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Evaluation of preeclampsia outcomes in de novo preeclampsia and superimposed preeclampsia: A case-control study from a tertiary center

De novo preeklampsi ve süperempoze preeklampside preeklampsi sonuçlarının değerlendirilmesi: Üçüncü basamak bir merkezden vaka kontrol çalışması

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ABSTRACT

Aim: To compare de novo and superimposed preeclampsia outcomes and evaluate the role of chronic hypertension in preeclampsia outcomes

Materials and Method: The present retrospective case-control study was conducted on 250 pregnant women diagnosed with preeclampsia, including 100 patients in the superimposed preeclampsia group and 150 in the de novo preeclampsia group. The control group comprised 200 low-risk pregnant women consecutively delivered in the same timeline. The demographic specialties and obstetric and neonatal outcomes of the de novo and superimposed preeclampsia groups were compared with the control group and also between preeclampsia groups. Parameters were then evaluated using the literature findings.

Results: Early onset preeclampsia and preterm delivery rates were higher in the superimposed preeclampsia group, with p-values of 0.046 and 0.026, respectively. Prodromal symptoms were lower in the superimposed preeclampsia group than in the de novo preeclampsia group (p=0.029). Fetal growth retardation was higher in both preeclampsia groups than in the control group, with a p-value of <0.001. Severe preeclampsia rates were similar in the preeclampsia groups, with a p-value of 0.278.

Conclusion: The presented study showed in a single tertiary center experience that chronic hypertension is an individual risk factor for early-onset preeclampsia occurrence and preterm delivery. Because the prodromal symptoms are seen less in a superimposed preeclampsia group than in the de novo preeclampsia group, obstetricians must be careful with severe preeclampsia in such a specific patient group.

Keywords: Superimposed preeclampsia outcomes; preeclampsia outcomes; adverse outcomes; chronic hypertension

ÖZ

Amaç: De novo ve superempoze preeklampsi sonuçlarını karşılaştırmak ve kronik hipertansiyonun preeklampsi sonuçlarındaki rolünü değerlendirmek.

Gereçler ve Yöntem: Mevcut retrospektif vaka-kontrol çalışması, 100'ü süperempoze preeklampsi grubunda, 150'si de novo preeklampsi grubunda olmak üzere, preeklampsi tanısı alan 250 hamile kadın üzerinde gerçekleştirildi. Kontrol grubu, aynı zaman aralığında ardı ardına doğum yapan 200 düşük riskli hamile kadından oluşuyordu. De novo ve süperempoze preeklampsi gruplarının demografik özellikleri, obstetrik ve neonatal sonuçları kontrol grubu ile karşılaştırıldı. Sonuçlar preeklampsi subgrupları arasında da karşılaştırıldı ve daha sonra parametreler literatür bulgularıyla birlikte değerlendirildi.

Bulgular: Erken başlangıçlı preeklampsi ve erken doğum oranları, süperempoze preeklampsi grubunda p değerleri sırasıyla 0,046 ve 0,026 ile daha yüksekti. Prodromal semptomların varlığı, süperempoze preeklampsi grubunda de novo preeklampsi grubuna göre daha düşüktü (p=0,029). Fetal büyüme geriliği her iki preeklampsi grubunda da p değeri <0,001 ile kontrol grubuna göre daha yüksekti. Şiddetli preeklampsi oranları preeklampsi gruplarında p değeri 0,278 ile benzerdi.

Sonuç: Sunulan çalışma, üçüncü basamak tek merkez deneyiminde, kronik hipertansiyonun erken başlangıçlı preeklampsi oluşumu ve erken doğum için bağımsız bir risk faktörü olduğunu göstermiştir. Süperempoze preeklampsi grubunda prodromal semptomlar de novo preeklampsi grubuna göre daha az görüldüğü için, bu spesifik hasta grubunda şiddetli preeklampsi konusunda kadın doğum uzmanlarının dikkatli olması gerekmektedir.

