VIA MEDICA

ORIGINAL PAPER / OBSTETRICS

Ginekologia Polska
2020, vol. 91, no. 5, 256–261

ISSN 0017–0011

DOI: 10.5603/GP.2020.0047

Nasal bone in screening for Trisomy 18 and 13 at 11–13 + 6 weeks of gestation — own experiences

Bartosz Czuba[1], Marek Maczka[2], Wojciech Cnota[1], Agata Wloch[1], Agnieszka Jagielska[1], Anna Niesluchowska-Hoxha[1], Dariusz Borowski[3]

[1]Department of Obstetrics and Gynecology in Ruda Slaska, Medical University of Silesia, Ruda Slaska, Poland

[2]Center for Prenatal Diagnostic, Opole, Poland

[3]Faculty of Health Sciences, Department of Obstetrics, Nicolaus Copernicus University in Torun, Collegium Medicum, Bydgoszcz, Poland

ABSTRACT

Objectives: The objective of the paper is the suitability assessment of screening for Trisomy 18 and 13 on the basis of NT measurement, FHR, double test and assessment of Nasal Bone.

Material and methods: The study was performed in 6,661 singleton pregnancies. In each fetus NT, FHR, DV-PIV were examined. Double test from maternal blood was examined. These ultrasound and biochemical factors were in combined screening investigated. Additional ultrasound marker — Nasal Bone was and its impact on Trisomies 18 and 13 screening was examined.

Results: Two groups of patients were compared — with chromosomal normal and chromosomal abnormalities — Trisomy 18 and 13. Detection Rate of Trisomies 18 and 13 at the risk cutoff 1/300 using combined screening was 84.1% and FPR was 7.1%. Detection Rates of examined chromosomal abnormalities using screening with additional marker — NB was 93.2% and False Positive Rate — 5.6%.

Conclusions: It should be noted that the qualitative analysis of the assessment of NB in the first trimester significantly influences the improvement of screening values focusing on Trisomy 18 and 13 detection. In summary, our research indicates a more effective type of Trisomy 13 and 18 screening using NT, double test, maternal age, CRL and FHR as well as nasal bone presence and absence.

Key words: combined test Trisomy 18 Trisomy 13; first trimester nuchal translucency thickness; Nasal Bone; Serum free β-hCG; Pregnancy-associated plasma protein A

Ginekologia Polska 2020; 91, 5: 256–261

INTRODUCTION

The main objective of screening tests in the first trimester of gestation is to assess the risk of chromosomal (most often Trisomy 21, 13 and 18) based on ultrasound examination (nuchal translucency [NT] assessment, fetal heart rate [FHR]). What is more, the assessment of the double test (the level of the free β- subunit of human chorionic gonadotropin and pregnancy plasma protein type A-PAPP-A are assessed) as well as maternal age [1, 2] were also taken into consideration.

By means of this methodology, the detection rate (DR) for Trisomy 21 is 87% at FPR (False-positive Results) 5.3%, whereas 90% at FPR 3.1% [1, 3]. The detectability of Trisomy 18 and 13 is 97% and 94%, respectively, at FPR 3.1% [1, 3]. Additional markers are used in screening for Trisomy 21: assessment of the presence of nasal bone, which increases detection of Trisomy 21 by about 5% in the case of FPR from 4.8 to 3.4% [4].

The objective of this retrospective study was

The work is a retrospective study assessing the use of an additional ultrasound marker in the prenatal examination of the first trimester (11^{+0}–13^{+6} weeks of gestation), which is the nasal bone, in the analysis of chromosomal aberration screening: Trisomy 18 and 13.

MATERIAL AND METHODS

We had 6,844 pregnant women included in the study with single pregnancies who underwent prenatal screening

Corresponding author:
Bartosz Czuba
Medical University of Silesia, 2 Lipa St, 41–712 Ruda Śląska, Poland
e-mail: bczuba@o2.pl

