VIA MEDICA
ORIGINAL PAPER / OBSTETRICS
Ginekologia Polska
2019, vol. 90, no. 10, 604–606

ISSN 0017–0011
DOI: 10.5603/GP.2019.0104

The absence of fetal nasal bones in ultrasound examination between 11 + 0 and 13 + 6 weeks of gestation versus the occurrence of trisomies 21, 18, and 13

Katarzyna M. Wojda[1], Hanna Moczulska[2], Piotr J. Sieroszewski[1]

[1]*Gynaecology and Fetal Medicine Department Medical University of Lodz, Poland*
[2]*Department of Clinical Genetics, Medical University of Lodz, Poland*

ABSTRACT

Objectives: One part of the ultrasound examination of fetuses in the first trimester of gestation is visualization of the nasal bones. Numerous studies have demonstrated a correlation between the absence of nasal bones and abnormal fetal karyotype. Aim: To assess the utility of ultrasound visualization of nasal bones during the first trimester of pregnancy as a marker of the most common chromosomal trisomies.

Material and methods: Ultrasound visualization of nasal bones was carried out in 941 fetuses from a high-risk group between 11 + 0 and 13 + 6 weeks of gestation. Amniocentesis was performed to determine karyotype in all 941 cases.

Results: Normal fetal karyotype was observed in 847 cases, trisomy 21 in 45 cases, trisomy 18 in 16 cases and trisomy 13 in 10 cases. Other abnormal karyotypes were detected in the remaining 23 cases. The absence of nasal bones demonstrated 27% sensitivity, 97% specificity and a positive predictive value of 35% as an indicator of trisomy 21 in the study group, and 12% sensitivity, 97% specificity and 12% positive predictive value for trisomies 18 and 13.

Conclusions: The absence of nasal bones in ultrasound examination in the first trimester of pregnancy is characterized by low sensitivity and high specificity as a marker of the most common trisomies. Visualization of fetal nasal bone is a poor marker of aneuploidy and should not be taken into account in risk calculation algorithms.

Key words: nasal bone; ultrasound trisomy marker; chromosomal trisomies

Ginekologia Polska 2019; 90, 10: 604–606

INTRODUCTION

Visualization of the nasal bones is one of the main stages of the fetal ultrasound examination between 11 + 0 and 13 + 6 weeks of pregnancy. Numerous studies have reported a correlation between the absence of nasal bone in the first trimester of pregnancy and abnormal fetal karyotype. This has been attributed to the nasal bone ossification process being delayed in fetuses with chromosomal aberrations such as trisomies 21, 18 or 13.

In 1866, Langdon Down observed that patients with trisomy 21, the most commonly occurring chromosomal aberration, were characterized by a typical facial appearance including a small, short nose [1]. In terms of frequency, Down's syndrome is followed by Edwards syndrome, i.e. trisomy 18, with an incidence rate of up to 1/6,000 live births [2]. Following this, trisomy 13 (Patau syndrome) is observed in 1/8,000 to 1/12,000 live births. Trisomies 18 and 13 are characterized by a much more severe clinical presentation than Down's syndrome, with less than 10% of children surviving the first year [3]. These trisomies are associated with the presentation of an abnormal profile together with multiple other serious defects [4]. It has been found that ultrasound scans performed between 11 + 0 and 13 + 6 weeks of gestation indicate an absence of nasal bones in more than 50% of fetuses with trisomy 18, as well as in about 30% of fetuses with trisomy 13 [5].

Aim

To assess the value of ultrasound visualization of nasal bones during the first trimester of pregnancy as a marker of the most common chromosomal trisomies.

Corresponding author:
Katarzyna M. Wojda
Gynaecology and Fetal Medicine Department Medical University of Lodz, 37 Wilenska St, 94–029 Lodz, Poland
e-mail: wojda.ka@tlen.pl

MATERIAL AND METHODS

Nasal bone visualization was performed in 941 fetuses between 11 + 0 and 13 + 6 weeks of gestation (ultrasound scan + biochemical markers: PAPP-A + free βhCG) by certified researchers at two independent referral centers. Voluson E8 and Philips iU22 ultrasound scanners and transabdominal probes were used for the examination. The procedure was performed according to the Fetal Medicine Foundation standards of assessing the presence of nasal bones.

The presence of nasal bones was recorded in ultrasound scan summaries. The risk of fetal chromosomal aberrations was calculated on the basis of maternal age, ultrasound parameters (crown-lump length CRL, nuchal translucency NT) and biochemical analyses (PAPP-A, free βhCG) using Astraia software.

Following the combined non-invasive first trimester screening, comprising ultrasound and biochemical testing, an invasive diagnostic procedure was performed in all 941 cases to assess fetal karyotype and identify any high risk of fetal aneuploidies.

RESULTS

In total, 941 fetal karyotype results were analyzed. A normal fetal karyotype was observed in 847 cases. Of the remainder, trisomy 21 was observed in 45 cases, trisomy 18 in 16 cases, trisomy 13 in 10 cases, and other karyotype anomalies in the remaining 23 cases.

