Experimental
&
Clinical Article

Obstetrics; *Maternal-Fetal Medicine and Perinatology*

Nuchal Translucency Measurement Did Not Significantly Predict Trisomy Cases in Tertiary Referral Center

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OBJECTIVE: We sought to determine the value of well defined screening method in predicting trisomy cases in our institution.

STUDY DESIGN: Totally 300 amniocentesis cases were screened from prospectively collected database. Subjects were referred to amniocentesis according to the sequential results of first and second trimester screening tests. Each case had nuchal translucency measurement between 11th to 14th weeks of gestation. All values of NT measurement were analyzed to predict trisomy cases.

RESULTS: There were 7 trisomy cases , non of the screening methods significantly predicted trisomy cases (p>0.05) rather than the simply age (Area under curve 0.724, p=0.043). Mean NT did not differ between groups with normal and abnormal chromosomes(p>0.05).

CONCLUSION: This data led us to conclude that in our country there is still need for more accurate and standardized method to predict abnormal cases with higher sensitivity and specificiy to decrease invasive procedures.

Key Words: Nuchal translucency, Trisomy, Prenatal tests

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Introduction

In prenatal ultrasound, the concept of quality assessment and certification has only recently a concern.[1] Nuchal translucency measurement has been shown to be a useful marker for Down syndrome in the late first trimester but only when accompanied by targeted training and ongoing quality assessment.[2] A continuous monitoring and careful evaluations of individual performance may improve NT measurement procedure. Although NT was frequently used to detect trisomies there are some reports of chromosomal deletions with increased NT.[3] The aim of this study is to analize the predictive value of nuchal translucency measurement by non certified sonographers to detect trisomies or other chromosomal aberrations.

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Material and Method

Three hundred amniocentesis were performed between January 2008 to May 2012 in Dr. Sami Ulus Maternity and Women's Heath Teaching and Research Hospital. Subjects were referred to amniocentesis according to the sequential results of first and second trimester screening tests. First trimester combined screening for Down syndrome (DS) was performed to all pregnant women attended in our Department during this period, including maternal age, biochemistry (Pregnancy-Associated Plasma Protein-A and free β-human Chorionic Gonadotrophin), and NT. The maternal serum biochemistry was measured using the Kryptor analyzer (Brahms Diagnostica) in a one or two-step strategy between 45 and 85 mm of crown rump length (CRL) measurements. Scans were carried out by 4 experienced sonographers without NT measurement certification transabdominally. Logic S6 (GE Medical Systems, Zipf, Austria) machines with a 5-MHz transabdominal was used. NT was measured in embryos with 40 to 85 mm of CRL. Combined risk was calculated by software. Cytogenetic study was recommended when combined risk index was higher than 1/270 at screening time. Between 16 and 20 weeks of gestation all subjects underwent second trimester serum screening including free β-human Chorionic Gonadotrophin, alfa-fetoprotein and estriol. E2 were measured using the Bayer ADVIA Centaur assay (Bayer Corp., Tarrytown, NY), a competitive immunoassay using direct chemiluminescent technology. Total E3 was measured using

fluorescence polarization immunoassay technology and the Abbott TDxFLx analyzer (Abbott Laboratories, Abbott Park, IL). Serum alfa fetoprotein levels were measured with electro chemiluminescence method on the commercially available ELECSYS 2010 analyzer from ROCHE. Amniocentesis results were retrieved from our database.

Results

Mean age of the study population was 30.9±6.8 years. Mean nuchal translucency of study population was 1.4±0.8 mm. Mean CRL at the time of measurement was 70.2±12.4 mm. There were 7 trisomy cases, NT measurements did not significantly predict trisomy cases (p>0.05) while simply the age significantly predicted trisomy cases. (Area under curve 0.724, p=0.043, Figure 1).