of 1st trimester assessing the risk of occurrence of Trisomy 18 and 13 in the years 2014–2019. It should be stressed that the fetuses with other syndromes (Trisomy 21 — 84 , Turner Syndrome — 14, Tetraploidy — 5, Unbalanced translocations — 6 cases respectively) and structural defects with normal karyotype, such as: heart defects — Hypoplastic Left Heart Syndrome — 13 , Atrioventricular Septal Defects — 7, Tetrallogy of Fallot — 4 and Transposition of the Great Arteries — 2 cases were excluded from the research. Other structural fetal defects excluding fetuses from the study were: Fetal Hydrops — 15, Spina bifida — 11, Hydrocephalus — 7, Palate or upper lips cleft — 7, Omphalocele — 4 and Gastroschisis — 4 cases. The study was performed in pregnancies scanned in the Department of Obstetrics and Gynecology in Ruda Śląska, Outpatient 'Sonomedico' Żory and in Outpatient Clinic 'GENOM' in Ruda Śląska. The risk was calculated using the Fetalmedicine Foundation (FMF) certified program The First Trimester Screening Program or Astraia (Astraia Software G.m.b.H., Munich, Germany). These pregnant women were retrospectively divided into two groups: patients with a low risk of chromosomal defects, who gave birth to healthy children were included in the control group (6617 pregnant), whereas, the study group included patients (44 pregnant women) whose fetuses were diagnosed with Trisomy 18 and 13.

All patients who were at increased risk of developing Trisomy 18 or 13 made decisions to undergo invasive diagnostics. Edwards Syndrome (Trisomy 18) and Patau Syndrome (Trisomy 13) were found after amniocentesis and cytogenetic tests. Amniotic fluid obtained during amniocentesis after genetic consultation and obtaining written consent of the patient for amniocentesis were used for these tests. Invasive diagnostics were performed in pregnant women with increased risk of Trisomy 18 and 13 in age-related risk.

Ultrasound examination during the first trimester was performed between 11^{+0} and 13^{+6} weeks of gestation according to the recommendations of FMF and the Ultrasonography Section of the Polish Gynaecological Society [3]. During the ultrasound examination, the following parameters were evaluated: crown-rump length (CRL), fetal heart rate (FHR), nuchal translucency (NT) and, additionally, nasal bone (NB), (nasal bone — its presence or absence). A Double Marker Test was performed, and the mother's age at the time of examination was noted. The first trimester ultrasound was performed by specialists in obstetrics and gynaecology certified by the Fetal Medicine Foundation and the Ultrasound Section of the Polish Society of Gynaecologists and Obstetricians. The ultrasound examination was performed with Volusion 730 Expert, Volusion E6, E8 and E10 (GE Healthcare). Each patient was serum examinated level to a double test on the day of ultrasound examination: assessment of the β-hCG free subunit level (human β- chorionic gonadotropin free subunit) and PAPP-A level (plasma protein A during pregnancy) in venous blood. Levels of the tested substances were individually calculated for each patient on MoM (multiples of the median). Biochemical tests were carried out using the Kryptor method of the Brahms company (Kryptor, Brahms Diagnostica GmbH, Berlin, Germany) and Delfia Express-Perkin Elmer USA.

The results were analysed using the PQStat statistical package ver. 1.4.2.324. The results of the analyses were presented in the tables of descriptive statistics and two-split tables and on the charts. The results of the β-hCG MoM, PAPP-A MoM scales depending on the group (testing and control) were compared using the Mann-Whitney U test. The presence and absence of the nasal bone in healthy fetuses and sick fetuses were analysed by determining detection rates and the number of false-positive results along with confidence intervals and using ROC analyzes. The risk of Trisomy 18 and 13 divided into > 1/300 > 1/200.1 > 100 > 1/50 and with coincident consideration of the presence or absence of the nasal bone of healthy fetuses and afflicted fetuses was analysed by estimating detection rates and the number of false positive results with confidence intervals. The risk of Trisomy of 18 and 13 was also analysed using ROC curve. The test probability on the level of $p < 0.05$ was considered statistically important and noticeable.

RESULTS

The control group included 6,617 pregnant women aged between 14 to 46 years of age (mean age of pregnant women was 31 years), ultrasound examination was performed between 11^{+0} and 14th weeks of gestation (on mean 12^{+3} weeks of gestation). The CRL size of the fetuses ranged from 45 to 84 mm (mean CRL of fetuses was 63.7mm). The mean nuchal translucency in the control group was 1.8 mm (min. 0.8 mm, max. 13.1 mm). In 200 (3.02%) of fetuses from the control group, the nasal bone was not present (Tab. 1, 4).

