Nasal bone in screening for T21 at 11-13+6 weeks of gestation - a multicenter study

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Objective
Trisomy 21 is one of the most common chromosomal defects diagnosed prenatally. Screening for Down syndrome is based on maternal age (MA), measurement of crown-rump length (CRL), nuchal translucency (NT) and fetal heart rate (FHR), together with free β-hCG and PAPP-A assessment (BC - first trimester biochemistry) at 11 to 13+6 wks. The aim of the study was to investigate the influence of introduction of additional ultrasound marker of Trisomy 21 (evaluation of the nasal bone - NB) on detection rate (DR) and invasive diagnostic testing rate (FPR – false positive rate).

Methods
Ultrasound scans were performed in 5814 fetuses as part of routine screening for chromosomal defects at 11 to 13+6 weeks of gestation. In all fetuses NB was evaluated according to FMF rules. CRL, MA, NT, FHR, free β-hCG and PAPP-A (results of first trimester biochemistry expressed as multiples of the median (MoMs)), values were entered into the Astraia software to assess the risk for Trisomy 21. In the high-risk group amniocentesis for karyotyping was performed. In the remaining cases, neonatologists phenotypically evaluated newborns for follow-up. DR and FPR coefficients were calculated for 3 levels of risk as cut-off points for screening model 1, based on MA, NT, and BC, and for screening model 2, based on MA, NT, BC and NB.

Results
There were 5708 normal cases, 71 cases of Trisomy 21 and 35 cases of other chromosomal defects that were excluded from the study. The presence and absence of NB was analyzed only in Trisomy 21 and normal cases. NB was absent in 46 (64.8%) cases and present in 25 (35.3%) cases of Trisomy 21, in comparison to present NB in 5463 (95.7%) and absent in 245 (4.3%) of normal cases. In screening model 1 (without NB) with a high-risk cut-off of 1:300, DR = 84.5%, FPR = 10.7%. When the additional marker (NB) was added to screening (model 2) DR increased to 93.0% for 2.0% FPR. For a cut-off of 1:100 DR = 80.3%, FPR = 5.7%, in model 1, and in model 2 - DR = 90.1% at 1.9% FPR. For the cut-off of 1:50, DR = 78.8%, FPR = 3.6% in model 1, and in model 2 - DR = 80.3%, FPR = 1.5%.

Conclusion
First-trimester screening with additional NB assessment significantly increases the detection rate for Trisomy 21 and decreases the rate of false-positive results. Adding NB evaluation at the risk level of 1:50 causes only a small increase in detection rate. Invasive procedures should be performed in that group regardless NB assessment.