9.2	ND	ND	ND	7.7	ND	8.3

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Conflict of interest: None.

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