Fourty-four pregnant women aged between of 20–41 were included in the study group (the mean age of pregnant women was 29). Ultrasound examination was performed between 11^{+0} and 13^{+6} weeks of gestation (on mean 12^{+2} weeks of gestation). CRL size of fetuses ranged from 47 mm to 81.1 mm (mean size of fetuses was 58.8 mm) The mean nuchal translucency in the study group was 5.1 mm (min 1.7 mm, max 8.3 mm). In the examined group nasal bone was found in 14 fetuses — in 8 fetuses with Edwards syndrome and in 6 fetuses with Patau syndrome. In 30 (68.18%) fetuses with Trisomy 18 and 13 the nasal bone was not found during ultrasound examination (Tab. 2, 4).

The differences in NT thickness, MoM β-hCG and MoM PAPP-A as well as the percentage of presence or absence of nasal bone in the control and study group was statistically significant (Tab. 3).

Table 1. Control group

	mean	SD	min.	max.	median	25th percentile (lower quartile)	75th percentile (upper quartile)
age [years]	31	5.54	14	46	31	27	36
CRL [mm]	63.7	8.47	45	84	63.4	57.8	69.5
NT [mm]	1.8	0.56	0.8	13.1	1.8	1.5	2
FHR [/min]	160	6.25	131	206	160	156	164
β-hCG MoM	1.238	0.814	0.08	9.181	1.023	0.702	1.538
PAPP-A MoM	1.076	0.576	0.052	6	0.958	0.671	1.354

CRL — crown-rump length; FHR — fetal heart rate; MoM — multiples of the median; NT — nuchal translucency; SD — standard deviation

Table 2. Study group

	mean	SD	min.	max.	median	25th percentile (lower quartile)	75th percentile (upper quartile)
age [years]	29	6.08	20	41	28	25	33
CRL [mm]	58.8	8.9	47	81.1	56.5	51.3	63.6
NT [mm]	5.1	1.66	1.7	8.3	5.7	3.9	6.4
FHR (/min)	159	11.7	135	179	158	150	170
β-hCG MoM	1.238	0.814	0.08	9.181	1.023	0.702	1.538
PAPP-A MoM	0.533	0.663	0.1	2.995	0.295	0.242	0.48

CRL — crown-rump length; FHR — fetal heart rate; MoM — multiples of the median; NT — nuchal translucency; SD — standard deviation

Table 3. Both groups selected parameters comparison

	Healthy fetuses	Trisomy 18 and 13 fetuses	p value
NT [median]	1.8 mm	5.7 mm	p < 0.001
β-hCG MoM [median]	1.023	0.46	p < 0.001
PAPP-A MoM [median]	0.958	0.295	p < 0.001
Percentage of nasal bone presence	93.98%	31.82%	p < 0.001

NT — nuchal translucency; MoM — multiples of the median

Table 4. Assessment of DR and FPR depending on the cut-off point for Trisomy 18 and 13

	DR		FPR	
	NT + PAPP-A	NT + NB + PAPP-A	NT + PAPP-A	NT + NB + PAPP-A
1:300	84.1%	93.2%	7.1%	5.6%
1:200	81.8%	90.9%	4.5%	3.8%
1:100	68.2%	81.8%	2.2%	2.2%
1:50	56.8%	75.0%	1.1%	1.1%

DR — detection rate; FPR — fetal heart rate; NB — nasal bone; NT — nuchal translucency

Table 5. The assessment of nasal bone presence

	All patients	Present nasal bone		Absent nasal bone	
The number of examined patients	6661	6431	95.54%	230	3.43%
Healthy fetuses	6617	6417	96.98%	200	3.02%
Trisomy 18 and 13 fetuses	44	14	31.82%	30	68.18%

As a result of further analysis, patients were divided into 4 groups depending on the level of risk of Trisomy 18 and 13: the first group with a risk above 1:300 and the second with a risk above 1:200, the third with a risk above 1:100 and the fourth group with a risk above 1:50 occurrence of Trisomy 18 and 13. DR and FPR as well as positive and negative ratio (LH + and LH-) were assessed in each group. Each group was divided into two subgroups, in one of them the risk of Trisomy 18 and 13 was assessed basing on the patient age, NT, FHR, and double PAPP-A test. In the second group, the same fetuses had an estimated risk based on the patient's age, NT, FHR, double test and nasal bone assessment. The highest DR was in the risk group > 1:300 and was 84% for fetuses in which the nasal bone was left beyond the scope of the study and 93% for fetuses in which the presence or absence of the nasal bone was assessed. In this group, we obtained a decrease in FPR from 7.1% (group without nasal bone assessment) to 5.6% (in the group with nasal bone assessment). The lowest DR was found in the group at risk > 1:50 i.e. 56% (screening without nasal bone assessment) and 75% (screening with nasal bone assessment) with a similar FPR of 1.1% (Tab. 5).

