Özgün Araştırma / **Original Article**

The utility of pulsatility index and diastolic notch presence in uterine artery doppler ultrasound between 18-24 weeks for preeclampsia prediction

18-24 hafta uterin arter doppler ultrasonografisinde pulsatilite indeksinin ve diyastolik çentik varlığının preeklampsi öngörüsündeki önemi

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ÖZ

Amaç: İkinci trimester uterin arter pulsatilite indeksi (Pİ) değerinin ve diyastolik çentik varlığının primigravid, düşük riskli gebe hastalarda preeklampsi öngörüsündeki önemini saptamaktır.

Gerekçeler ve Yöntem: Primigravid, tekil, 18-24 haftası arasında olan 244 gebe hasta çalışmaya dahil edildi. Doppler ultrason ölçümleri transabdominal olarak yapıldı. Uterin arter Pİ değeri ve diyastolik çentik varlığı not edildi. Daha önce normotansif olan bir gebede, 20. gebelik haftası ve sonrasında yeni başlayan hipertansiyon (> 140/90 mmHg) ve proteinüri (24 saatlik idrarda 300 mg ve üzeri), proteinüri yokluğunda hipertansiyona eşlik eden sistemik bulguların bulunması preeklampsi olarak değerlendirildi. 32 gebelik haftası öncesi preeklampsi gelişmesi erken preeklampsi olarak tanımlandı.

Bulgular: Preeklampsi gözlenen 15 gebenin ortalama Pİ değeri (1,51), preeklampsi gözlenmeyen gebelerinkinden (0,89) anlamlı olarak yüksek bulundu (p<0,001). Preeklampsi öngörüsü için duyarlılığı ve özgüllüğü en yüksek olan eşik Pİ değeri 1,13 olarak hesaplandı. Diyastolik çentik gözlenen gebelerde preeklampsi ve erken preeklampsi gelişme oranı, çentik negatif olan gebelere göre anlamlı olarak artmıştı (p<0,001). Preeklampsi gözlenen 15 gebenin 13'ünde iki taraflı, ikisinde ise tek taraflı çentik pozitifti.

Sonuç: Uterin arter Doppler değerlendirmesi, yüksek riskli gebelikleri belirlemek için kullanılabilecek non-invaziv ve basit bir araçtır. Özellikle anormal UA-PI değerlerine (> 1,13) eşlik eden bilateral diyastolik çentik saptanan gebelerde preeklampsi gelişme riski daha yüksektir. Yakın hasta izlemi, yüksek risk gruplarında hem maternal hem de fetal morbidite ve mortaliteyi azaltmaya yardımcı olabilir.

Anahtar kelimeler: Diyastolik çentik, Uterin arter doppleri, Preeklampsi, Pulsatilite indeksi

ABSTRACT

Aim: To determine the importance of second trimester uterine artery pulsatility index (PI) value and the presence of diastolic notch in the prediction of preeclampsia in primigravid, low-risk pregnant women.

Materials and Methods: Primigravid, singleton, 244 pregnant women between 18-24 weeks of gestation included the study. Doppler ultrasound measurements were done transabdominally. Uterine artery PI value and the presence of diastolic notch were noted. Presence of new-onset hypertension (> 140/90 mmHg) and proteinuria (300 mg or more in 24-hour urine) or systemic findings accompanying hypertension in the absence of proteinuria in a pregnant woman who was normotensive before was considered preeclampsia. The development of preeclampsia before 32 weeks of gestation was defined as early preeclampsia.

Results: The mean PI value of the 15 pregnant women with preeclampsia (1,51) was found to be significantly higher than that of the pregnant women without preeclampsia (0,89) (p<0.001). The threshold PI value with the highest sensitivity and specificity for the prediction of preeclampsia was calculated as 1,13. The preeclampsia and early preeclampsia rates in pregnant women with diastolic notch were significantly higher than in pregnant women with negative notch (p<0.001). Bilateral notch was positive in 13 of 15 pregnant women with preeclampsia, and unilateral notch was positive in two.

Conclusion: Uterine artery Doppler is a non-invasive and simple tool to identify high-risk pregnancies and may improve patient-specific practice. Especially pregnant women with a bilateral uterine diastolic notch accompanying with abnormal UA-PI values (> 1,13) have higher risk to develop preeclampsia. Closer monitoring may help to reduce both maternal and fetal morbidity and mortality in high-risk groups.