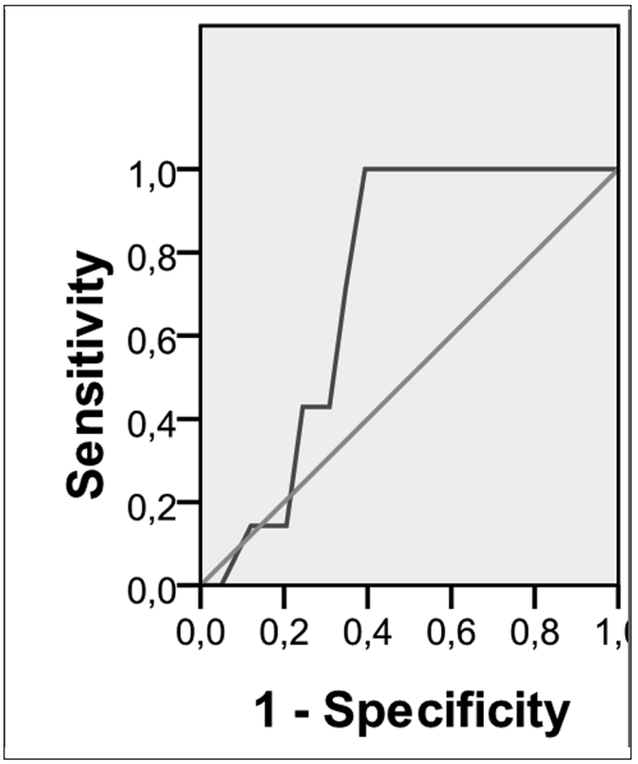

Figure 1: ROC curve of age to predict trisomies

Neither age nor NT significantly predicted any chromosomal abnormality (trisomies, deletions, inversions, Figure 2). Nuchal translucency measurement was not significanly correlated with trisomy, any chromosomal abnormality or age (p>0.05). Out of 7 trisomies there were trisomy 21 (n=5), trisomy 18 (n=1) and trisomy 13 (n=1) cases. Other chromosomal abnormalities were as follows;14p+ (n=2), 1 46, XX, inv (9) (p11q13) (n=1), 1 46, XY, 16qh+ (n=1), 46, XY, inv(12) (p11.2q13) (n=1), 46, XY, inv (Y) (p11.3q11.2) (n=1), del (18) (q12.2q12.3) (n=1), level II mozaic inv (7) (p1(n=1), levelII mozaic t (2;11) (q(n=1), levelII mozaic trisomy 3 (n=1). There were 3 cases with high nuchal translucency (>3.5 mm). One of them was measured to be 7.7 mm, other two were 4.8 and 3.9 mm. All of them had normal karyotype and their echocardiographic evaluation revealed normal cardiac findings. Mean NT values did not differ between normal and abnormal cases (p>0.05).

