J. Fetal Med. (March 2018) 5:13–16
https://doi.org/10.1007/s40556-018-0151-9

ORIGINAL ARTICLE

Nasal Bone Assessment and Credibility of Visualization Between 11 and 14 Weeks: Experience in a Tertiary Fetal Medicine Center

Subapriya Kandasamy[1] · **Sherina Paul Raj**[1]

Received: 23 October 2017 / Accepted: 3 January 2018 / Published online: 6 February 2018

Abstract The objective of our study was to assess the visualization of nasal bone in the first trimester and its credibility, by an experienced operator in a Tertiary Fetal Medicine Center. A total of 1245 women with singleton and multiple pregnancies, who were referred for routine first trimester ultrasound at 11–14 weeks of gestation were assessed for the presence or absence of nasal bone in the fetus. The study was conducted at a Fetal Medicine Center in South India, by a highly experienced Fetal Medicine Consultant, during the period from October 2015 to December 2016. The fetal nasal bone was imaged in 1200 of these fetuses (NB +). Twenty-three patients had isolated absence of nasal bone, with no other associated markers like tricuspid regurgitation (TR), ductus venosus reversal or associated anomalies and three patients had an associated finding of TR. In 19 patients, nasal bone was imaged with difficulty. However, biochemical screening turned out to be negative in these patients and during the second trimester scan, nasal bone was present in all cases. Apart from this, five cases for which we had reported that the nasal bone was visualized normally in the 11–14 weeks scan, nasal bone was found to be absent in the second trimester scan. These patients were given the option of direct sampling. Three were found to have normal karyotype. One patient chose to terminate the pregnancy and the other patient was lost for follow up. The study points the difficulties faced by even experienced sonographers in the application of the fetal nasal bone as an additional screening tool in the first trimester scans. In order to improve the efficacy of nasal bone assessment in the prediction of trisomy 21, we recommended that the nasal bone be re-assessed during the performance of anomaly scan. The detection rate remains the same, however, the errors due to the first trimester technical difficulties can be avoided with re-assessment.

Keywords Nasal bone · Absence of · Prenatal screening · Prenatal ultrasonography · 11–14 weeks scan · Visualization · Credibility · Nasal bone assessment

Introduction

The first trimester screening of Down syndrome is based on the combination of maternal age, nuchal translucency (NT) measurement, and maternal serum biochemical screening. Currently, imaging of the nasal bone (NB) has been added as an additional ultrasound marker in screening for chromosomal abnormalities. The sensitivity of nasal bone in detecting Down syndrome is 73% with a false positive rate of 0.5% in high-risk pregnant women by Cicero et al. [1] and when combined with nuchal translucency, the sensitivity increased to 85% with false positive rate of 1%. This has also shown that the likelihood ratio of absent nasal bone is 145, which makes it a strong marker for Down syndrome. Many studies [1–4] have suggested that nasal bone imaging improves Down syndrome screening. Although the imaging of nasal bone is standardized by the Fetal Medicine Foundation (FMF), it is technically demanding in the first trimester. The nasal bone was

Electronic supplementary material The online version of this article (https://doi.org/10.1007/s40556-018-0151-9) contains supplementary material, which is available to authorized users.

✉ Subapriya Kandasamy
ksubapriya@gmail.com

[1] Fetoscan Fetal Medicine Center, No. 129 AE/80 A, Fourth Avenue, Shanthi Colony Main Road, Anna Nagar, Chennai 600040, India

difficult to assess in 6% of the cases in a study by Otano et al. [5]. The visualization of nasal bone had intra and inter-observer variability and inclusion of nasal bone in routine screening is controversial according to Senat et al. [6]. In a recent study by Lakshmi Ravi, retrospective analysis of nasal bone images in first trimester showed only 76% correlation due to observer variability [7]. However, studies on false positive imaging of nasal bone in first trimester in spite of following standard guidelines are limited. The aim of our study was to assess the visualization of nasal bone in the first trimester and its credibility, by an experienced operator in a tertiary Fetal Medicine Center.

Materials and Methods

This is a retrospective study conducted at a Fetal Medicine Center in South India during the period October 2015 through December 2016. The ultrasound was performed by an experienced Fetal Medicine Consultant, certified by the Fetal Medicine Foundation (FMF) for nasal bone assessment. The ultrasonography was performed transabdominally and transvaginally when required, by Voluson E6 (GE Healthcare, Kretztechnik, Zipf, Austria).

A total of 1245 women with singleton and multiple pregnancies, who were referred for routine first trimester ultrasound at 11–14 weeks of gestation were included in the study. The patients were scanned in the first trimester, according to FMF guidelines. The information about the purpose of the scan and screening was provided to each patient. Biochemical screening was offered to all patients and risk was calculated based on maternal age, nuchal translucency (NT) and biochemistry. If the patient was found to have absent nasal bone, increased NT and any other associated marker with the former two, they were given the option of direct fetal sampling.

