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Original Article

Fetal Nasal Bone Length Nomogram at 11-13week +6 Days in Upper Egyptian Pregnant Women

Mostafa Mahmoud Hassan Mohamed [1], Abdou Saeed Ait-Allah [1], Mostafa Hussein Mohamed[2], Mohamed Nour El- Dien Salem[1]

1- Department of Obstetrics and Gynecology, Faculty of Medicine, Sohag University, Egypt.
2- Department of Obstetrics and Gynecology, Faculty of Medicine, Assiut University, Egypt.

. **Abstract**

Background: Lack of ossification of the nasal bone (NB) is a prominent skeletal marker associated with trisomy 21. Assessing the NB has also been found to enhance the accuracy and reliability of first-trimester screening methods for identifying this genetic disorder. The purpose of this research was to determine a normative reference range for fetal nasal bone length (NBL) among pregnant women in Upper Egypt which has a value in prediction of chromosomal abnormalities as down syndrome.

Methods: This study employed a cross-sectional design involving 986 pregnant women between 11 weeks and 13 weeks + 6 days of gestation , singleton pregnancy, viable fetus and no gross fetal malformation. All patents were subjected to real-time ultrasound to measure NBL and crown rump length (CRL).

Results: The study demonstrated a statistically significant direct relationship between NBL and CRL (r=0.442, < 0.001). NBL was significantly lower in CRL (40-50mm) than (50.1-60 mm, 60.1-70 mm and 70.1-79.6mm), higher in CRL (60.1-70 mm and 70.1- 80mm) than CRL (50.1-60 mm) and higher in CRL (70.1-80mm) than CRL (60.1-70 mm).

Conclusions: Normgram of NBL can be used as stander in prediction of chromosomal abnormalities.

Keywords: Fetal Nasal Bone Length, Nomogram, Crown Rump Length, Pregnant Women

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Corresponding Author: Mostafa Mahmoud Hassan **E-mail**: faithandeducation7@gmail.com

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Introduction:

In the early phases of embryonic development, genetic factors predominantly influence the formation of the fetal face. As development progresses, environmental factors become increasingly significant. Facial anomalies may arise due to chromosomal abnormalities or exposure to teratogenic agents. Consequently, facial dysmorphism can serve as a critical indicator of potential genetic or chromosomal disorders. In postnatal settings, diagnosing facial dysmorphism is a recognized pediatric practice, typically relying on pattern recognition involving one or more characteristic facial traits, including craniofacial markers such as low-lying ears , altered orbital spacing—either hypotelorism or hypertelorism , reduced orbital size, micrognathia, retrognathia, among others. Notably, several of these features can be identified during the prenatal period. [1]

The nasal bones (NB), originating from neural crest cell aggregates, become histologically detectable once the fetal crown–rump length measures reaches approximately 42 mm, corresponding to 10.9 weeks of gestation. [2] Failure of nasal bone (NB) ossification is considered a characteristic skeletal finding in cases of trisomy 21. [3] Consequently, nasal bone assessment is incorporated into fetal sonographic protocols for trisomy 21 screening .[4] The inclusion of nasal bone assessment has been proven to increase the diagnostic accuracy of trisomy 21 detection during the first trimester. [5]

The measurement of nasal bone length is limited by variation between and within observers, and the effectiveness of using the nasal bone as a supplementary ultrasound-based indicator used during first-trimester screening is highly dependent on the operator's level of experience. [6]

The standard approach to first-trimester Down syndrome screening involves integrating maternal age, nuchal translucency (NT), and biochemical markers such as PAPP-A and free β-hCG, achieving a detection rate of 85% to 90% with a corresponding false-positive rate of 5%. [7] According to previous studies. [8], estimates suggest that integrating nasal bone examination into the screening protocol to standard first-trimester screening methods could improve achieving a detection rate of up to 97% for trisomy 21, without increasing the 5% false-positive rate. In a separate investigation, second-trimester ultrasound detection of nasal bone hypoplasia displayed a sensitivity rate of of 77.7% and a false-positive rate of 0.7% . [9]

This investigation was conducted to determine standard measurements for fetal NBL in Upper Egyptian women at 11 to 13 weeks + 6 days of pregnancy, which has a value in prediction of chromosomal abnormalities as down syndrome.