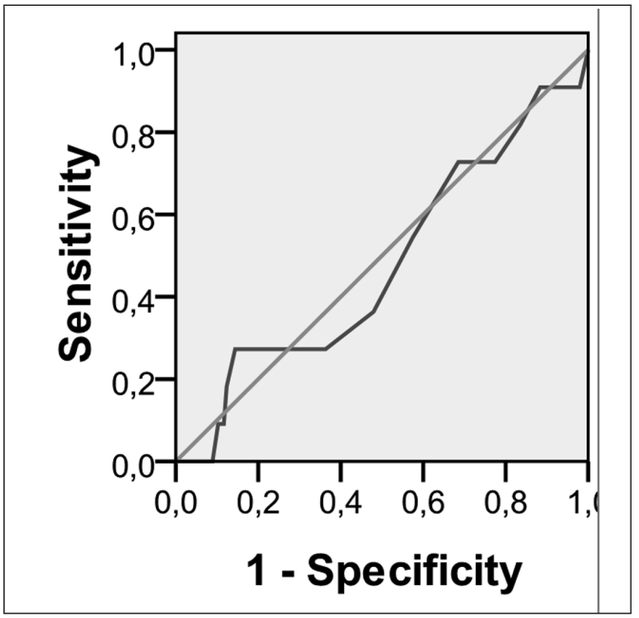

Figure 2a: ROC curve of NT to predict any chromosomal abnormality

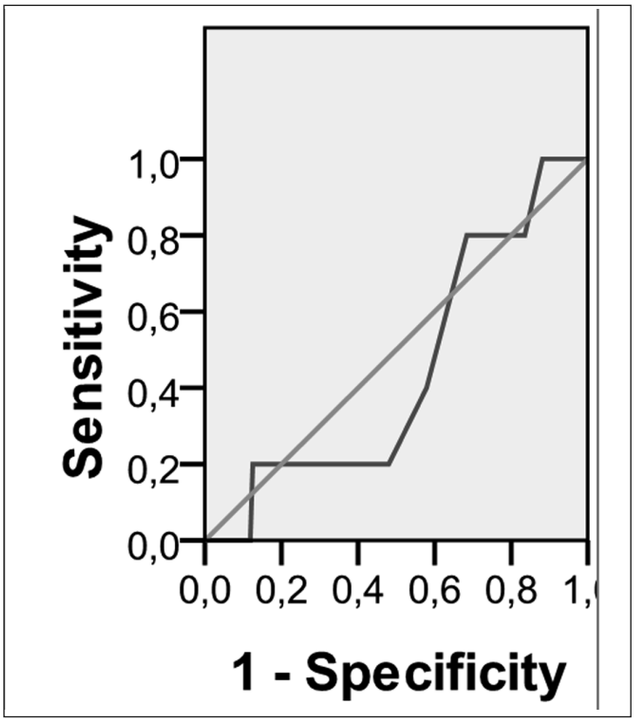

Figure 2b: ROC curve of NT to predict trisomies

Discussion

In this study 300 amniocentesis results were screened from database and prospectively collected NT results were analyzed for chromosomal abnormality prediction. This study was conducted to show the importance of NT measurement certification in detecting chromosomal abnormalities. In this study we have shown that without certification simply age can predict chromosomal abnormalities with higher sensitivity compared to NT. Studies have shown that increased NT is recognized as a sensitive marker for fetal chromosomal abnormalities.[4,5] However, NT screening is subject to high variability due to a lack of automation and significant operator factor. International guidelines and quality review programs are being increasingly recommended for standardiazation of the procedure.[6-8] According to the previous study CRL range has also an impact, and measurements of NT in fetuses over 60 mm length seem to be more accurate.[6] As a result an increase in the variation of NT measurements may be associated with suboptimal screening results. There are several published papers indicating the effect of deviation of NT measurements on the performance of screening.[1,9,10,11] Recently published study concluded that centers should routinely monitor the quality of NT measurements used to estimate trisomy screening risk.[12] And it was suggested that the use of practitioner-specific medians corrects for practitioner bias in measuring nuchal translucency. Practitioner-specific medians improve screening performance and help meet detection rate goals.[13] Several publications have shown less success for trisomy screening, probably, this related to the lack of standardization of NT measurements.[14,15] Another study has shown that when well-trained certified examiners perform nuchal translucency screening, continuous evaluation of the distribution of the nuchal translucency multiples of the median seems to be a good method to assess the quality for a center and may also be used to identify individual examiners deviating from the mean performance.[16] In previous study it was concluded that the prenatal detection rate of trisomy 21 cases was poor and remained unchanged throughout the 18-year study period with maternal age and second trimester screening. If improvement in detection rates is desired, additional programs are necessary.[17] Previous study stated that not all single-gene disorders are associated with enlarged NT, therefore NT cannot be regarded as a generic marker for single-gene disorder but only for a limited number of these conditions, in our series NT significantly predicted the neither trisomies nor single gene disorders.[18] Previous study aimed to examine the effectiveness of a combination of parameters at first-trimester screening for fetal aneuploidies, including ultrasound assessment of the nasal bone (NB), blood flow in the ductus venosus (DV) and flow across the tricuspid valve. The individual areas under the ROC curves of NT, NB, DV or TR were found to range between 0.7 and 0.8, representing acceptable discrimination. The area under the ROC curve of combined first-trimester screening was 0.87, At a risk cutoff of 1/275, the detection rate for aneuploidy increased from 87% to 92% .[19] In another recently published study it was concluded that around 65% of the fetuses with an increased NT have normal karyotype.[20] In our literature search, we recognized that, although some studies revealed controversial results, generally nuchal translucency measurement is valuable if it is standardized and performed by certified sonographers. In our study we concluded that without standardization sensitivity of the test in predicting chromosomal anomalies is very low.

Ense Saydamlığı Ölçümü Üçüncü Basamak Referans Merkezinde Trizomi Vakalarını Anlamlı Öngöremedi

AMAÇ: Biz bu çalışmada iyi tanımlanmış tarama yönteminin merkezimizdeki trizomi vakalarını öngörmedeki değerini belirlemek istedik.

GEREÇ VE YÖNTEM: Toplamda prospektif olarak toplanmış 300 amniyosentez sonucu kayıtlardan tarandı. Hastalar ikinci ve üçüncü trimester tarama ardışık sonuçlarına göre amniyosenteze yönlendirildiler. Her hastada 11-14. haftalar arasında ense saydamlığı ölçümü vardı. Tüm değerler trizomi vakalarını öngörmedeki değeri açısından değerlendirildi.

BULGULAR: Yedi tane trizomi vakası izlendi, hiçbir tarama yöntemi trizomi vakalarını anlamlı öngöremedi (p>0,05) basit olarak yaşın dışında (eğri altında kalan alan: 0,724, p=0,043). Ortalama ense saydamlığı ölçümü normal ve anormal kromozom yapılı vakalarda farklılık göstermedi (p>0,05).

SONUÇ: Bu data bizi şu kararı almamıza yönlendirdi; ülkemizde invazif prosedürleri azaltabilmek için anormal vakaları daha iyi öngören sensitivite ve spesifisitesi yüksek daha kesin, standardize bir metoda ihtiyaç vardır.

Anahtar Kelimeler: Ense saydamlığı, Trizomi, Prenatal tarama

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