The nasal bones were observed to be absent in 39 fetuses, including 22 with a normal karyotype; however, the nasal bones were visualized in 33 out of 45 T21 patients. In addition, they were observed in all fetuses with trisomy 18, and in seven of ten fetuses with trisomy 13 (Tab. 1).

Two study groups were defined for the purposes of statistical analysis: the group of fetuses with T21 syndrome (n = 45) and the combined group of fetuses with T18 and T13 syndromes (n = 26). The control group consisted of 847 fetuses with a normal karyotype. The frequencies of absence of nasal bones in the T21 group and the T18 and T13 group were compared with that of the control group.

In the group of T21 patients, the nasal bones were found to be absent in 12 cases (Tab. 2). The absence of nasal bones demonstrated 27% sensitivity and 97% specificity as a marker of T21, with a positive predictive value of 35%.

In the combined group of T18 and T13 patients, nasal bones were found to be absent in only three cases (Tab. 3). Lack of nasal bones was found to offer the 12% sensitivity and 97% specificity in the detection of trisomies 18 and 13, with a positive predictive value of 12%.

DISCUSSION

Current non-invasive risk assessment of fetal chromosomal aberrations is based on maternal age, ultrasound markers (NT, FHR) and biochemistry (PAPP-A, free βhCG). This algorithm allows the detection of 85–90% of fetuses with trisomies 21, 18, or 13, with some publications recording a detection rate of 90–95% [6–8]. More sophisticated algorithms incorporating additional markers such as the presence of nasal bones, analysis of ductus venous or tricuspid valve flow have been proposed to reduce the false positive rate (FPR); however, these are the subject of ongoing research.

Many reports have proposed the absence of nasal bones as a potential marker of fetal chromosomal defects. Our present results obtained by ultrasound examination of fetuses with Down's syndrome support those of previous studies indicating that the absence of nasal bones may be a promising marker of fetal trisomy 21. This has been confirmed in many reports, including data from multicenter studies [9, 10]

A paper published in The Lancet in 2001 reported the absence of nasal bones in 43 out of 59 (73%) ultrasound scans in the first trimester of pregnancy; however, while the study also reports that nasal bones were found to be absent in only 0.5% of examined fetuses with normal karyotype [9]. This figure was found to be 2.6% in the present study. Węgrzyn et al. [10] (2016) reported nasal bones to be absent in 64.8% of fetuses with trisomy 21, but only 4.3% of fetuses with normal karyotype. Similarly, a higher rate of absence was also confirmed among fetuses with trisomy 21 (70%) in studies conducted in

Table 1. Presence of nasal bones vs. fetal karyotype: results of the analysis

	NB +	NB –
Normal karyotype	825	22
T21	33	12
T18	16	0
T13	7	3
Other karyotypic anomaly	21	2
Total	902	39

Table 2. Presence of nasal bones in T21 fetuses (n = 45) and controls

	Nasal bones present, NB+	Nasal bones absent, NB -
Normal karyotype	825 (97.4%)	22 (2.6%)
T21	33 (73%)	12 (27%)

Table 3. Absence of nasal bones in T18 and T13 fetuses (n = 26) compared to controls

	Nasal bones present, NB +	Nasal bones absent, NB –
Normal karyotype	825 (97.4%)	22 (2.6%)
T18, T13	23 (88.5 %)	3 (11.5 %)

much smaller study groups [11], and elsewhere, absence was noted in 70% of Down's syndrome fetuses scanned in the first trimester of pregnancy [12]. Interestingly, while the authors of the mentioned article reported the absence of nasal bones in 80% of fetuses with trisomy 18, this was observed in only 11.5% of fetuses from the combined group of trisomy 18 or 13 cases identified in the present study: the vast majority (88.5%) of fetuses tested between 11 + 0 and 13 + 6 weeks of pregnancy were found to possess nasal bones. In addition, another ultrasound study found nasal bones to be absent in 52.8% of fetuses with trisomy 18, 45% of fetuses with trisomy 13, and only 59.8 % of fetuses with trisomy 21 [13]. Sepulveda et al. [14] reported nasal bone hypoplasia in 53% of a group of 53 fetuses with trisomy 18, while Wagner et al. [15] reported a lack of nasal bones in 60% of fetuses with trisomy 18 and 69% of fetuses with trisomy 13.

Our data on the absence of nasal bones in ultrasound examination acquired in T21 syndrome fetuses between 11 + 0 and 13 + 6 weeks of pregnancy are similar to those obtained by other authors. As an ultrasound marker of trisomy 21, ultrasound identification of a lack of nasal bones is characterized by low sensitivity (27%) and high specificity (97%). Likewise, Sieroszewski et al. [16] found such an approach to be characterized by low sensitivity (40%) but very high specificity (100%) in assessing the risk of chromosomal aneuploidies.

Our present findings indicate a much lower percentage of fetuses presenting an absence of nasal bones among the combined group of fetuses with less common aberrations, i.e. those with trisomies 13 or 18; in addition, the presence of nasal bones was detected in all fetuses with trisomy 18. The sensitivity and specificity of the absence of nasal bones as a predictive factor of these trisomies were 12% and 97%, respectively.