Anahtar Kelimeler: Süperempoze preeklampsi, preeklampsi sonuçları, olumsuz gebelik sonuçları, kronik hipertansiyon

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INTRODUCTION

Preeclampsia is accepted as a pregnancy-specific multisystem disorder accompanied by hypertension, permeability increase, and microvascular thrombosis (1). Preeclampsia prevalence is 5-8% and is the leading cause of both fetal and maternal morbidity and also mortality (2). There are two possible ways in which it can occur: in previously healthy women by de novo preeclampsia or pregnancies with chronic hypertension called superimposed preeclampsia (3).

Prediction of de novo preeclampsia in healthy pregnancies before it occurs is challenging. Some risk factors for having preeclampsia in pregnancies were determined, and high-risk pregnancies are defined by ACOG guidelines (4). Recently, studies have been continuing to predict and prevent preeclampsia, focusing on clinical and laboratory markers. However, the only preventive situation whose effectiveness is accepted today is starting aspirin from 12 weeks onwards in patients with risk factors and performing appropriate blood pressure and pregnancy checks (5).

Chronic hypertension has become one of the most frequent diseases seen in the reproductive age, with increasing maternal age. All chronic hypertension patients are candidates for superimposed preeclampsia. Superimposed preeclampsia develops in up to 30% of chronic hypertensive pregnancies. Diagnosis is made by new onset of proteinuria or worsening preexisting proteinuria, blood pressure control, and/or laboratory abnormalities (3). Generally, superimposed preeclampsia occurs earlier and is more severe than preeclampsia without chronic hypertension etiology.

Prevention and prediction of superimposed preeclampsia before it develops is a major task for obstetricians. None of the laboratory or ultrasonography findings has specified the prediction of superimposed preeclampsia occurring in patients with chronic hypertension. The only preventive choice, similar to de novo preeclampsia, is accepted as starting aspirin from 12 weeks onwards in patients with chronic hypertension and performing appropriate blood pressure control with appropriate medication. The termination of pregnancy is the only effective way of certain treatment.

This study hypothesized and evaluated whether the underlying gestational or chronic hypertension has a determining effect on pregnancy outcomes in pregnant women with preeclampsia who were followed up in the same tertiary center and managed in the same manner.

MATERIAL AND METHODS

The present retrospective case-control study was conducted on pregnant women with preeclampsia and low-risk pregnant women as the control group. Patient demographic information and neonatal-obstetric outcomes were taken from the hospital database. Patients with preeclampsia and delivered between January 2021 - June 2023, having a singleton pregnancy, maternal age between 18-45 years, and no chronic systemic diseases except for hypertension were included in the study. Patients were categorized according to having de novo preeclampsia or superimposed preeclampsia. The control group comprised 200 low-risk pregnant women consecutively delivered in the same timeline. Chronic hypertension diagnosed before mid-pregnancy with a new onset of proteinuria or worsening preexisting proteinuria, blood pressure control, and/or laboratory abnormalities was defined as superimposed preeclampsia. New-onset hypertension after mid-pregnancy with accompanying either proteinuria or end-organ failure was defined as de novo preeclampsia. Severe preeclampsia criteria were determined based on ACOG guidelines (6). Severe headache, visual disturbance and epigastric pain were defined as prodromal symptoms. All high-risk patients in the de novo group and those in the superimposed preeclampsia group were given acetylsalicylic acid prophylaxis. All severe preeclampsia-diagnosed patients were administered magnesium sulfate treatment for eclampsia prevention. Preeclampsia development before 34 weeks was accepted as early-onset preeclampsia as in the literature (7). This study was approved by the "Institutional Review Board of the University of Health Sciences Turkey, Ankara Bilkent City Hospital Ethics Committee" (approval number: E2-24-6138).

Hypertensive patients were followed closely and multidisciplinary by cardiology and perinatology departments with appropriate antihypertensive treatments for blood pressure, proteinuria, and laboratory abnormalities.