Patients and Methods:

This cross-sectional study enrolled 986 pregnant women with singleton, viable fetuses and no evident structural anomalies, between 11 weeks and 13 weeks + 6 days of gestation. The research was conducted over the period from April 2021 to April 2023 following ethical approval from the Ethics Committee of Sohag University Hospitals, Sohag, Egypt (ClinicalTrials.gov ID: NCT04798170). Consent to participate was obtained in writing from all individuals included in the study. Exclusion criteria encompassedwomen with pre-existing medical conditions, multiple pregnancies, fetal anomalies, or missed abortions.Each participant underwent comprehensive medical history evaluation, general and abdominal examination, and real-time ultrasonographic assessment for measuring both nasal bone length (NBL) and crown-rump length (CRL).Inclusion criteria:Pregnant women between 11 to 13week +6days of gestation ,Singltone pregnancy,Viable fetus,No gross fetal malformation.

Exclusion criteria:Medical diseased women, Multiple gestations, Fetal malformations,Missed abortion.

Methods**:**Patients were subjected to:Complete history taking,Personal history including Name, Age,address and consanguinity ,Menstrual history: last menstrual period and expected date of delivery,Obstetric history :Parity, mode of delivery,History of present illness : of current pregnancy .,Previous history of congenital anomalies in her fetuses or genetic diseases ,History of exposure to radiation in current pregnancy,Exposure to teratogenic drugs in current pregnancy .,Family history of congenital anomalies or genetic diseases.

Examination:General examination:Vital signs (pulse ,blood pressure, temperature and respiratory rate),Signs of (Pallor, Cyanosis, Jaundice, and Lymph node enlargement).Abdominal examination: visible skin abnormalites or palpaple organ.

Ultrasound examinations were performed using a transabdominal curved transducer with a frequency of 3.5 MHz, under low brightness settings, during the first trimester, specifically from 11 to 13 weeks and 6 days gestation. The ultrasound systems utilized in this study included the Mindray DC-30 (China), Alpinion (Korea), Voluson 8C (India), and Medison Sonace X8 (South Korea).

Crown-rump length measurement:

A mid-sagittal view of the entire fetus was acquired. The fetus was positioned horizontally on the ultrasound screen, ensuring that the crown–rump axis was perpendicular (90°) to the direction of the ultrasound signal path. Calipers were accurately placed to obtain measurements with the structure in a non-flexed crown-rump length, with both anatomical landmarks—the crown and the rump—clearly visualized and defined. [10] **Figure 1**

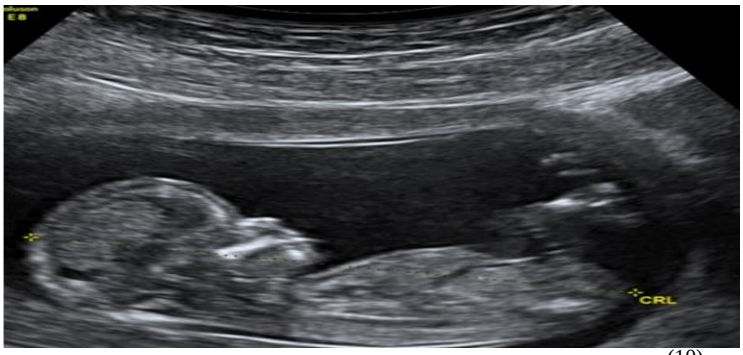

Figure 1: Sonographic evaluation of CRL length [10]

Nasal bone length measurement:

For nasal bone (NB) measurement purposes, a mid-sagittal view of the fetal facial profile was acquired via transabdominal ultrasound , with the ultrasound beam oriented perpendicular to the NB. This specific view was characterized by a hyperechoic nasal tip and a rectangular-shaped palate anteriorly, a translucent diencephalon centrally, and the posterior aspect showing the nuchal membrane. A true midline image was acquired, ensuring that the nasal bone was visualized as a distinct, thin echogenic line. To differentiate the NB from the overlying skin, the transducer was gently tilted laterally until the two structures were clearly visualized as separate.

The ultrasound beam was directed at an angle near 45° in relation to the fetal face was applied to avoid falsely interpreting the nasal bone as absent.

The NB was measured using calipers positioned from outer edge to outer edge. Image magnification was adjusted so that the fetal head and upper thorax occupied around 75% of the screen. The angle of insonation was maintained at 90° in alignment with the longitudinal orientation of the of the nasal bone, ensuring the transducer's face was parallel to this axis. The NB was identified as the echogenic line at least equal in brightness to the overlying skin. In the mid-sagittal plane, a third bright line, indicative of the skin over the nasal tip, appeared anterior to the echogenic 'equal sign' configuration . [11] A statistical regression model was developed to quantify the regarding the correlation between NBL and CRL . **Figure 2**