The FMF guidelines were strictly adhered to, in the assessment of fetal nasal bone. The magnification of the image was such that the head and upper thorax occupied the whole screen and a mid-sagittal view of the fetal profile was obtained. The ultrasound transducer was placed parallel to the direction of the nose and the probe was gently tilted from one side to the other of the fetal nose. When these criteria were satisfied, three distinct lines were seen at the level of the fetal nose. The top line represented the skin. The bottom one, which is thicker and more echogenic than the overlying skin represented the nasal bone and the third line in front of the bone and at a higher level than the skin represents the tip of the nose. The nasal bone was considered to be present if it was more echogenic than the overlying skin and absent if it was either not visible or its echogenicity was the same or less than that of the skin.

Results

Among 1245 women, the fetal nasal bone was imaged in 1200 (NB +). Twenty-three patients had isolated absence of nasal bone. In these 23 patients, NT was less than 95th percentile, but no other associated markers like tricuspid regurgitation (TR), ductus venosus (DV) reversal or associated anomalies were found. These 23 patients were counseled about the option of direct sampling.

Sixteen patients opted for biochemical screening in which absent nasal bone was included for risk calculation in screening and six patients were lost for follow up. Fourteen of these patients had low risk on biochemical screening. Of the two patients who were screen positive with isolated absent nasal bone, one underwent direct sampling and had normal karyotyping report. The other patient with isolated absent nasal bone and screen positive was lost to follow up. In the 14 cases with absent nasal bone and low risk biochemical screening, nasal bone was ossified in 13 cases in second trimester. In one of these cases, nasal bone was absent in the second trimester scan and was given the option of direct fetal sampling but she was lost to follow up. One of the patients with isolated nasal bone was a triplet gestation with missed abortion of one fetus. In this pregnancy, only NT based risk was given in which the fetus with absent nasal bone was under high-risk category. The patient was lost for further follow up.

The nasal bone was imaged with difficulty in 19 patients. All these patients underwent biochemical screening and were advised to have reassessment of nasal bone in second trimester. The screening test report was found to be screen-negative and nasal bone was present in second trimester scan in all these cases.

However, three patients among the 25 absent nasal bone cases were associated with tricuspid regurgitation. These three patients were counseled about the findings and the opinion of direct sampling was given. Among the three, none of them preferred karyotyping. One case opted for biochemical screening and other case chose to do non-invasive prenatal testing (NIPT). Both of them turned out to fall under low risk category. One among the three cases with associated TR was not willing for any type of screening procedure. However, in the follow up scan at 17 weeks and 6 days, TR was persistent but the nasal bone was present in this patient.

In five cases in which we had reported that the nasal bone was visualized normally in the 11–14 weeks scan, nasal bone was absent in the second trimester scan. These patients were given the option of direct sampling (amniocentesis), of which three were found to have normal karyotype. One patient chose to terminate the pregnancy. One patient was lost for follow up.

Discussion

The prevalence of absent nasal bone varies in cases of Down syndrome population varies from 0 to 80% [1]. Visualization of the nasal bone in the 11–14 weeks scan plays a major role in estimating the risk for trisomy 21 because of its high positive (nasal bone absent) and negative (nasal bone present) likelihood ratio. This calls for the accurate assessment of nasal bone.

In 2003, Larose et al. pointed out that the false positive rate of nasal bone identification by ultrasound was 40%, using postmortem radiograph as the gold standard [8]. The Fetal Medicine Foundation (FMF) provides software for first-trimester risk assessment. It also provides certification of nasal bone assessment. According to the Fetal Medicine Foundation, at 11–13 weeks, the nasal bone is considered to be absent in 60% of fetuses with trisomy 21, 50% of fetuses with trisomy 18, 40% of fetuses with trisomy 13 and 1–3% of normal fetuses. The assessment of the nasal bone at 11–13 weeks improved the performance of combined screening, increasing the detection rate of Down syndrome (trisomy 21) from 90% without inclusion of nasal bone to 93% with inclusion of nasal bone and decreasing the false positive rate from 3 to 2.5% (FMF).

Bernard et al. observed that among 1040 fetus examined, nasal bone was identified by ultrasound in 948 cases, not seen in eight and impossible to assess in 84 fetuses. They noted a significant intra- and inter-observer variability in the reproducibility of nasal bone by ultrasound, which could be attributed to the sonographer's skill and ability to identify the nasal bone [6]. High expertise is required to produce reproducible results of nasal bone examination. The accuracy in imaging of the nasal bone depends on various factors. Few of them include quality of the ultrasound machine, maternal obesity, experience of the sonographer, use of standardized technique in imaging of the nasal bone and fetal position [9]. Moreover, since the nasal bone is a small, bifid structure, it can be easily missed if the image is not exactly in the mid sagittal view, or the nasal bone is parallel to the ultrasound beam. Variance in nasal bone echogenicity and discrimination between echoes of nasal skin and bone lead to difficulties in nasal bone measurement even by an experienced sonographer [9].

