

The Effect of Down Syndrome Biochemical Markers on Predicting Severity of Preeclampsia

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Research Article

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Abstract

Objective: This study aims to determine whether it is possible to predict preeclampsia by comparing postpartum results and test results of the pregnant women diagnosed with preeclampsia, whose first and/or second trimester screening tests were accessible, and to demonstrate the predictability of severity and week of onset.

Background: 204 patients underwent renal transplantation in our center and 84 of them were female. Five of our patients (one of them had two births) gave birth to a total of 6 pregnancies.

Method: 135 patients were diagnosed with preeclampsia and their first and/or second trimester screening tests were accessible, and 366 control participants gave birth to a healthy baby between 37-41 weeks after standard follow-up period for pregnancy and their screening tests were also accessible.

Results: The study results show that the first trimester maternal serum PAPP-A level is significantly low in preeclamptic pregnant women, and that the second trimester maternal serum AFP and hCG levels are significantly high and uE3 levels are significantly low. The results also suggest that the first and second trimester Down syndrome biochemical markers can be used in preeclampsia screening.

Conclusion: Among these markers, uE3 is the parameter which affects the possibility of preeclampsia the most. However, the first and second trimester Down syndrome biochemical markers are not effective in predicting the severity and onset week of preeclampsia.

Introduction

Preeclampsia is an important complication of pregnancy with a frequency of 2-4% and is the most important cause of maternal and fetal mortality and morbidity. Preterm labor, fetal growth retardation, and perinatal death are among fetal complications and maternal complications include placental abruption, disseminated coagulopathy, pulmonary oedema, acute renal failure, and convulsions (eclampsia). Its etiology remains uncertain and impaired early trophoblast invasion, decreased placental perfusion, placental ischemia and oxidative stress are important factors in its pathophysiology. Some placental factors (balance of angiogenic and prothrombotic factors) play an important role in inducing this systemic maternal endothelial dysfunction. Diffuse endothelial dysfunction and systemic inflammatory response lead to hypertension and proteinuria, which are the characteristic findings of maternal preeclampsia in the late stages of pregnancy. Early diagnosis and full-term delivery reduce maternal morbidity [1].

There are various tests proposed to evaluate the risk of preeclampsia. Studies have focused on non-biochemical markers; however, in recent years, an increasing number of biochemical markers have been tested to predict preeclampsia [2]. Second trimester serum screening is common for Down syndrome and there is evidence on that these biomarkers can be useful for screening preeclampsia [3,4]. Integrated testing (measurement of pregnancy-associated plasma protein (PAPP-A) and nuchal translucency (NT)),

which is a combined screening performance of the first and second trimester prenatal markers, and the measurement of maternal serum alpha-fetoprotein (MSAFP), human chorionic gonadotropin (hCG), non-conjugated estriol (uE3), and inhibin-A in the second trimester are the most effective and safe method for screening test in fetal Down syndrome.

This study aims to determine whether it is possible to predict preeclampsia by comparing postpartum results and test results of the pregnant women diagnosed with preeclampsia, whose first and/or second trimester screening tests were accessible, and to demonstrate the predictability of severity and week of onset.

Material Method

This study included patients admitted to Dr. Zekai Tahir Burak Women's Health Education and Research Hospital. Of these patients, 135 patients were diagnosed with preeclampsia and their first and/or second trimester screening tests were accessible, and 366 control participants gave birth to a healthy baby between 37-41 weeks after standard follow-up period for pregnancy and their screening tests were also accessible.

All pregnant women underwent a detailed ultrasonography to determine the gestational week and eliminate congenital fetal anomalies. Criteria of preeclampsia included a blood pressure above 140/90 mmHg tested at least twice every 6 hours and 300 mg (0.3 g) or higher level of protein in a 24-hour urine sample, or presence of proteinuria of 0.1 g/L or higher in two spot urine samples taken at 4-hour intervals. Those with multiple pregnancy, aneuploidy, neural tube defect, abdominal wall defect or serious anatomical defects, diabetes mellitus, premature rupture of membranes, intrauterine infection and chronic maternal disease in their follow-up were excluded from the study. The demographic data of the patients associated with pregnancy were recorded and evaluated.

