

**Prenatal Screening Test Parameters Can Be Affected By Either Placental Location Or Fetal Gender**

Prenatal Tarama Test Parametreleri Plasental Lokalizasyon Yada Fetal Cinsiyetten Etkilenebilir

Melahat YILDIRIM<sup>1</sup>, Aydın KÖŞÜŞ<sup>2</sup>, Nermin KÖŞÜŞ<sup>2</sup>, Hanife SAĞLAM<sup>1</sup>, Müzeyyen DURAN ERDOLU<sup>3</sup><sup>1</sup> Yıldırım Beyazıt University, Department of Obstetrics and Gynecology, Ankara, Turkey<sup>2</sup> Turgut Özal University Faculty of Medicine, Department of Obstetrics and Gynecology Ankara, Turkey<sup>3</sup> Muğla University Faculty of Medicine, Department of Obstetrics and Gynecology, Muğla, Turkey**ÖZ****Amaç:** Bu çalışma ilk trimester ve ikinci trimester tarama testi parametreleri ile plasental lokalizasyon ve fetal gender arasında ilişki olup olmadığını araştırmaktadır.**Gereç ve Yöntemler:** Fetal ense kalınlığı (NT) ölçümü ve ilk trimester maternal serum serbest beta human koryonik gonadotropin (b-HCG), pregnancy-associated plasma protein-A (PAPP-A) değerleri ile ikinci trimester maternal serum alfa-fetoprotein (AFP), human koryonik gonadotropin (hCG) and ankonjuge estriol (uE3) düzeyleri tesbit edildi ve fetal cinsiyet ve plasenta lokalizasyonu ile ilişkisini göstermek için karşılaştırıldı.**Bulgular:** Kız fetuslarda NT değerleri daha yüksekti ( $p = 0.04$ ). Posterior plasenta grubunda AFP değerleri anlamlı bir şekilde yüksek idi ( $p = 0.04$ ), ve ilk trimester hCG değerleri posterior plasenta grubunda sınırda anlamlılık gösterdi ( $p = 0.05$ ).**Sonuç:** İlk trimester ve ikinci trimester tarama test parametreleri fetal cinsiyet ve plasenta lokalizasyonundan etkilenebilir.**Anahtar Kelimeler:** Prenatal tarama testleri, fetal cinsiyet, plasental lokalizasyon, plasenta**ABSTRACT****Aim:** This study aims to investigate the relationship between first and second trimester screening test parameters and placental location together with fetal gender.**Material and Methods:** Fetal nuchal translucency (NT) measurement and maternal serum free beta human chorionic gonadotropin (b-HCG) and pregnancy-associated plasma protein-A (PAPP-A) values in the first trimester and maternal serum alpha-fetoprotein (AFP), human chorionic gonadotropin (hCG) and unconjugated estriol (uE3) levels in the second trimester were determined and compared to fetal gender and placental location for demonstrating the relationship between them.**Results:** NT values were higher among female fetuses ( $p = 0.04$ ). AFP values were significantly higher in the posterior placenta group ( $p = 0.04$ ), and first trimester hCG values were higher in the posterior placenta group with a borderline level of significance ( $p = 0.05$ ).**Conclusion:** First and second trimester screening test parameters can be affected by fetal gender and placental location.**Keywords:** Prenatal screening tests, fetal gender, placental location; placenta**Introduction**

Screening for fetal chromosomal abnormalities and structural congenital malformations is an essential part of antenatal care. Prenatal screening tests are routinely offered to expectant mothers of all ages in most developed countries. These tests usually combining with maternal ages can be performed either in the first trimester (ultrasonic measurement of nuchal translucency combined with serum measurements of pregnancy-associated plasma protein A (PAPP-A) and human chorionic gonadotropin (hCG), or in the second trimester.

Second-trimester triple screening test consists of the measurement of maternal serum alpha-fetoprotein (AFP), hCG and unconjugated estriol (uE3) levels (1). In addition to maternal ages various factors such as maternal weight, maternal insulin-dependent diabetes mellitus, smoking habit can affect on the result of prenatal screening tests. Furthermore, the results of first and second trimester screening tests can be related to adverse pregnancy outcomes (2-4). The relationship between placental location fetal gender, and prenatal screening tests and pregnancy outcomes has been a focus of interest for many scientists in order to reveal any relation between. Studies investigating the rela-

Yazışma Adresi/ Correspondence Address:  
Melahat Yıldırım  
Beyazıt University, Kadın Hastalıkları ve Doğum Departmanı,  
Ankara, Türkiye  
Tel/Phone: 0535 557 99 78  
E-mail: melahatyildirim@yahoo.com