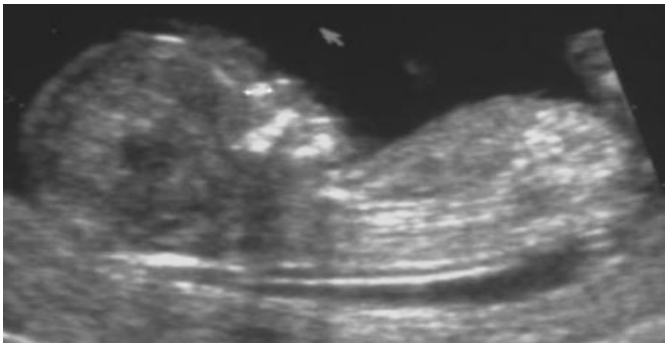

Figure 2: Sonographic measurement of the nasal bone using electronic calipers positioned from outer edge to outer edge [10]

Anatomical scan in second trimester was done for all studied cases to exclude congenital anomalies and genetic diseases which were not discovered in the early scan and to detect correlation between NBL and congenital or genetic diseases.

Statistical analysis

Statistical evaluation was conducted using IBM SPSS Statistics version 26 (IBM Corp., Chicago, IL, USA). Quantitative data were presented as mean values with standard deviation (SD) and analyzed between groups using an independent samples t-test.Categorical data were reported as frequencies and percentages and analyzed using the Chi-square test or Fisher's exact test, as appropriate. The receiver operating characteristic (ROC) curve was utilized to assess diagnostic performance, including sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV). Correlations between variables were analyzed using the Pearson correlation method, with significance set at a two-tailed p-value of less than 0.05.**Results:**

Demographic data, obstetric history and indication of 1st trimester ultrasound examination were enumerated in this table. **Table 1**

Table 1: Demographic data, obstetric history and indication of 1st trimester ultrasound examination of the studied patients

			N=986
Age (years)			29 ± 6.04
BMI (Kg/m^2)	**Underweight**		0 (0%)
	Normal		767 (77.78%)
	Overweight		219 (22.21%)
Residence	**Sohag 926(93.1%)**	**Urban**	254(27.42%)
		Rural	672(72.57%)
	Assiut 60(6.08%)	**Urban**	18(30%)
		Rural	42(70%)
Obstetric history			
Parity	**Primigravida**		400 (41.32%)
	Multipara		586 (59.43%)
Mode of delivery	**Vaginal delivery**		270 (46.07%)
	CS 304(51.87%)	**Previous 1 CS**	103 (33.88%)
		Previous 2 CS	70 (23.02%)
		> previous 2 CS	131 (43.09%)
	Vaginal delivery after CS		12 (2.04%)
Abortions 210(21.2%)	**1st trimester**		126 (60%)
	2nd trimester		84 (40%)
Indication of 1st trimester ultrasound examination			
Family history of CFMF			9 (0.91%)
Previous child with CFMF			74 (7.48%)
Drug intake			47 (4.75%)
Consanguinity			21 (2.12%)
ICSI			84 (8.49%)
Family history of Down syndrome			1 (0.1%)
Previous child with Down syndrome			48 (4.85%)
Routine			701 (70.88%)

Data are summarized as mean with standard deviation for continuous variables, and as counts and percentages for categorical variables. BMI: body mass index, CS: Cesarean section, CFMF: congenital fetal malformation, ICSI: Intracytoplasmic sperm injection.

A positive significant association was identified between nasal bone length (NBL) and crown–rump length (CRL) ($r = 0.442$, $p < 0.001$).

Table 3: Distribution of NBL according to CRL as percentiles

	N	CRL (mm)	5th	50th	95th	P
40-50mm	108	2.4 ± 0.18	2.1	2.5	2.8	**<0.001***
50.1-60 mm	179	2.6 ± 0.17	2.4	2.6	2.9	
60.1-70 mm	255	2.7 ± 0.17	2.5	2.7	3.1	
70.1-80mm	444	2.9 ± 0.21	2.6	2.9	3.2	

Results are shown as mean ± SD; * denotes a statistically significant difference ($p \leq 0.05$)., NBL: nasal bone length, CRL: crown-rump length.