The patients were divided into two groups; mild and severe preeclamptic patients based on the severity of preeclampsia; those with early and late onset preeclampsia based on the week of onset. A At blood pressure level of $\geq 160/110$ mmHg of at least two tests, measured at 6-hour intervals, of a patient at bed rest, proteinuria >5 g/24 hours, oliguria (≤ 400 ml/24 hours), cerebral and visual symptoms, pulmonary edema, thrombocytopenia (≤ 100000 /mm³), increased liver enzymes, serum creatinine >1.2 mg/dl, and increased microangiopathic hemolysis (increased LDH) were considered severe preeclampsia criteria. Nuchal translucency (NT), PAPP-A, and free β -hCG were evaluated in patients with a gestational age of 11 weeks to 13 weeks 6 days as the first trimester screening test. AFP, hCG and Ue3 were evaluated in those with a gestational age of 16 weeks to 19 weeks 6 days as the second trimester screening test.

PAPP-A, free β -hCG, AFP, hCG, Ue3 values were studied in venous blood samples taken in appropriate week. After ultracentrifugation, serum samples with hemolysis and without lipemia were taken. The measurements of the markers were performed using a solid-phase enzyme-labeled chemiluminescent immunometric assay technique using Immulite 2000 kit. The sensitivity of the kit was 0.025 Miu/ml for

PAPP-A, 0.1 ng/ml for free β -Hcg, 0.2 IU/ml for AFP, 0.4 Miu/ml for Hcg, and 0.1 ng/ml for Ue3. The values were recorded as MOM values adjusted according to age, weight, and gestational week.

A written informed consent was obtained from the patients and from healthy participants. The study protocol was approved by the Dr. Zekai Tahir Burak Women's Health Education and Research Hospital Ethics Committee. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. This study was no funding. There is no conflict of interest.

STATISTICAL ANALYSIS

The data were analysed using SPSS (statistical Package for Social Sciences, SPSS Inc., Chicago, IL, United States for Windows 22) software. Student's t test was used to identify whether there was a statistically significant difference in continuous variables distributed normally between the control and study groups, and the significance of the difference in non-normally distributed continuous variables was evaluated using Mann Whitney-u test. Kruskal Wallis test was used to analyse whether there was a statistically significant difference in double and triple screening test levels between the control group and the study groups formed based on the severity of preeclampsia and the development time of preeclampsia. Nominal variables were compared with Pearson's chi-square test.

The area under the ROC curve was calculated to evaluate whether double and triple screening test components were a determiner in predicting preeclampsia development. Cut-off points corresponding to the 5% false positive level for each component were determined in predicting the development of preeclampsia in case that the area under the curve was found to be significant. Sensitivity, positive and negative predictive values were calculated for the cut-off points.

Multivariate Logistic Regression analysis was used to determine the test component with the highest predictive level in the development of preeclampsia between the double and triple screening tests. Odds Rate, 95% confidence interval and significance levels of each test component were calculated. A p value of ≤ 0.05 for the results was considered statistically significant.

Results

The mean age of normal pregnant and preeclamptic pregnant was 27.1, and there was no statistically significant difference ($p=0,955$). The weight of preeclamptic pregnant was higher than that of normotensive pregnant ($p<0,001$). Examining the birth weight, there were statistically significant differences in low birth weight and neonatal intensive care need in the preeclamptic group. Demographic data and statistical significance values of these data are summarized in Table 1.

The first trimester biochemical screening test was performed on a total of 310 pregnant women and 67 of these women were preeclamptic. A mean level of 0.84 MOM was found for PAPP-A in in the normotensive

group, while it was 0.63 MOM in the preeclamptic group ($p=0.001$). The mean level of free β -Hcg was 1.09 MOM in the normotensive group and it was 1.04 MOM in the preeclamptic group ($p=0.925$). The level of PAPP-A in the preeclamptic group lower than that of the control group was statistically significant; however, there was no statistically significant difference in free β -Hcg between the groups (Table 2).

The results show that preeclamptic pregnant with 11.9% sensitivity, 95% specificity, and 79.7% negative predictive value could be predetermined when a value of 0.34 MOM at the 5th percentile was taken as cut-off for PAPP-A (Table 3).

The lower and upper limits of the ROC curve, in which serum PAPP-A levels were evaluated, were found to be 0.616 and 0.758, respectively, with a confidence interval of 95%, while the area under the curve was 0.687 ($p=0.001$) (Table 4).

The selectivity of serum PAPP-A levels determined by ROC analysis in preeclampsia is shown in Figure 1.

A PAPP-A level of <0.34 MOM significantly increases the risk of preeclampsia ($p=0.045$ Odds ratio 2.61 [1.02-6.67]) (Table 5).