CONCLUSIONS

1. The absence of nasal bones between 11 + 0 and 13 + 6 weeks of gestation, identified by ultrasound examination, can be used as a marker of the most common trisomies with low sensitivity and high specificity.
2. Visualization of the fetal nasal bone is a poor marker of aneuploidy and should not be taken into account in risk calculation algorithms.

REFERENCES

1. Langdon Do. Observations on an ethnic classification of idiots. Clinical Lectures and Reports, London Hospital. 1866; 3: 259–262.
2. Cereda A, Carey JC. The trisomy 18 syndrome. Orphanet J Rare Dis. 2012; 7: 81, doi: 10.1186/1750-1172-7-81, indexed in Pubmed: 23088440.
3. Rasmussen SA, Wong LYC, Yang Q, et al. Population-based analyses of mortality in trisomy 13 and trisomy 18. Pediatrics. 2003; 111(4 Pt 1): 777–784, doi: 10.1542/peds.111.4.777, indexed in Pubmed: 12671111.
4. Bruns DA, Campbell E. Nine children over the age of one year with full trisomy 13: a case series describing medical conditions. Am J Med Genet A. 2014; 164A(12): 2987–2995, doi: 10.1002/ajmg.a.36689, indexed in Pubmed: 25323598.
5. Nicolaides KH. Nuchal translucency and other first-trimester sonographic markers of chromosomal abnormalities. Am J Obstet Gynecol. 2004; 191(1): 45–67, doi: 10.1016/j.ajog.2004.03.090, indexed in Pubmed: 15295343.
6. Kagan KO, Etchegaray A, Zhou Y, et al. Prospective validation of first-trimester combined screening for trisomy 21. Ultrasound Obstet Gynecol. 2009; 34(1): 14–18, doi: 10.1002/uog.6412, indexed in Pubmed: 19526452.
7. Kagan KO, Wright D, Maiz N, et al. Screening for trisomy 18 by maternal age, fetal nuchal translucency, free beta-human chorionic gonadotropin and pregnancy-associated plasma protein-A. Ultrasound Obstet Gynecol. 2008; 32(4): 488–492, doi: 10.1002/uog.6123, indexed in Pubmed: 18726925.
8. Wright D, Syngelaki A, Bradbury I, et al. First-trimester screening for trisomies 21, 18 and 13 by ultrasound and biochemical testing. Fetal Diagn Ther. 2014; 35(2): 118–126, doi: 10.1159/000357430, indexed in Pubmed: 24356462.
9. Cicero S, Curcio P, Papageorghiou A, et al. Absence of nasal bone in fetuses with trisomy 21 at 11-14 weeks of gestation: an observational study. Lancet. 2001; 358(9294): 1665–1667, doi: 10.1016/S0140-6736(01)06709-5, indexed in Pubmed: 11728540.
10. Węgrzyn P, Czuba B, Serafin D, et al. Nasal bone in screening for T21 at 11-13 + 6 weeks of gestation - a multicenter study. Ginekol Pol. 2016; 87(11): 751–754, doi: 10.5603/GP.2016.0082, indexed in Pubmed: 27958633.
11. Otaño L, Aiello H, Igarzábal L, et al. Association between first trimester absence of fetal nasal bone on ultrasound and Down syndrome. Prenat Diagn. 2002; 22(10): 930–932, doi: 10.1002/pd.431, indexed in Pubmed: 12378580.
12. Zoppi MA, Ibba RM, Axiana C, et al. Absence of fetal nasal bone and aneuploidies at first-trimester nuchal translucency screening in unselected pregnancies. Prenat Diagn. 2003; 23(6): 496–500, doi: 10.1002/pd.628, indexed in Pubmed: 12813765.
13. Kagan KO, Cicero S, Staboulidou I, et al. Fetal nasal bone in screening for trisomies 21, 18 and 13 and Turner syndrome at 11-13 weeks of gestation. Ultrasound Obstet Gynecol. 2009; 33(3): 259–264, doi: 10.1002/uog.6318, indexed in Pubmed: 19248005.
14. Sepulveda W, Wong AE, Dezerega V. First-trimester sonographic findings in trisomy 18: a review of 53 cases. Prenat Diagn. 2010; 30(3): 256–259, doi: 10.1002/pd.2462, indexed in Pubmed: 20112232.
15. Wagner P, Sonek J, Hoopmann M, et al. First-trimester screening for trisomies 18 and 13, triploidy and Turner syndrome by detailed early anomaly scan. Ultrasound Obstet Gynecol. 2016; 48(4): 446–451, doi: 10.1002/uog.15829, indexed in Pubmed: 26611869.
16. Sieroszewski P, Baś-Budecka E, Perenc M. [Nasal bone (NB) length measurement in the first trimester of pregnancy in Polish population and its validity as fetal aneuploidy indicator]. Ginekol Pol. 2007; 78(8): 616–620, indexed in Pubmed: 18050610.