Table 6. Nuchal Translucency above 95th percentile in study group

	Control group	Edward's Syndrome	Patau Syndrome
NT percentage above 95th percentile	4.9%	81%	91%

NT — nuchal translucency

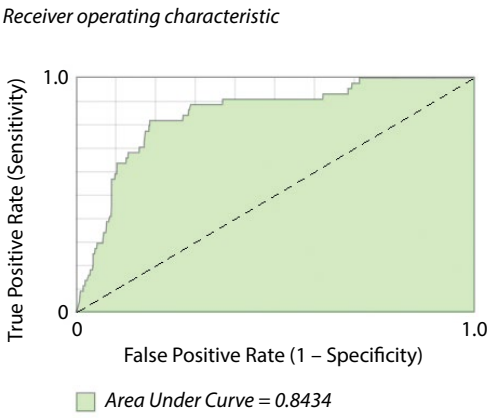

Figure 1. ROC curve for Trisomy 18 and 13 prediction using risk 18 and 13 in the group in which the patient's age, NT FHR and PAPP-A test were assessed

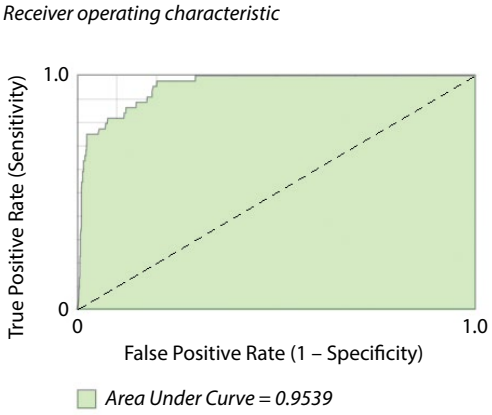

Figure 2. ROC curve for Trisomy prediction 18 and 13 using risk 18 and 13 in the group in which the patient's age, NT, FHR, NB and PAPP-A test were assessed

In every the assessed groups according to risk (> 1:300, > 1:200, > 1:100, > 1:50) an increase in the study's correctness and a decrease in FPR after including the nasal bone screening was obtained: for groups at risk > 1:300 DR increased from 84% to 93% with a decrease in FPR from 7.1% to 5.6%; and for the group at risk > 1:50 DR increased from 56% to 75% at the FPR level of 1.1% for both groups (Tab. 4).

The risk of Trisomy 18 and 13 is in relation to maternal age, CRL, nuchal translucency scan and fetal heart rates, as well as a double test. In our studies, we additionally evaluated the presence or absence of the nasal bone. Thanks to the evaluation of the nasal bone, we have obtained both an increase in the sensitivity of the examination as well as a decrease in FPR (Chart 1, 2).

Nuchal translucency was above 95th percentile in 4.9% of cases in the control group. In fetuses with Trisomy 18 in 81% and in fetuses with Trisomy 13 in 91% of cases. (Tab. 6).

In the group in which the nasal bone was not assessed, but only the nuchal translucency and the double test (control group) were evaluated, the area under the curve in the ROC analysis was 0.8434. On the contrary, the area under the curve in the group with nasal bone assessment (study group) in the ROC analysis was 0.9539. The absence of a nasal bone is a very good marker of Trisomy 18 and 13 because the area under the curve in ROC analysis when the screening nasal bone assessment is included increased from 0.8434 to 0.9593 (Fig. 1, 2).

DISCUSSION

The most frequent human chromosomes are Down syndrome (Trisomy 21) — 1 case for 800 live births, Edwards Syndrome (Trisomy 18 — 1 case for 3,500 to 8,000 live births) and Patau Syndrome (Trisomy 13) — 1 case out of 6,500 live births [5, 6]. Most fetuses with genetic abnormalities die intrauterine at various stages of development, and the incidence of genetic is estimated to be significantly higher [6]. The risk of Edwards and Patau Syndrome depends on the age of the mother and increases with it [7]. However, about 80% of fetuses with genetic abnormalities occur in women under 35 years of age [8]. According to Kroes [1], 69% of mothers whose fetuses had a Trisomy were under 35 years old.