The second trimester screening test was performed on 453 pregnant women and 114 of these women were preeclamptic. The mean level of AFP was 0.82 MOM in the normotensive group, while it was 1.03 MOM in the preeclamptic group ($p=0.001$). A level of 1.02 MOM was found for hCG in the normotensive group, and 1.41 MOM in the preeclamptic group ($p=0.001$). The mean level of uE3 was 1.67 MOM in the normotensive group and it was 1.37 MOM in the preeclamptic group ($p=0.001$). It was found that AFP and hCG levels were significantly higher in the preeclamptic group than in the control group, and uE3 level was lower (Table 6).

The study results show that preeclamptic pregnant with 21.1% sensitivity, 95% specificity and 78.2% negative predictive value could be predetermined when a level of 1.47 MOM at 95th percentile was taken as cut-off for AFP, that those with 25.4% sensitivity, 95% specificity, and 79.1% negative predictive value could be predetermined when a level of 2.14 MOM at 95th percentile was taken as cut-off for hCG, and that those with 27.2% sensitivity, 95% specificity, and 79.5% negative predictive value could be predetermined when a level of 1.06 MOM at 5th percentile was taken as cut-off for uE3 (Table 3). The area under the ROC curve was calculated as 0.674 for AFP, 0.684 for hCG, and 0.684 for uE3, and the result was statistically significant ($p=0.001$) (Table 7) (Figure 2).

An AFP level of >1.47 MOM ($p=0.001$ Odds ratio 3.81 [1.82-7.95]), a hCG level of >2.14 MOM ($p=0.001$ Odds ratio 3.84 [1.88-7.87]), and an uE3 level <1.06 MOM ($p=0.001$ Odds ratio 6.57 [3.36-12.84]) significantly increase the risk of preeclampsia. Furthermore, uE3 is the parameter affecting the possibility of preeclampsia among the triple screening markers the most (wald=30.37) (Table 4). Combining AFP, hCG and uE3 values, preeclamptic pregnant can be detected with a specificity level of 93.8%, a sensitivity level of 36.8%, and a negative predictive value of 81.5%. Combined test alone increases the success of uE3 more.

There were 46 preeclamptic and 216 control patients whose the first and second trimester screening tests were accessible. When the double and triple screening tests were combined to predict preeclampsia, the level of specificity increased to 96.3%, that of sensitivity to 60.9%, and negative predictive level to 92%. Odds values and 5-95% confidence intervals for PAPP-A ≤ 0.34 MOM, AFP > 1.47 MOM, hCG > 2.14 MOM, and uE3 ≥ 1.06 MOM were found to be 3.83 [1.05-13.89], 19.65 [4.57-84.54], 5.63 [1.85-17.14], and 25.42 [7.78-83.05], respectively. uE3 was the marker affecting the development of preeclampsia the most (wald: 28.71), while the marker affecting the least was PAPP-A (wald = 4.19) (Table 8).

The first trimester screening test was performed on 67 preeclamptic patients, 38 of whom were with mild preeclampsia and 29 were with severe preeclampsia. The mean level of PAPP-A was 0.84 MOM in the control group, 0.68 MOM in the mild preeclampsia group, and 0.62 MOM in the severe preeclampsia group. The difference between the control group and the mild preeclampsia group, and the difference between the control group and severe preeclampsia group were statistically significant ($p \leq 0.001$). However, the difference between the mild and severe preeclampsia group was not statistically significant. The mean level of free β -hCG was 0.96 MOM in the control group and 1.14 MOM in the severe preeclampsia group. There was no statistically significant difference between the groups ($p=0.954$). Therefore, the first trimester screening test markers failed to predict the severity of preeclampsia. The second trimester screening test was performed on 114 patients, 58 of which were mild preeclampsia and 56 were severe preeclampsia. The mean level of AFP was 0.82 MOM in the control group, while it was 1.10 MOM in the mild preeclamptic group and 0.99 MOM in the severe preeclamptic group. The mean level of hCG was 1.02 MOM in the control group, and it was 1.47 MOM in the mild preeclamptic group and 1.26 MOM in the severe preeclamptic group. The mean uE3 level was 1.67 MOM in the control group, while it was 1.27 MOM in the mild preeclamptic group and 1.39 MOM in the severe preeclamptic group. A significant difference was found between the control group and the mild preeclampsia group, and between the control group and the severe preeclampsia group for all three markers ($p \leq 0.001$). However, there was no statistically significant difference between the mild and severe preeclampsia groups in AFP, hCG, and uE3 levels. The second trimester screening test markers also failed to predict the severity of preeclampsia (Table 9).