Preeclampsia and superimposed preeclampsia groups' demographic specialties and obstetric and neonatal outcomes were compared between groups. Parameters were then compared with the literature.

The statistical analyses used IBM Inc., Armonk, NY, USA's Statistical Package for the Social Sciences version 23. All descriptive statistics were presented as the mean and standard deviations (SD) due to the consistency with a normal distribution. The ANOVA test was used to compare the parameters between the groups. Categorical variables were presented as numbers and percentages. Statistical significance was a two-tailed P value of 0.05 with a 95% confidence interval.

RESULTS

The study was conducted on 150 patients with de novo preeclampsia, 100 patients with superimposed preeclampsia, and 200 low-risk pregnant women in the control group. Demographic parameters were similar between de novo preeclampsia and control groups. However, maternal age and gravida were higher in the superimposed preeclampsia group compared to the control group. Maternal demographic characteristics of groups are shown in Table 1.

Adverse neonatal outcomes were all found to be statistically higher both in de novo preeclampsia and in the superimposed preeclampsia groups compared to the control group. The only statistical difference observed between preeclampsia and superimposed preeclampsia was gestational age at birth. Neonatal outcomes characteristics of groups are shown in Table 2.

When the groups were evaluated according to the obstetric outcomes, neonatal invasive care unit admission and fetal growth retardation ratios were higher in both preeclampsia groups than in the control group. Early onset preeclampsia was higher in the superimposed preeclampsia group, and the presence of prodromal symptoms was lower than in the de novo preeclampsia group. Obstetric outcomes characteristics of groups are shown in Table 3.

Other obstetric complications seen in preeclampsia groups were placenta abruption, fetal demise, posterior reversible encephalopathy syndrome (PRESS), sinus vein thrombosis, and the need for re-laparotomy. The distribution of these complications in groups is presented below.

In the preeclampsia group, there were three placenta abruption cases in which two fetuses died intrauterine. Also, 1 PRESS, one pleural effusion, and one sinus vein thrombosis cases were observed, and two patients were gone to re-laparotomy because of post-operation intra-abdominal bleeding.

In the superimposed preeclampsia group, there was one PRESS syndrome, two patients with superficial infections and hematomas of incision, and two patients who went to re-laparotomy because of post-operation intra-abdominal bleeding.

Table 1. Maternal demographic characteristics and laboratory findings

Variable (Maternal indices)	Control group (n=200)	De novo Preeclampsia group (n=150)	Superimposed Preeclampsia group (n=100)	P value	P value[a]	P value[b]	P value[c]
Maternal age (years)	27.67 (5.33)	28.85 (5.96)	31.36 (5.99)	<0.001	0.134	<0.001	0.002
Gravidity	2.18 (1.26)	2.35 (1.70)	2.89 (1.81)	<0.001	0.537	0.001	0.021
Parity	1.00 (1.06)	0.89 (1.13)	1.30 (1.29)	0.018	0.627	0.081	0.014
Living Child	0.98 (1.05)	0.85 (1.12)	1.26 (1.25)	0.019	0.575	0.096	0.014

*All variables were presented as means and standard deviations (SD). P value[a], between control and De novo Preeclampsia groups; P value[b], between control and superimposed preeclampsia groups; P value[c], between superimposed preeclampsia and De novo Preeclampsia groups

Table 2. Neonatal Outcomes

Variable	Control group (n=200)	De novo Preeclampsia group (n=150)	Superimposed Preeclampsia group (n=100)	P value	P value[a]	P value[b]	P value[c]
Gestational age at birth. (weeks)	38.74 (1.23)	34.41 (4.06)	33.38 (3.77)	<0.001	<0.001	<0.001	0.026
Fetal birth weight. (g)	3281.58 (381.58)	2214.01 (950.60)	2085.35 (909.06)	<0.001	<0.001	<0.001	0.371
APGAR. first-minute	7.60 (0.59)	6.31 (1.99)	6.31 (1.48)	<0.001	<0.001	<0.001	1.00
APGAR. fifth-minute	8.95 (0.49)	7.97 (1.83)	8.07 (1.33)	<0.001	<0.001	<0.001	0.827