Screening tests used to assess the risk of Trisomy of 21, 18 and 13 are performed between 11^{+0} and 13^{+6} weeks of gestation. The detection of Trisomy 21, 18 and 13 depends on the test method, i.e. the number of ultrasound markers evaluated, and biochemical tests performed. The basic ultrasound marker for chromosomal aberration assessment is nuchal translucency and fetal heart rate (FHR) [7]. Nuchal translucency above the 95th percentile occurs in approximately 72% of Down Syndrome cases [8], while in Edwards and Patau Syndrome only in 66% and 44% of cases assessed in prenatal tests during the first trimester of pregnancy respectively [9]. In our study, nuchal translucency above the 95th percentile occurred in 81% of Edwards' Syndrome and 91% of Patau Syndrome.

Detection (DR) of Trisomy 18 and 13 in screening tests in the first trimester of pregnancy, i.e. based on basal markers (maternal age, NT, fetal heart rate and assessing the double test) is approximately 87% at FPR 5.3% [4]. According to Kagan et al. [13], when examining mother's age, nuchal

translucency and performing a biochemical test (double test), the detection of Trisomy 18 and 13 is 97% and 94% respectively at FPR 3.1%. In our studies, assessing maternal age, nuchal translucency, fetal heart function and performing a double test at 4.5% FPR a detection rate (DR) of 81% for Trisomy 18 and 13 was obtained (Tab. 4).

The nasal bone is an additional ultrasound indicator assessed in screening tests in the first trimester of pregnancy to assess the risk of Trisomy 21, 18 and 13 [11–13]. The nasal bone does not occur in approximately 0.1–2.8% of healthy fetuses [14]. Absence of the nasal bone in healthy fetuses depends on the mother's ethnicity [12]: most often it does not occur in African-Americans (10.4%), less often in Asians (6.8%), while the most rarely absence of the nasal bone is found in Caucasians (2.8%) [15]. In our material, no nasal bone in 3.02% of healthy foetuses was found. The nasal bone is more often absent in the Trisomy 21 than in Trisomy 18 and 13 [12, 14]. In Edwards' Syndrome, the nasal bone is absent in about 52–80% of cases [15, 16], while in Patau's Syndrome in about 31–67% of cases [8, 12, 15]. Our results show similar values — in 68% of fetuses with Trisomy 18 and 13 we did not find the presence of nasal bone.

In our study, after including the nasal bone assessment into the screening, the sensitivity of the examination in each case was increased by about 10–20% (DR for risk > 1: 300 from 84.1% to 93.2%, for risk > 1: 200 from 81.8% to 90.9%, for risk > 1: 100 from 68.2% to 81.8%, and for risk > 1:50 from 56.8% to 75%) . At the same time the false positive results were reduced FPR from 7.1% at cut-off point for risk > 1: 300 to 1.1% at cut-off point for risk > 1:50 (Tab. 4).

After including the presence or absence of the nasal bone assessment into the screening Kagan et al. [13] did not observe in their studies changes in the detection of Trisomy 18 and 13 — at a cut-off point for 1:100 the detection of Trisomy 18 and 13 remained on this level (DR for Trisomy 18:92%; DR for Trisomy 13:83%) with an FPR of 2.5%. In our study, for a cut-off point of > 1:100 taking into account the assessment of the nasal bone compared to the test without assessment of the nasal bone, the sensitivity increased from 68% to 81%, with the same level of FPR — 2.2% .

We stated that the absence of a nasal bone was a very accurate additional marker of Trisomy 18 and 13. The area under the curve in the ROC analysis is statistically important and noticeable ($p < 0.0001$). After including the nasal bone screening an increase in DR was obtained with a decrease in FPR. Therefore, we believe that the assessment of the risk of Trisomy 18 and 13 should be carried out not only in scope of mother's age, fetal heart rate and nuchal translucency thickness but also using an additional ultrasound marker which is the presence or absence of the nasal bone. For this reason, we agree with other authors [17] that nasal bone assessment is a good marker of Trisomy 18 and 13, but we disagree that it should not be considered in the trisomy risk assessment algorithm.

CONCLUSIONS

Concluding, it should be noted that the qualitative analysis of the assessment of the nasal bone in the first trimester significantly influences the improvement of screening values focusing on Trisomy 18 and 13 detection. In summary, our research indicates a more effective type of Trisomy 13 and 18 screening using NT, double test, maternal age, CRL and FHR as well as nasal bone presence and absence.