Cicero et al. proposed a learning curve for sonographic examination of the fetal nasal bone at 11–14 weeks and suggested that the minimum number of scans required for an experienced sonographer to become competent in examining the fetal nasal bone is on average 80, with a range of 40–120 [10]. In the present study, although the ultrasound was performed by a highly experienced consultant and in a well-equipped tertiary setting, in 19 cases (1.5%) the nasal bone was imaged with difficulty and in five cases (0.4%), the nasal bone was falsely reported to be present (Figs. 1, 2, 3).

A valuable screening test in addition to demonstrating good sensitivity and specificity should be both feasible and reproducible in routine settings and the criteria that should be evaluated before its introduction into general practice. False-positive results in screening for trisomy 21 in the general population have a major impact on the positive predictive value, as the prevalence of the disease is less than 1% [6]. If nasal bone assessment is added to maternal age, NT and maternal serum biochemistry then this is likely to have an impact on risk calculation by increasing it by up to 146 times when nasal bones are not seen and decreasing this risk when they can be identified [6]. Thus inaccurate nasal bone assessments would lead to significant change in Down syndrome risk calculation.

In the present study, there was a false positive reporting of presence of nasal bone in 0.4% of the cases in the hands of an experienced operator. Malone et al. had highlighted the difficulty in consistent visualization of nasal bone. Lakshmi Ravi et al. also showed increased number of false positives in routine inclusion of NB in first trimester risk assessment with conventional mid sagittal view [7].

Limitation of the present study is that it involved a small number of cases. Also, the entire study is based, from the perspective of a single-operator. Apart from this, transvaginal scan was not routinely used in all cases and was used only for technically difficult cases. However, when nasal bone is going to be used universally, on one hand, the accessibility to transvaginal scan is difficult in rural areas and other hand, in certain cultural backgrounds, women deny its use unless strongly indicated.