*All variables were presented as means and standard deviations (SD). P value[a], between control and De novo Preeclampsia groups; P value[b], between control and superimposed preeclampsia groups; P value[c], between superimposed preeclampsia and De novo Preeclampsia groups

Table 3. Obstetric Outcomes

Variable	Control group (n=200)	De novo Preeclampsia group (n=150)	Superimposed Preeclampsia group (n=100)	P value	P value[a]	P value[b]	P value[c]
NICU. %	14 (7.0)	82 (54.7)	52 (52.0)	<0.001	<0.001	<0.001	0.679
FGR. %	6 (3.0)	20 (13.3)	14 (14.0)	<0.001	<0.001	<0.001	0.880
Oligohydramnios. %	16 (8.0)	15 (10.0)	4 (4.0)	0.368	0.560	0.325	0.079
PPROM. %	3 (1.5)	6 (4.0)	3 (3.0)	0.347	0.144	0.382	0.678
Early preeclampsia. %	-	46 (30.7)	43 (43.0)	-	-	-	0.046
Severe preeclampsia. %	-	78 (52.0)	45 (45.0)	-	-	-	0.278
HELLP. %	-	15 (10.0)	10 (10.0)	-	-	-	1.000
Prodromal symptom	-	40 (26.7)	15 (15.0)	-	-	-	0.029
Eclampsia	-	4 (2.7)	3 (3.0)	-	-	-	0.876

* Categorical variables were presented as numbers (percentages). P value[a], between control and De novo Preeclampsia groups; P value[b], between control and superimposed preeclampsia groups; P value[c], between superimposed preeclampsia and De novo Preeclampsia groups. NICU, neonatal intensive care unit; FGR, fetal growth retardation; PPROM, preterm premature rupture of membranes; HELLP, hemolysis, elevated liver enzymes and low platelet.

DISCUSSION

The presented study showed in a single tertiary center experience that chronic hypertension etiology is an individual risk factor for early preeclampsia occurrence and preterm delivery. There are limited studies in the literature on the prevention of superimposed preeclampsia. In a systematic review, acetylsalicylic acid was found to be neither beneficial in preventing superimposed preeclampsia nor decreasing the early onset preeclampsia (8). In this study, all patients in the superimposed preeclampsia group and high-risk patients in the de novo preeclampsia group were used acetylsalicylic acid and managed with similar hospital manner for both delivery decision and control on hypertension but early preeclampsia and preterm delivery rates were higher in superimposed preeclampsia group, similar with the literature findings. In early onset preeclampsia, patients were followed by appropriate antihypertensive treatment and fetal ultrasound and Doppler findings. Delivery decisions were taken in uncontrolled hypertensive patients and fetal distress conditions in line with guidelines.

In the presented study, severe preeclampsia, HELLP, and eclampsia rates were similar in both preeclampsia groups. In contrast to the presented research, severe preeclampsia and eclampsia rates were found to be higher in the literature (9). This difference may occur from following all patients by the perinatology unit, managing them meticulously, and giving magnesium sulfate treatment as eclampsia prevention to all severe preeclampsia cases for 24 hours.

Prodromal symptoms like headache, visual disturbance, epigastric pain, etc., were seen significantly lower in the superimposed preeclampsia group than in the de novo group. This situation may be explained by the fact that the preeclampsia group is more sensitive to hypertension symptoms because of the no exposure to hypertension without pregnancy.

De novo preeclampsia was higher in nulliparous patients, and superimposed preeclampsia was higher in advance-aged pregnancies and multiparous patients as convenience with the literature (10,11).

Neonatal outcomes for APGAR scores, gestational weeks at birth, birth weights, and admission to the neonatal invasive care unit were similar and higher in both preeclampsia groups than in the control group in convenience with the literature (9, 12, 13).