REFERENCES

1. Brown R. Trisomy 13: 13+ Syndrome (Patau Syndrome). Encyclopedia of Special Education. 2014, doi: 10.1002/9781118660584.ese2442.
2. Ghaffari SR, Tahmasebpour AR, Jamal A, et al. First-trimester screening for chromosomal abnormalities by integrated application of nuchal translucency, nasal bone, tricuspid regurgitation and ductus venosus flow combined with maternal serum free β-hCG and PAPP-A: a 5-year prospective study. Ultrasound Obstet Gynecol. 2012; 39(5): 528–534, doi: 10.1002/uog.10051, indexed in Pubmed: 21793085.
3. zespół z. Polish Gynecological Society – Ultrasound Section Guidelines on ultrasound screening in gynecology – 2015. Polish Gynaecology. 2015; 86(8): 635–639, doi: 10.17772/gp/58975.
4. Nicolaides K, Węgrzyn P. Nicolaides K, Węgrzyn P, Badanie ultrasonograficzne między 11+0-13+6 tygodniem ciąży, Fetal Medicine Foundation, London. ; 2004.
5. Adiego B, Martinez-Ten P, Illescas T, et al. First-trimester assessment of nasal bone using retronasal triangle view: a prospective study. Ultrasound Obstet Gynecol. 2014; 43(3): 272–276, doi: 10.1002/uog.12525, indexed in Pubmed: 23733531.
6. Kozlowski P, Knippel AJ, Froehlich S, et al. Additional performance of nasal bone in first trimester screening. Ultraschall Med. 2006; 27(4): 336–339, doi: 10.1055/s-2005-858880, indexed in Pubmed: 16596511.
7. Cicero S, Longo D, Rembouskos G, et al. Absent nasal bone at 11-14 weeks of gestation and chromosomal defects. Ultrasound Obstet Gynecol. 2003; 22(1): 31–35, doi: 10.1002/uog.170, indexed in Pubmed: 12858299.
8. Karadzov-Orlic N, Egic A, Filimonovic D, et al. Screening for aneuploidies by maternal age, fetal nuchal translucency and maternal serum biochemistry at 11-13+6 gestational weeks. Srpski arhiv za celokupno lekarstvo. 2012; 140(9-10): 606–611, doi: 10.2298/sarh1210606k.
9. Springett AL, Morris JK. Antenatal detection of Edwards (Trisomy 18) and Patau (Trisomy 13) syndrome: England and Wales 2005-2012. J Med Screen. 2014; 21(3): 113–119, doi: 10.1177/0969141314543128, indexed in Pubmed: 24993362.
10. Maiz N, Valencia C, Kagan KO, 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.
11. Kagan KO, Wright D, Valencia C, et al. Screening for trisomies 21, 18 and 13 by maternal age, fetal nuchal translucency, fetal heart rate, free beta-hCG and pregnancy-associated plasma protein-A. Hum Reprod. 2008; 23(9): 1968–1975, doi: 10.1093/humrep/den224, indexed in Pubmed: 18544579.
12. Borenstein M, Persico N, Kagan KO, et al. Frontomaxillary facial angle in screening for trisomy 21 at 11 + 0 to 13 + 6 weeks. Ultrasound in Obstetrics and Gynecology. 2008; 32(1): 5–11, doi: 10.1002/uog.5334.
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. 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.
15. Cicero S, Spencer K, Avgidou K, et al. Maternal serum biochemistry at 11-13(+6) weeks in relation to the presence or absence of the fetal

nasal bone on ultrasonography in chromosomally abnormal fetuses: an updated analysis of integrated ultrasound and biochemical screening. Prenat Diagn. 2005; 25(11): 977–983, doi: 10.1002/pd.1211, indexed in Pubmed: 16245371.
16. Czuba B, Cnota W, Wloch A, et al. Frontomaxillary facial angle measurement in screening for trisomy 18 at 11 + 0 to 13 + 6 weeks of pregnancy: a double-centre study. Biomed Res Int. 2013; 2013: 168302, doi: 10.1155/2013/168302, indexed in Pubmed: 24195065.
17. Wojda KM, Moczulska H, Sieroszewski PJ. 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. Ginekol Pol. 2019; 90(10): 604–606, doi: 10.5603/GP.2019.0104, indexed in Pubmed: 31686418.