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tionship between fetal gender and prenatal screening tests found that prenatal screening test parameters were significantly different between female fetuses and male ones (5). In addition to that the earliest studies examining the impact of the placental location on the pregnancy stretch back to late 1970s (6). Moreover there is plenty of research studying the effect of placental location on the pregnancy and its outcome as well (7-9). It has been shown that there is a strong relationship between placental location and presence of pre-eclampsia (10). Another study (9) clearly demonstrated that the incidence of preeclampsia and intrauterine growth retardation (IUGR) increased 2.8 - fold and 2.7 - fold in patients with unilateral placentas when comparing to patients with central located placentas. Pregnancies complicated by IUGR are found to be more likely to have lateral placentation than non-IUGR pregnancies in the second trimester (11). It is needless to say that the location of placenta plays an important role in determining the mode of delivery (12,13) and the fetal presentation (14) In addition to these findings mentioned above, placental location has an effect on the approach to prenatal diagnostic testing as well (15). Even though the effect of placental position-either anterior or posterior- on the prenatal screening test parameters is unknown, increased perinatal risks have been reported to be associated with anterior located placenta previa (16,17) Although there are number of studies investigating the relationship between placental location and pregnancy outcome, there is no study, as far as we know, demonstrating particularly the association between prenatal screening test parameters and placental location. The aim of current study is to investigate the relationship between first or second trimester screening test parameters and placental location and fetal gender as well.

## Material And Methods

This analysis was carried out as a retrospective study at Obstetrics and Gynecology Clinic of Turgut Özal University Hospital between January 2010 and October 2011. Approval of the study protocol was obtained from the ethics committee at Turgut Özal University. Each participant gave written informed consent. The study population comprised of 300 pregnant women with singleton pregnancies. Pregnant women with, polyhydramni oligohydramni, fetal death, existence of congenital anomalies, any systemic disease and pregnancy complications such as diabetes or hypertensive disorders, smoking habits and multiple pregnancies were excluded from the study.

Maternal characteristics including age, gravida, parity, gestational age, and fetal gender, fetal birth weight were recorded prior to any further analysis. NT measurement and maternal serum b-hCG and PAPP-A values in the first trimester and maternal serum AFP, hCG, and uE3 levels in the second trimester were obtained.

All study participants were evaluated in the first and second trimester as a part of routine prenatal care. The ultrasonographic measurement of fetal nuchal translucency between 11-14 weeks of gestation was made by the same clinician by using an HDI 3000 ultrasound system (ATL Ultrasound, Bothell, WA, USA) At the very same day, venous blood sample were obtained from all participant in order to determine maternal serum PAPP-A and b-hCG levels.

At the 16-18 weeks of gestation, transabdominal measurements of fetal biparietal diameter (BPD) was made by the same clinician using aforementioned ultrasound device. Retrospective fetal ultrasound data were used to examine fetal growth. Maternal serum AFP, hCG and uE3 levels were measured from the serum samples of pregnant women. Plasma samples were analyzed

using the Siemens Immulite 2000 immunoanalyzer with IMMULITE® Free  $\beta$ -HCG and IMMULITE® PAPP-A kits , IMMULITE® Unconjugated Estriol Kit, IMMULITE® AFP kit , IMMULITE® HCG kit (Siemens Medical Solutions Diagnostics Limited, UK). The risk assesment of fetuses was made by using Prenatal screening program (PRISCA Typolog Software GmbH, Hamburg, Germany).

All resulting values were recorded for further analysis. Placental location in the uterine cavity was determined by transabdominal ultrasound screening (HDI 3000 ultrasound system (ATL Ultrasound, Bothell, WA, USA) ). Fetal biometric parameters and placental localization were recorded. Placental position was categorized as anterior and posterior based on their localization in the uterus. Fetal gender was recorded to determine fetal sexing precision after the delivery. After all these recording procedures, first or second trimester screening test parameters were compared to the placental location and the fetal gender in order to demonstrate whether there is a relationship between them.

The Statistical Package Program for the Social Sciences (SPSS 16.0; SPSS Inc., Chicago, IL, USA) was used for statistical analysis. Shapiro-Wilk test was used to verify if parameters were normally distributed. This test showed that the quantitative variables did not exhibit normal distribution. Results of continuous variables were expressed as median (minimum-maximum). The Mann-Whitney test was used for comparison of groups in the study. Values of  $p < 0.05$  were considered significant.