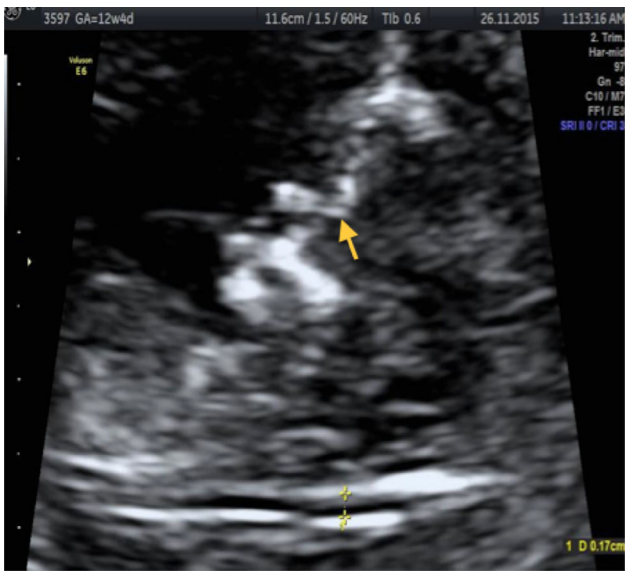

Fig. 1 Nasal bone (shown by arrow) present at 12 weeks

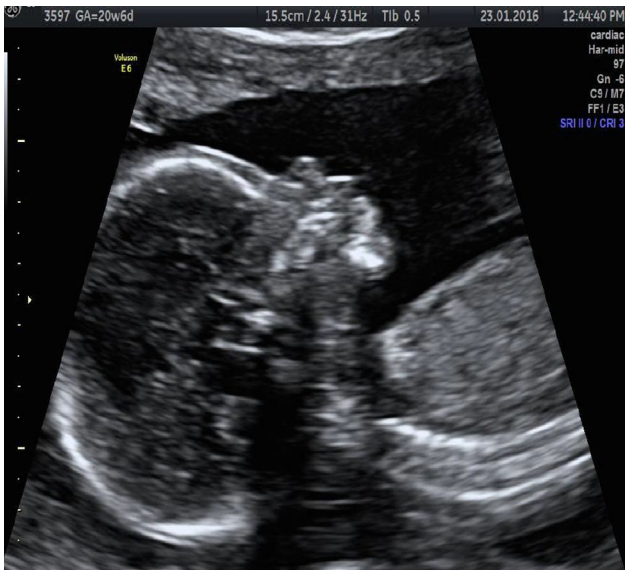

Fig. 2 Absence of nasal bone in the same patient during anomaly scan

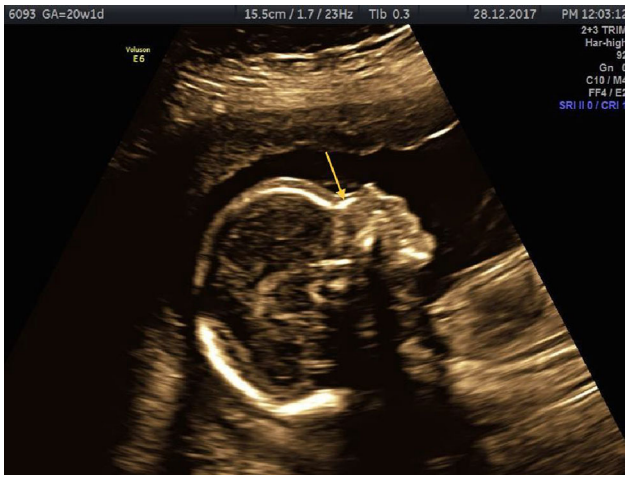

Fig. 3 Figure showing presence of nasal bone (shown by arrow) in another patient, during the anomaly scan

Kanellopoulos et al. showed that the length of nasal bone increases with crown-rump length (CRL). So, the detection of nasal bone becomes progressively easier as the gestational age advances [11]. To eliminate the technical difficulties of nasal bone imaging in the first trimester, Lakshmi Ravi et al. has suggested the inclusion of nasal bone in the second trimester. Thus, in order to improve the efficacy of nasal bone assessment in the prediction of trisomy 21, we recommended that the nasal bone be re-assessed during the performance of anomaly scan.

Conclusion

In view of the uncertainties and difficulties faced by even experienced sonographers, the application and implementation of the fetal nasal bone as an additional screening tool in the first trimester scans in routine setting is questionable. Similar studies by skilled sonographers in larger settings are encouraged prior to incorporating the nasal bone screening method into risk calculation algorithms. This study would certainly bring to light the degree of difficulty faced by physicians and sonographers in the field, even after proper training and expertise in the examination of nasal bone.

References

1. Cicero S, Longo D, Rembouskos G, Sacchini C, Nicolaides KH. Absent nasal bone at 11–14 weeks of gestation and chromosomal defects. Ultrasound Obstet Gynecol. 2003;22(1):31–5.
2. Ferriman E, Cuckle H. Case report: clinical utility of ultrasound nasal bone determination in the prenatal diagnosis of Down syndrome. Prenat Diagn. 2003;23:433–4.
3. Zoppi MA, Ibba RM, Axiana C, Floris M, Manca F, Monni G. Absence of fetal nasal bone and aneuploidies at first-trimester nuchal translucency screening in unselected pregnancies. Prenat Diagn. 2003;23(6):496–500.
4. 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.
5. Otano L, Aiello H, Igarzabal L, Matayoshi T, Gadow EC. Association between first trimester absence of fetal nasal bone on ultrasound and Down syndrome. Prenat Diagn. 2002;22(10):930–2.
6. Senat MV, Bernard JP, Boulvain M, Ville Y. Intra- and inter-operator variability in fetal nasal bone assessment at 11–14 weeks of gestation. Ultrasound Obstet Gynecol. 2003;22(2):138–41.
7. Lakshmy SR, Shobana U, Rose N. Sensitivity of nasal bone as aneuploidy marker—first trimester versus second trimester assessment. J Fetal Med. 2017;4(3):109–17. https://doi.org/10.1007/s40556-017-0128-0.
8. Larose C, Massoc P, Hillion Y, Bernard JP, Ville Y. Comparison of fetal nasal bone assessment by ultrasound at 11–14 weeks and by postmortem X-ray in trisomy 21: a prospective observational study. Ultrasound Obstet Gynecol. 2003;22(1):27–30.
9. Suwanrath C, Pruksanusak N, Kor-Anantakul O, Suntharasaj T, Hanprasertpong T, Pranpanus S. Reliability of fetal nasal bone length measurement at 11–14 weeks of gestation. BMC Pregnancy Childbirth. 2013;13(1):7. http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=3565861&tool=pmcentrez&rendertype=abstract.
10. Cicero S, Dezerega V, Andrade E, Scheier M, Nicolaides KH. Learning curve for sonographic examination of the fetal nasal bone at 11–14 weeks. Ultrasound Obstet Gynecol. 2003;22(2):135–7.
11. Kanellopoulos V, Katsetos C, Economides DL. Examination of fetal nasal bone and repeatability of measurement in early pregnancy. Ultrasound Obstet Gynecol. 2003;22(2):131–4.