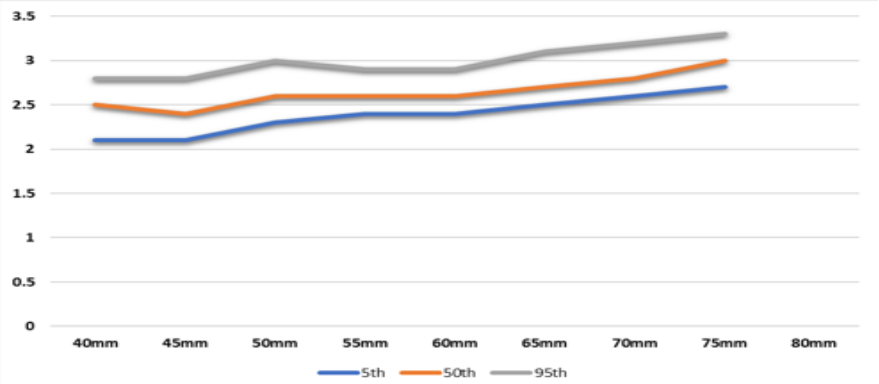

Figure 3: Distribution of NBL according to CRL as percentiles

Discussion

Screening for fetal chromosomal anomalies has become an essential component of prenatal assessment. Nuchal translucency (NT) measurement remains the most widely utilized sonographic parameter applied in early prenatal screening. However, the evaluation of the fetal nasal bone (NB) has recently emerged as a complementary tool to enhance the detection of chromosomal abnormalities [12]. Cicero et al . [8] were the initial researchers to explore the possibility of nasal bone evaluation as a marker in first-trimester trisomy 21 screening.

In our study, NBL showed a significant direct association with CRL (r=0.442, < 0.001) of the studied fetuses (n=986). This is in accordance with Cansu et al. [13] reported that regression analysis of nasal bone length (NBL) in relation to crown–rump length (CRL) yielded the equation y = 0.781 + 0.030 × CRL, with a correlation coefficient (R) of 0.533 and a statistically significant p-value (< 0.001), demonstrating a positive linear relationship. Prabha et al. [14] reported that, based on Pearson correlation analysis, nasal bone length exhibited a weak positive correlation demonstrating a positive association with gestational age (r = 0.346). Orlandi et al,[15] demonstrated that, among unaffected fetuses with clearly measurable nasal bones, a regression equation was constructed.In our study, as regard NBL values stratified by CRL and expressed in percentiles (n=986); NBL measurements ranged from 2 to 2.8 mm with a mean value (± SD) of 2.4 (± 0.18) mm in CRL (40-50mm), ranged from 2.1 to 3.1 mm with a mean value (± SD) of 2.6(± 0.17) mm in CRL (50.1-60 mm) and ranged from 2.4 to 3.2mm with a mean value (± SD) of 2.7 (± 0.17) mm in CRL (60.1-70 mm) and ranged from 2.9 ± 0.21mm with a mean value (± SD) of 2.9 (± 0.21)mm in CRL (70.1-80 mm). NBL was significantly lower in CRL (40-50mm) than (50.1-60 mm, 60.1-70 mm and 70.1-79.6mm), higher in CRL (60.1-70 mm and 70.1- 80mm) than CRL (50.1-60 mm) and higher in CRL (70.1-80mm) than CRL (60.1-70 mm). In comparison to international data, the present study demonstrated comparable mean NBL measurements within the 11+0 to 13+6-week gestational range reported by Orlandi et al. [15] and Sonek et al. [16] Moreover, Cansu et al.[13] established a nomogram following the examination of 479 fetuses with no detected anomalies originating from the Eastern part of the Black Sea region of Turkey.Their values for the 12th week, and the 13th week were 2.2, 2.5 and 2.9 mm, respectively. Moreover, Prabha et al. [14] demonstrated that NBL increased linearly with

advancing gestational age and CRL , consistent with findings from previous research. Specifically, their analysis showed that NBL increased by 0.014 mm for every 1 mm increase in CRL. Our findings showed that the mean NBL in relation to CRL exceeded those reported in the study by Kelekci et al.[17] and Sivri et al. [18] Our findings were inconsistent with those of Colloda et al, [19] since, in his study, Asian fetuses were found to have comparatively shorter nasal bones.

Limitations of the study included that NBL measurement may be influenced by other clinical and diagnostic factors that were not accounted for in the analysis. The predictive power of NBL measurement for Down syndrome may be limited by its sensitivity and a strong negative predictive value. Incorrectly identified positive and negative outcomes can occur, and confirmatory testing may be needed to confirm a diagnosis of Down syndrome. The normogram of NBL of upper Egyptian women do not reflect the normogram of NBL of Egyptian pregnant women.

Conclusions:

NBL measurements increase with CRL, with significantly higher measurements at larger CRLs. NBL can be utilized as a screening parameter for Down syndrome, with an established cut-off value indicating increased risk of >2.4 mm showing high sensitivity and positive predictive value. Normgram of NBL can be used as stander in prediction of chromosomal abnormalities. Our NBL normogram supports the existence of ethinc variability in NBL.

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Conflict of Interest: Nil

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