The first trimester screening test was performed on 67 patients, 16 of whom were with early-onset preeclampsia and 51 were with late-onset preeclampsia. PAPP-A level was 0.84 MOM in the control group, it was 0.64 MOM in the early-onset preeclampsia group and 0.62 MOM in the late-onset preeclampsia group. The difference between the control group and the early-onset preeclampsia group and the difference between the control group and the late-onset preeclampsia group were statistically significant ($p \leq 0.001$). However, no statistically significant difference was found between the early-onset and late-onset preeclampsia groups. The mean level of free β -hCG was 1.09 MOM in the control group, while it was 1.12 MOM in the early-onset preeclampsia group and 1.04 MOM in the late-onset preeclampsia group. There was no statistically significant difference between the groups ($p=0.737$). The first trimester screening test markers failed to predict the onset week of preeclampsia. The second trimester screening test was performed on 114 patients, 29 of whom were with early-onset preeclampsia and 85 were with late-onset preeclampsia. The mean level of AFP was 0.82 MOM in the control group,

1.11 MOM in the early-onset preeclampsia group, and 1.01 MOM in the late-onset preeclampsia group. The mean level of hCG was 1.02 MOM in the control group, 1.41 MOM in the early-onset and late-onset preeclampsia group. The mean level of uE3 was 1.67 MOM in the control group, 1.42 MOM in the early-onset preeclampsia group, and 1.36 MOM in the late-onset preeclampsia group. There was a significant difference between the control group and the early-onset preeclampsia group, and between the control group and the late-onset preeclampsia group for all three markers ($p \leq 0.001$). However, there was no statistically significant difference between the early-onset and late-onset groups in AFP, hCG, and uE3 levels. The second trimester screening test markers failed to predict the onset week of preeclampsia (Table 10).

Discussion

Although the etiology of preeclampsia, which is a multisystem disease of maternal and placental origin, has not been clarified yet, it is the most emphasized mechanism of insufficiency in early trophoblastic invasion. A decrease in placental perfusion due to a defect in the trophoblastic invasion of spiral arteries, placental ischemia, oxidative stress, and imbalance between angiogenic and prothrombotic placental factors stimulate systemic maternal endothelial dysfunction. Generalized endothelial dysfunction and systemic inflammatory response cause hypertension and proteinuria, which are the characteristic symptoms of preeclampsia in the later stages of pregnancy [5]. The best and precise treatment for preeclampsia is delivery and complete removal of placenta. Although there are studies indicating that calcium supplementation, antithrombotic agents (low-dose aspirin), and antioxidants (vitamin E and vitamin C) can be used in preeclampsia prophylaxis, their protective effects have not been fully demonstrated [6,7]. The present study was based on the hypothesis that steroids and/or proteins such as PAPP-A, Hcg, AFP, Ue3 in maternal circulation in early pregnancy may be indicators of preeclampsia in late pregnancy.

In the analysis using MOM values of the first trimester screening test biochemical markers PAPP-A and free β hCG adjusted according to maternal weight, age, smoking habit, and gestational week, PAPP-A was significantly lower in the preeclamptic group, while there was no statistically significant difference between the control and the study group in free β hCG. When a level of 0.34 MOM at the 5th percentile was taken as the cut-off for free β hCG, sensitivity was found to be 11.9% with a rate of 5% false positive. It was identified that a PAPP-A level of <0.34 MOM significantly increased the risk of preeclampsia. It was concluded that PAPP-A was an effective parameter in distinguishing pregnant women with the possibility to develop preeclampsia.

In the literature, the study which was conducted by Spencer et al. compared the first trimester screening test biochemical markers of 222 preeclamptic pregnant women and 47770 controls; similar to the present study, PAPP-A was found to be significantly lower in the group with the disease, but there was no difference between the two groups in free β hCG [8]. Yaron et al. evaluated 1622 pregnant women, 27 of whom were with preeclampsia, and indicated that a PAPP-A level of <0.25 MOM showed an increasing relative risk for preeclampsia [9]. PAPP-A is a protease for insulin-like growth factor-binding protein 4

(IGFBP 4) synthesized by trophoblasts. In its deficiency, serum level increases as IGFBP cannot be destroyed in its deficiency. Increased IGFBP binds more IGF-1 and IGF-2. As free IGF decrease, it negatively affects fetal growth. Therefore, a low level of PAPP-A in the first trimester indicates insufficient placentation and/or placental function, and may predict preeclampsia that will occur in the later period of pregnancy in the first trimester.