## Results

In this current study, median age was found as 31 (20-43) years, gravity was 2 (1-6), parity was 1 (1-5), and median gestational age was 21 (19-23) weeks. Of the 300 pregnant women 171 (57 %) had female fetuses and 129 (43 %) had male fetuses. One hundred five women (55 %) had anterior and 135 women (45 %) had posterior placental position. AFP values were found to be significantly higher in the posterior placenta group comparing to anterior ones (33.25 (13.60-74) IU/mL, 33.20 (3.05-255) IU/mL respectively;  $P = 0.04$ ) (Table 1), and first trimester hCG values were higher in the posterior placenta group with a borderline level of statistical significance (posterior placenta : 43.95 (10.10-116) ng/mL, anterior placenta : 33.40 (8.40-110) ng/mL ( $P = 0.05$ ) (Table 1). PAPP-A and NT values were identified as higher in anterior placenta group (2.22 (0.47-11.70) mIU/mL, 1.30 (0.6-2.5) mm respectively) but this finding turned out to be statistically insignificant ( $P > 0.05$ ). Although high-level second trimester hCG values were observed in the anterior placenta group, and uE3 values were predominantly high in the posterior placenta group however these results failed to demonstrate the statistical differences between study groups ( $P > 0.05$ ) (Table 1).

When comparing groups based on fetal gender, NT values were found higher among female fetuses (male fetus group: 1.3 (0.60-2.70) mm, female fetus group: 1.35 (0.60-2.50) mm) ( $p = 0.04$ ) (Table 2). Even though PAPP-A and first trimester hCG values were found as higher among female fetuses, these results couldn't reach the statistically significant levels ( $P > 0.05$ ).

While AFP and uE3 values were high in the male fetus group and second trimester hCG values were high in the female fetus group, all findings were not found to be significantly difference.

( $P > 0.05$ ) (Table 2)

## Discussion:

In the present study, higher maternal serum AFP levels were detected in the presence of posterior placenta. First trimester hCG values were found higher in the posterior placenta group, however this finding resulted in borderline statistical significance. On the other hand, first trimester maternal serum PAPP-A levels and fetal NT measurement were detected as higher in the anterior placenta group, but these results couldn't reach the statistical significance. Similarly, maternal serum uE3 values were higher in the posterior placenta group with a insignificant statistical difference. When comparing prenatal screening test parameters to fetal gender, NT values were found significantly higher in pregnant women with female fetuses. Although uE3 levels were detected higher in the male fetus group this result was barely detectable statistically significant difference. Many studies have investigated the effect of fetal gender on prenatal screening test results ( 5,18 ) Yaron et al indicated that maternal serum hCG levels in the first trimester were higher in female fetus than those in the male fetus ( 5 ). Another study demonstrated that maternal serum hCG levels at 10-14 weeks of gestation are significantly higher in the presence of female fetus ( 19 ) Although the current study reached the same result as expectant mothers with female fetuses had higher first trimester PAPP-A and hCG values these result turned out to be statistically insignificant. Reason why we couldn't obtain the same result as aforementioned study did can be due to our relatively small study population.

Another study found that pregnancies with female fetuses had higher first trimester maternal serum free beta hCG levels and also the second trimester free beta hCG levels were found to be increased both in the maternal serum and in the amniotic fluid when compared with male fetuses ( 20 ). Similar to our study, Spencer et. al showed that female fetuses had higher maternal serum PAPP-A levels than male fetuses in the first trimester ( 21 ). They demonstrated that, maternal serum free b-hCG levels in the first trimester were higher by about 15% in the pregnancies with female fetuses those in the pregnancies with male fetuses This study also demonstrated that in first trimester pregnancies with female fetuses, compared with male fetuses, maternal serum PAPP-A levels were higher by about 10% in the chromosomally normal fetuses.

In our study we attained the similar result as Spencer et. al ( 21 ) did however why we failed to demonstrate the statistical differences between female and male fetuses can be the most likely due to small sample size of our study.

While in the study of Spencer et. al, fetal NT was found as about 3-4% lower in female fetuses when comparing them to male ones, in this current study fetal NT was measured as higher in the female fetus group. In the present study, 55% of the pregnancies had anterior placenta while 45% of them had posteriorly located placenta. The findings of Magann et. Al ( 22 ) which, posterior placental implantation was detected to be more common, than anterior implantation at 18 weeks' gestation did not match with what we found in our study ( 22 ). Another study confirmed that antepartum hemorrhage was more common in women with complete placenta previa particularly when the placenta was located on the anterior wall of the uterus ( 23 ).

In conclusion, even though this study can be criticized for not having a strong statistical result, it has clearly revealed that there is some close relation between prenatal screening test parameters and either placental location or fetal

gender. We can assume that first and second trimester screening test parameters can be affected by fetal gender and placental location. However future research should be directed toward attempting to pin down this casual relationship between these parameters by extending sample size.

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