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First-trimester nuchal translucency, nasal bones, and trisomy 21 in selected and unselected populations

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KEY WORDS
First trimester
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Objective: The purpose of this study was to assess the role of fetal nasal bones evaluation in first-trimester screening for trisomy 21 in selected and unselected pregnancies.

Study design: Visualization of the nasal bones was attempted in women attending for routine nuchal translucency screening (unselected population, n = 7116, 12 cases of trisomy 21), as well as in high-risk pregnancies referred to our tertiary care center (selected population, n = 510, 23 cases of trisomy 21).

Results: The sensitivity, specificity, positive and negative predictive value of absent nasal bones for trisomy 21 were 16.7%, 97.3%, 1.1%, 99.8% and 47.6%, 95.3%, 33.3%, 97.4% in the unselected and selected population, respectively. At logistic regression analysis including nuchal translucency and nasal bones findings, the latter resulted to be an independent predictor of trisomy 21 in the selected but not in the unselected population.

Conclusion: First-trimester nasal bones assessment for trisomy 21 screening has a very different performance in selected and unselected pregnancies.

Screening for Down syndrome has become an integral part of routine antenatal care. First-trimester screening using first-trimester fetal nuchal translucency, alone[1] or in combination with maternal serum free β human chorionic gonadotropin (βhCG) and pregnancy associated plasma protein A (PAPP-A),[2,3] has been proven to provide effective screening for Down syndrome.[4] It was also reported that the failed visualization of the fetal nasal bones by ultrasound at 11 to 14 weeks of gestation may be associated with chromosomal abnormalities.[5-12] Some authors suggested that nasal bones assessment, in association with currently available first-trimester screening methods, is likely to result in increased screening sensitivity and reduced false-positive rates.[13]

However, most of the studies reporting a strong association between the failed visualization of the fetal nasal bones and trisomy 21 are based on selected high-risk cases referred to specialist centers.[5-9,11,12] Recent data from a large unselected population challenged the

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Table I Maternal demographic characteristics

	All cases (n = 7626)	Selected (n = 510)	Unselected (n = 7116)	*P* value
Maternal age (y)	31.6 (14.5-50.2)	35.5 (17.1-45.9)	31.4 (14.5-50.2)	< .001
Nullipara	53.0%	39.4%	54.0%	< .001
Ethnicity				< .001
white	63.6%	83.5%	62.1%	
black	14.4%	4.9%	15.1%	
Asian	16.1%	6.5%	16.9%	
Other	5.8%	5.1%	5.9%	
Smoking	8.0%	7.5%	8.0%	.74
Gestational age at scan (wk)	12.4 (11.1-14.0)	12.6 (11.1-14.0)	12.4 (11.1-14.0)	< .001

predictive value of nasal bones assessment for population screening of trisomy 21.[14]

The aim of this study was to compare the value of nasal bones assessment in improving first-trimester nuchal translucency screening for Down syndrome in selected and unselected pregnancies.

Material and methods

This was a prospective observational study including all singleton pregnancies having first-trimester nuchal translucency screening over a period of 24 months, from December 2001 to November 2003. Nuchal translucency thickness was measured in viable pregnancies with a crown-rump length (CRL) of between 45 and 84 mm, employing a standardized technique.[15] Nasal bones assessment was undertaken as part of a controlled introduction into clinical practice of a new technique in order to evaluate the ability of our sonographers to produce technically adequate images, and to validate the performance of this assessment in our local population. The individual risks of Down syndrome were calculated based on maternal age and nuchal translucency thickness.[1] Computerized hospital records were reviewed to determine delivery outcomes for each subject. Results were also cross-matched with the registry of the Regional Genetics Service, covering genetic and cytogenetic testing for the entire Health region.

For nasal bones assessment, a mid-sagittal view of the fetus was obtained, with the beam of the ultrasound transducer perpendicular to the nasal bones. To avoid misinterpretation of the skin of the nose as the nasal bones, the ultrasound transducer was gently tilted from side to side to ensure that the nasal bones were seen separate from the nasal skin. The sonographer first recorded whether the examination of the fetal profile was technically satisfactory. If the examination was satisfactory, then the visualization of the nasal bones was recorded as 'present.' If the nasal bones were not visualized, they were recorded as 'absent.' The total examination time for nasal bones assessment was limited to a maximum of 5 minutes, and only fetuses quiescent at the time of scan were enrolled. Nasal bones were not used to evaluate risk of trisomy 21. During the ultrasound examination, a full structural survey was undertaken. The study was approved by the Clinical Governance lead for the unit.

Within the study population, 2 groups of pregnancies were identified. An unselected group was constituted only by women receiving routine antenatal care at our Institution. All women lived within a predetermined geographic area characterized by postal codes. A selected group was constituted by patients referred from other hospitals to our Fetal Medicine Unit. The most common indications for referral were an increased risk (more than 1:300) for trisomy 21 based on maternal age and nuchal translucency screening, maternal age $\geq$35 years, previous pregnancy history or family history of chromosomal abnormalities or genetic disease, and a previous adverse pregnancy outcome. The same ultrasound systems were used for both groups. All cases in the selected group were scanned by a physician certified or training in maternal-fetal medicine. The unselected cases were scanned by sonographers with FMF certification for nuchal screening and a long-standing experience in first-trimester ultrasound. No formal auditing of nasal bone assessment was implemented.

The sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) for trisomy 21 were calculated for each marker. The likelihood ratio for trisomy 21 in case of positive and negative findings for each marker and their different combinations was also calculated. Logistic regression analysis was performed to assess the association between trisomy 21 and nuchal translucency and nasal bones findings. All calculations were performed using the SPSS software package (release 11.5, SPSS, Inc, Chicago, IL).

Results

A total of 7626 consecutive fetuses were evaluated during the study period. Demographic and baseline