In a study conducted by Smith et al. with a total of 8839 pregnant women, 331 of whom were with preeclampsia, PAPP-A level was found to be significantly lower in the preeclamptic group compared to the control group, while the risk of preeclampsia increased in pregnant women with PAPP-A below the 5th percentile, which is in accordance with the present study [10].

In the analysis of the second trimester screening test markers AFP, hCG and Ue3 using MOM values adjusted according to maternal age, smoking habit, and gestational age, the results were in accordance with the literature. Among the triple scanning markers, uE3 was the parameter affecting the probability of preeclampsia the most. When AFP, hCG and uE3 values were combined, it was concluded that preeclamptic pregnant could be predetermined with a specificity level of 93.8%, a sensitivity level of 36.8%, and a negative predictive value of 81.5%.

Specificity increased to 96.3%, sensitivity to 60.9%, and negative predictive value to 92% when the double and triple screening tests were combined to predict preeclampsia. Marker uE3 (wald=28.71) was the most predictive of preeclampsia development and PAPP-A was the least predictive (wald=4.19). In the literature, Kang et al., who combined these tests in predicting preeclampsia, found a sensitivity level of 41% and a specificity level of 95% in the combined test.

The present study also aims to determine the relation between the first and second trimester Down syndrome biochemical markers and the week, and the severity of preeclampsia. When the mild and severe preeclampsia groups were compared, it was concluded that there was no significant difference between the groups in the first and second trimester screening test biochemical markers, and that these markers failed to predict the severity of preeclampsia. In a study conducted by Kang et al., it was concluded that there was no significant difference between the mild and severe preeclampsia groups in PAPP-A, hCG and AFP level, which was similar to the results of the present study [11].

When the early-onset and late-onset preeclampsia groups were compared, it was concluded that there was no significant difference between the groups in the first and second trimester screening test biochemical markers, and that these markers failed to predict the onset week of preeclampsia. In a study conducted by Poon et al. on 34 early-onset and 123 late-onset preeclamptic pregnant women, it was identified that PAPP-A level was significantly lower in the early-onset preeclampsia group, and stated that PAPP-A levels were higher than the early-onset group as the late-onset preeclampsia was not related to insufficient placentation [12].

In conclusion, the study results show that the first trimester maternal serum PAPP-A level is significantly low in preeclamptic pregnant women, and that the second trimester maternal serum AFP and hCG levels

are significantly high and uE3 levels are significantly low The results also suggest that the first and second trimester Down syndrome biochemical markers can be used in preeclampsia screening. Among these markers, uE3 is the parameter which affects the possibility of preeclampsia the most. However, the first and second trimester Down syndrome biochemical markers are not effective in predicting the severity and onset week of preeclampsia.

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Tables

Table 1. Demographic data

Variables	Control Group (n:366)	Patient Group (n: 135)	p
Age	27,1±5,4	27,1±6,2	0,955 ^a
Maternal weight	64,8±11,4	74,5±12,5	<0,001 ^c
Parity			<0,001 ^b
<i>Primigravid</i>	157 (%42,9)	90(%67,2)	
<i>Multigravid</i>	209 (%57,1)	44 (%32,8)	
Smoking	32 (%8,7)	9 (%6,7)	0,452 ^b
Intermarriage	51 (%13,9)	10 (%7,4)	0,047 ^b
Birth week	38,8±1,4	35,3±3,7	<0,001 ^c
Type of birth			<0,001 ^b
<i>NVB</i>	206 (%56,3)	39 (29,3)	
<i>C/S</i>	160 (%43,7)	94 (%70,7)	
Birth weight	3413,7±415,7	2275,7±871,7	<0,001 ^c
NICU requirement	30 (%8,2)	67 (%50,4)	<0,001 ^b

a Student's t test. **b** Pearson's chi square test. **c** Mann Whitney U test.

Table 2. Biochemical marker levels by double screening test according to groups

Variables	Control Group	Patient Group	p
Dual scan test	n=243	n=67	
PAPP-A	0,84 (0,23-2,69)	0,63 (0,25-2,37)	<0,001 ^a
free-β-hCG	1,09 (0,17-3,77)	1,04 (0,31-3,84)	0,925

1. Mann Whitney U test

Table 3. The cut-off points of the biochemical markers (5% false positivity) and the sensitivity, positive and negative predicted value levels of the double and triple screening test in predicting preeclamptic cases.