Keywords: diastolic notch, uterine artery doppler, preeclampsia, pulsatility index

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INTRODUCTION

Preeclampsia (PE) is a multisystemic disease characterized by the new onset of hypertension plus proteinuria and/or end-organ dysfunction after 20 weeks of gestation and a common risk factor for both perinatal and maternal morbidity, mortality worldwide (1). Since the only effective treatment is delivery, prediction and intervention of PE become very important to improve maternal and perinatal outcomes.

Prophylactic use of aspirin in high-risk women presents reduce risk of preterm PE (2). Thus, the determination of high-risk group becomes crucial but, the complexity of pathogenesis make it difficult. Placenta-mediated pregnancy complication has been widely used recently in the literature and includes pre-eclampsia, placental abruption, intrauterine growth restriction, and late fetal loss (3). Abnormal placentation due to inadequate trophoblastic invasion is accused in these cases (4, 5). This process ended up with high resistance in uteroplacental circulation and reflected abnormal uterine artery (UA) Doppler patterns. Angiogenic modulators like vascular endothelial growth factor (VEGF), placental induced growth factor (PlGF), soluble endoglin (sEng), and soluble fms-like tyrosine kinase 1 (sFlt-1) were widely investigated for PE prediction but, blood and urine levels of these factors have not been proven to be clinically useful for this purpose (6). A meta-analysis reported that an increased pulsatility index (PI) with diastolic notching (DN) especially in the second trimester provides the best overall PE prediction in both low-risk and high-risk patients (6). Whether ultrasonographic screening does not recommend for the low-risk population, finding a cut-off value for UA PI and the effect of DN presence on PE development risk would allow early intervention for possible PE complications in this group.

This study aims to determine the utility of second trimester UA PI values and DN presences in primigravid, low-risk pregnant women for PE prediction.

MATERIALS AND METHODS

This is a prospective cohort study conducted in the Turkish Ministry of Health Okmeydanı Research Hospital, Obstetrics and Gynecology Clinics with primigravid pregnant women. Primigravid, singleton, healthy, between 18-24 gestational weeks pregnant women selected as a study population. Women known to have multifetal pregnancies, fetal structural anomalies, maternal systemic diseases, maternal uterine anomalies were excluded. Written informed consent was obtained from all participants. The applied protocol was approved by the Medical Research Ethics Department.

The last menstrual period or first-trimester crown–rump length was used to determine gestational age. Doppler measurements were performed between 18 and 24 weeks of gestation by the same obstetrician using software of the Toshiba Xario Ultrasound (USG) machine, transabdominal PVU-375BT6C1 convex probe (1.9–6 Mhz). All USG examinations were performed by the same obstetricians (SGA, RA). Patients were examined in a semi-Fowler position to avoid orthostatic hypotension. UA was identified at the level where they cross the external iliac artery bilaterally. Pulsed wave Doppler is then applied with an insonation angle < 30° and a sampling volume of 2 mm. At least three uniform waves were analyzed. PI is then obtained using the average PI measurement of both right and left arteries and DN was noted if it was found.

Diagnostic criteria for pre-eclampsia were new-onset persistently high systolic (140 mm Hg) or diastolic (90 mm Hg) blood pressure and proteinuria (0.3 g of protein in 24-hour urine collection) or hypertension and end-organ dysfunction after 20 weeks of gestation. Early PE was defined as the development of PE before 32 weeks gestation.

SPSS 17 was used for statistical analysis. The Shapiro- Wilk test, Kolmogorov–Smirnov test were used to determine the distribution of normality. The continuous variables were presented as mean and standard deviations. Groups were compared with The Student's t-test and Mann-Whitney U test. A type-1 error below 0.05 was considered statistically significant. ROC curve was used to evaluate the UA-PI cut-off value for PE prediction.