Variables	Sensitivity	Selectivity	PPV	NPV
PAPP-A (<0,345)	%11,9	%95,1	%40,0	%79,7
AFP (>1,475)	%21,1	%95,0	%58,5	%78,2
hCG (>2,415)	%25,4	%95,0	%58,5	%79,1
uE3 (<1,065)	%27,2	%95,0	%64,6	%79,5

PPV: Pozitive predictive value, NPV: Negative predictive value.

Table 4. The area under the curve and the 95% confidence interval for the double-screening test biochemical marker levels to differentiate between control and patient groups

Variables	AUC (%95 CI)	p
Dual screening test		
PAPP-A	0,687 (0,616-0,758)	<0,001
free- β -hCG	0,504 (0,423-0,584)	0,925

AUC: Area under the curve, CI: Confidence interval

Table 5. Effects of binary and triple test components on the development of preeclampsia according to multivariate logistic regression analysis

Independent variables	Odds ratio (OR)	Wald	p	%95 Güven	
				Alt sınır	Üst sınır
PAPP-A (<0,345)	2,610	4,009	0,045	1,020	6,676
AFP (>1,475)	3,811	12,713	<0,001	1,827	7,950
hCG (>2,415)	3,849	13,634	<0,001	1,882	7,871
uE3 (<1,065)	6,573	30,370	<0,001	3,365	12,842

Table 6. Triple screening test biochemical marker levels by groups

Variables	Control group	Patient group	p
Triple screening test	n=339	n=114	
AFP	0,82 (0,33-1,68)	1,03 (0,44-3,26)	<0,001 ^a
hCG	1,02 (0,20-3,60)	1,41 (0,28-4,85)	<0,001 ^a
uE3	1,67 (0,73-3,29)	1,37 (0,40-3,65)	<0,001 ^a

Mann Whitney U test.

Table 7. The area under the curve of the triple screening test biochemical markers and 95% confidence interval levels to differentiate between control and case groups

Variables	AUC (%95 CI)	p
Triple screening test		
AFP	0,674 (0,617-0,732)	<0,001
hCG	0,684 (0,626-0,742)	<0,001
uE3	0,684 (0,621-0,746)	<0,001

AUC: Area under the curve, CI: Confidence interval

Table 8. Combined effects of binary and triple test components on the development of preeclampsia according to multivariate logistic regression analysis

Independent variables	Odds ratio (OR)	Wald	p	%95 Confidence interval (OR)	
				lower limit	upper limit
PAPP-A (<0,345)	3,835	4,191	0,041	1,059	13,892
AFP (>1,475)	19,656	16,009	<0,001	4,570	84,549
hCG (>2,415)	5,633	9,266	0,002	1,851	17,147
uE3 (<1,065)	25,429	28,715	<0,001	7,786	83,051

Table 9. Kontrol, hafif ve şiddetli preeklampsi gruplarına göre ikili ve üçlü tarama testi biyokimyasal marker düzeyleri

Variables	Control group	Mild preeclampsia	Severe preeclampsia	p
Dual screening test	n=243	n=38	n=29	
PAPP-A	0,84 (0,23-2,69) ^{b,c}	0,68 (0,25-1,79) ^b	0,62 (0,31-2,37) ^c	<0,001 ^a
free-β-hCG	1,09 (0,17-3,77)	0,96 (0,31-3,84)	1,14 (0,36-2,25)	0,594 ^a
Triple screening test	n=339	n=58	n=56	
AFP	0,82 (0,33-1,68) ^{b,c}	1,10 (0,55-3,26) ^b	0,99 (0,44-2,49) ^c	<0,001 ^a
hCG	1,02 (0,20-3,60) ^{b,c}	1,47 (0,28-4,61) ^b	1,26 (0,44-4,85) ^c	<0,001 ^a
uE3	1,67 (0,73-3,29) ^{b,c}	1,27 (0,58-3,65) ^b	1,39 (0,40-3,36) ^c	<0,001 ^a

1. Kruskal Wallis,

2. The difference between the control group and mild preeclampsia group was statistically significant. (p<0,001),

3. The difference between the control group and severe preeclampsia group was statistically significant. (p<0,001)

Table 10. Kontrol, erken ve geç başlangıçlı preeklampsi gruplarına göre ikili ve üçlü tarama testi biyokimyasal marker düzeyleri

Variables	Control group	Early preeclampsia	Late Preeclampsia	p
Dual screening test	n=243	n=16	n=51	
PAPP-A	0,84 (0,23-2,69) ^b	0,64 (0,28-2,37)	0,62 (0,25-1,79) ^b	<0,001 ^a
free-β-hCG	1,09 (0,17-3,77)	1,12 (0,35-3,849)	1,04 (0,31-2,25)	0,737 ^a
Triple screening test	n=339	n=29	n=85	
AFP	0,82 (0,33-1,68) ^{b,c}	1,11 (0,46-2,36) ^c	1,01 (0,44-3,26) ^b	<0,001 ^a
hCG	1,02 (0,20-3,60) ^{b,c}	1,41 (0,44-4,61) ^c	1,41 (0,28-4,85) ^b	<0,001 ^a
uE3	1,67 (0,73-3,29) ^{b,d}	1,42 (0,40-2,93) ^d	1,36 (0,58-3,65) ^b	<0,001 ^a

1. Kruskal Wallis

2. The difference between the control group and late preeclampsia group was statistically significant. (p<0,001).
3. The difference between the control group and early preeclampsia group was statistically significant. (p<0,001).

Figures

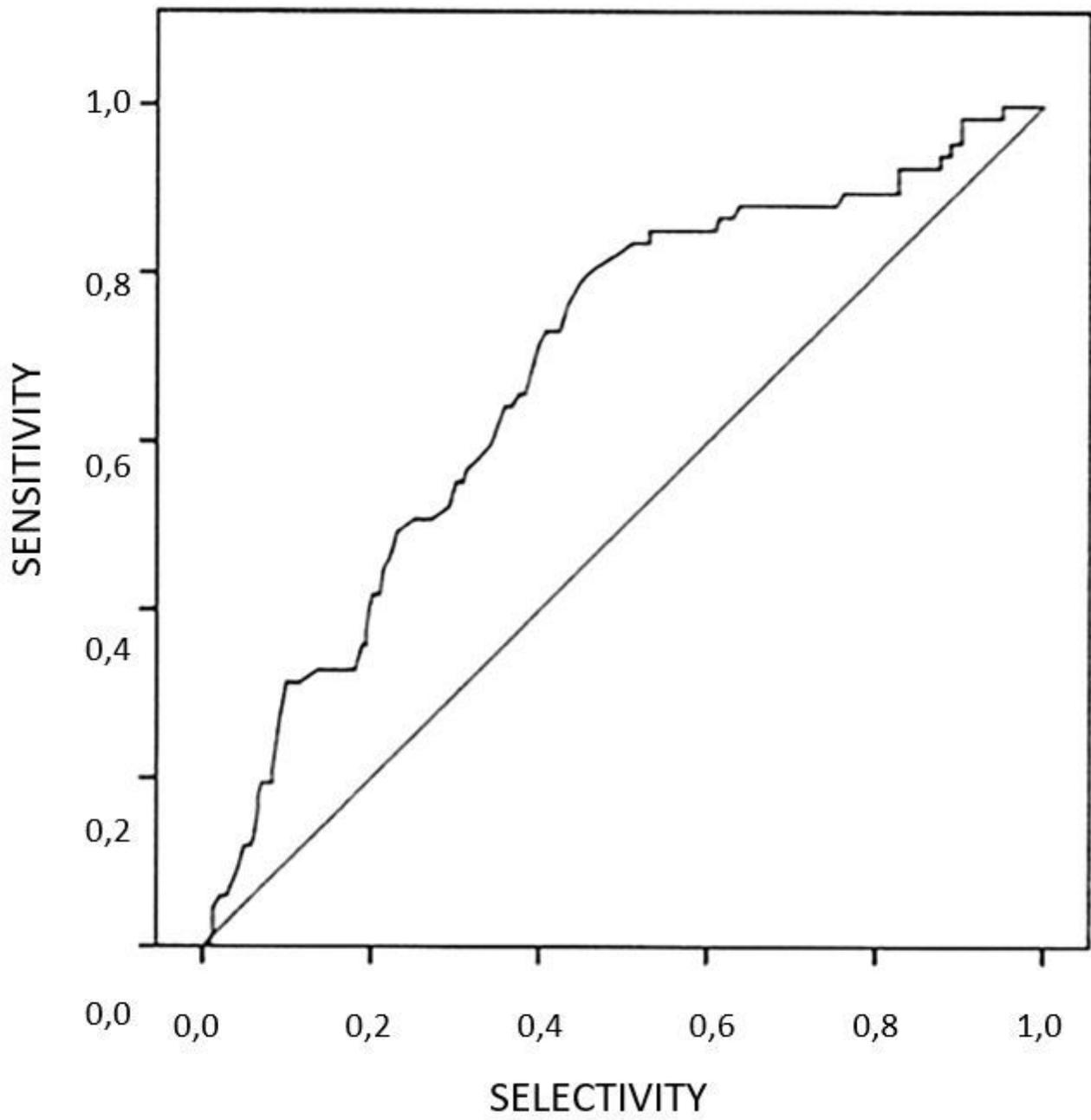


Figure 1

ROC curve for serum PAPP-A levels

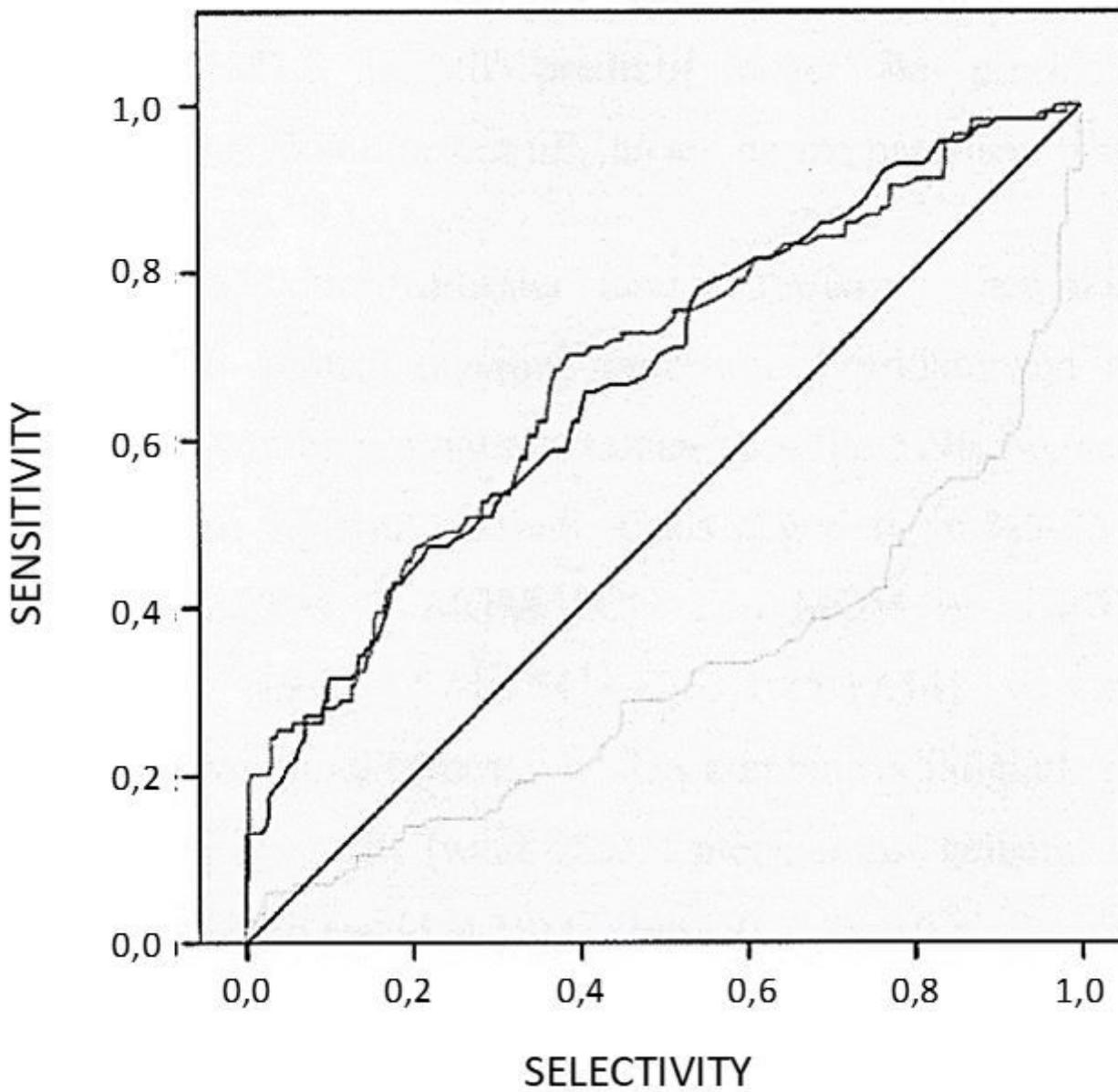


Figure 2

ROC curve for serum AFP, hCG, uE3 levels