RESULTS

Of the 244 primigravid pregnant women, 15 (6,1 %) developed PE. When Preeclampsia positive (PEP) group and the preeclampsia negative (PEN) group were compared, there was no difference in demographic data. PEP group mean UA-PI value was significantly higher (p< 0,01) when mean time of the delivery week (p< 0,01) and fetal birth weight (p< 0,01) were significantly lower than PEN group. Table 1 shows the basic characteristics of patients with PE (n = 15) and without PE (n = 229).

Table 1. Basic Characteristics of Patients with and without Pre-eclampsia (n=244, %)

Basic Characteristics	Preeclampsia Negative (n=229, %93,9) Mean +/-SD	Preeclampsia Positive (n=15, %6,1) Mean +/-SD	P
Age	22,99 ± 3,58	22,23 ± 3,89	0,290
Gestational Week (USG)	21,74 ± 1,33	21,07 ± 1,10	0,055
Pulsatility Index	0,890 ± 0,20	1,510 ± 0,42	<0,001*
Birth Week	38,27 ± 1,58	35,60 ± 2,64	<0,001*
Fetal Birth Weight (gr)	3221 ± 547	1952 ± 713	<0,001*
*p<0,05			

DN was negative (NN) in 163 (66,8 %) pregnant women, and found positive (NP) in 81 (33,2%) pregnant women (Table 2). Table 3 provides a relation between DN and early PE. Unilateral notch positivity was 48 (19,7%), while 33 of the patients (13,5%) had bilateral notch positivity. Bilateral DN and early PE relation was given in Table 4, and Table 5 shows bilateral DN and PE relation.

Table 2. Diastolic Notch and Preeclampsia Relation (n=244, %)

	PEN	PEP	
NN	163(%66,8)	0	
NP	66 (%27,1)	15 (%6,1)	p<0,0001
NN: Notch Negative, NP: Notch Positive,			
PEN: Preeclampsia Negative, PEP: Preeclampsia Positive			

Table 3. Diastolic Notch and Early Preeclampsia Relation (n=244, %)

	EPEN	EPEP	
NN	163(%66,8)	0	
NP	76 (%31,1)	5 (%2,1)	p=0,0037
NN: Notch Negative, NP: Notch Positive,			
EPEN: Early Preeclampsia Negative EPEP: Early Preeclampsia Positive			

Table 4. Bilateral Diastolic Notch and Early Preeclampsia Relation (n=244, %)

|	EPEN	EPEP	
NN + UNP	211(%86,5)	0	
BNP	28 (%11,4)	5(%2,1)	p<0,0001
NN: Notch Negative, UNP: Unilateral Notch Positive, BNP: Bilateral Notch Positive,			
EPEN: Early Preeclampsia Negative, EPEP: Early Preeclampsia Positive			

Table 5. Bilateral Diastolic Notch and Preeclampsia Relation (n=244, %)

	PEN	PEP	
NN + UNP	209(%85,7)	2 (%0,8)	
BNP	20 (%8,2)	13 (%5,3)	p<0,0001
NN: Notch Negative, UNP: Unilateral Notch Positive, BNP: Bilateral Notch Positive, PEN: Preeclampsia Negative, PEP: Preeclampsia Positive			

Figure 1 shows Roc analyses to establish cut of UA-PI for PE prediction and 1,13 found most sensitive (93 %) and specific (88%) value for this purpose.

Figure 1. ROC Curve
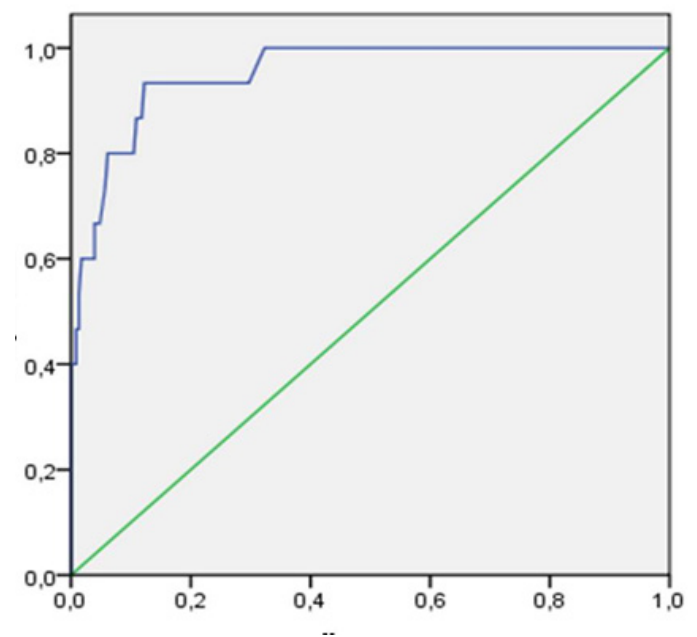
AUC: 0,952, most sensitive (93%) and specific (88%) value of UA-PI for PE prediction found 1,13

DISCUSSION

In the present study, we found a 1,13 value as a cut-off for UA-PI to PE prediction between 18-26 GW in primigravid, low-risk pregnant women. In addition, the presence of bilateral DN increases the risk of PE in this group.

UA Doppler evaluation has been used to determine advanced pregnancy outcomes for many years (7-10). Due to physiological changes in spiral arteries between 6-24 weeks, the Doppler flow velocity shows high capacitance and low resistance pattern (11-13). Therefore, inadequate placentation causes high impedance in UA and results abnormal UA Doppler parameters. Several studies investigated the value of uterine artery Doppler indices in predicting the development of adverse pregnancy outcomes and results varied widely. Schwarze et al. evaluated the role of uterine artery Doppler ultrasound in predicting adverse outcomes in pregnancy in low-risk women at 23–26 gestational weeks and, found low sensitivity for predicting PE, using resistance index (RI) cutoff of 0.58 or 0.7 or any notch in one or both uterine arteries. On the other hand, Bhattacharyya et al. (14) and Espinoza et al. (15) reported that UA Doppler abnormalities are an independent predictor of the development of PE. In the present study, PEP group mean UA-PI value was significantly higher (p< 0,01) when the mean time of the delivery week (p< 0,01) and fetal birth weight (p< 0,01) were significantly lower than PEN group. This is consistent with high resistance blood flow in UA and adverse outcomes of insufficient placentation in PE.

Roc analyses determined, 1,13 UA-PI as a most sensitive (93 %) and specific (88%) cut-of value for PE prediction (figure 1) in the present study. AUC calculated 0,952 ± 0,022 (p<0,001).

UA notch pathophysiology has not been clarified completely and increased compliance of the arterial wall or UA endothelial cell dysfunction blamed previous studies (16, 17). Ratiu et.al published a study that points, pregnant women with bilateral uterine notching had higher maternal and fetal morbidity compared to women presenting only unilateral uterine notching in the second trimester (18). In the present study, we found similar results. Notch positivity increased PE and early PE risk significantly when compared to notch negativity (p<0,001).

Of to 15 PEP group, 13 had bilateral uterine notching and 2 had unilateral uterine notching. Additionally, the mean PI value found 1,51 in the bilateral uterine notching group when it was 1,06 and 0,84 in unilateral uterine notching and notch negative group respectively. However, 48 of unilateral uterine notching group only 2 developed PE. Mean PI was less than 1,13 in this group which may be the explanation of this result.

The utility of UA Doppler analyses for PE prediction was demonstrated in a systematic review of 74 studies including almost 80,000 women (7). Both low-risk and high-risk pregnant women for PE and 15 UA Doppler indices were involved in the study and reported that UA Doppler evaluation was more accurate when performed in the second trimester than in the first trimester. Also, UA-PI was the best predictive tool for PE prediction when accompanied with UA notching. In the present study second trimester, pregnant women were examined for PE prediction using UA-PI and notching together consistent with this systematic review.

The main strength of this study is a prospective design with adequate follow-up until delivery and, a homogenous group about demographic features. The small sample size was the main limitation of the present study.

 In conclusion, whether UA doppler examinations do not recommend for routine PE screening, it is a non-invasive and simple tool for identifying high-risk pregnancies and may improve patient-specific practice. Prophylactic use of aspirin, closer monitoring, and determining the best time for intervention to high-risk groups enables to reduce both maternal and fetal morbidity and mortality (2, 8, 18-21). Especially pregnant women with a bilateral uterine notch plus abnormal UA-PI values resulted a higher prevalence to develop these severe adverse outcomes (18, 21).

Conflict of interest statement: All authors state that they have no conflict of interest in this study.

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