Fetal growth retardation rates were higher in both preeclampsia groups than in the control group. However, oligohydramnios was not an accompanying condition of the same severity and were similar in all groups. In the literature, in many studies, fetal growth retardation and accompanying oligohydramnios was found as a result of preeclampsia (14, 15).

Other pregnancy complications like placenta abruption, intrauterine fetal demise, posterior reversible encephalopathy syndrome, or sinus vein thrombosis were not higher in the superimposed preeclampsia group. In the literature, superimposed preeclampsia patients were found to be at more risk than preeclampsia patients for per partum complications, such as placental abruption and cerebrovascular incidents (3). Conversely to the literature, all abruption cases, the sinus vein thrombosis case, and fetal demises were seen in the de novo preeclampsia group.

The presented study is one of the few studies that evaluate preeclampsia outcomes compared to de novo and superimposed preeclampsia. In the literature, many studies about preeclampsia etiology point out that the inflammatory processes occur before the clinical diagnosis of the disease. The literature demonstrated an increased inflammatory process for preeclampsia in the first trimester (16). It is known that placental insufficiency and hypertension secondary to defective trophoblastic invasion develop in preeclampsia (17). This study evaluated the effect of underlying chronic hypertension on preeclampsia outcomes when external variables were excluded as much as possible and where gestational hypertension was monitored and managed most appropriately in the tertiary center. It has been shown that early-onset preeclampsia is more common in patients with chronic hypertension. This finding indicates that the underlying chronic hypertension condition plays a determining and accelerating role in the process leading to preeclampsia. Further studies are needed for this purpose.

The present study's strengths were being a referral center for managing preeclampsia and having obstetric and neonatal outcomes for all preeclampsia patients. Its limitations were its single-center retrospective study design and limited patient numbers.

CONCLUSION

In light of this study's findings, chronic hypertension is an individual risk factor for early-onset preeclampsia. Because the prodromal symptoms are seen less in a superimposed preeclampsia group than in the de novo preeclampsia group, obstetricians must be careful with severe preeclampsia and the faster eclampsia process in such a valuable patient group.

Ethics Committee Approval

This study was approved by the "Institutional Review Board of the University of Health Sciences Turkey, Ankara Bilkent City Hospital Ethics Committee" (approval number: E2-24-6138).

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Conflict of interests

The authors have no conflicts of interest.

REFERENCES

1. Lyall, F. and I.A. Greer, Pre-eclampsia: a vascular disorder of pregnancy. J Hypertens, 1994. 12(12): p. 1339-45.
2. Chaiworapongsa, T., et al., Pre-eclampsia part 1: current understanding of its pathophysiology. Nat Rev Nephrol, 2014. 10(8): p. 466-80.
3. Garovic, V.D., The role of angiogenic factors in the prediction and diagnosis of preeclampsia superimposed on chronic hypertension. Hypertension, 2012. 59(3): p. 555-7.
4. Gestational Hypertension and Preeclampsia: ACOG Practice Bulletin, Number 222. Obstet Gynecol, 2020. 135(6): p. e237-e260.
5. ACOG practice bulletin. Diagnosis and management of preeclampsia and eclampsia. Number 33, January 2002. American College of Obstetricians and Gynecologists. Int J Gynaecol Obstet, 2002. 77(1): p. 67-75.
6. ACOG Practice Bulletin No. 202: Gestational Hypertension and Preeclampsia. Obstet Gynecol, 2019. 133(1): p. 1.
7. Lisonkova, S. and K.S. Joseph, Incidence of preeclampsia: risk factors and outcomes associated with early- versus late-onset disease. Am J Obstet Gynecol, 2013. 209(6): p. 544.e1-544.e12.
8. Richards, E.M.F., et al., Low-dose aspirin for the prevention of superimposed preeclampsia in women with chronic hypertension: a systematic review and meta-analysis. Am J Obstet Gynecol, 2023. 228(4): p. 395-408.
9. Boneh, H.R., et al., Superimposed versus de novo pre-eclampsia: Is there a difference? Int J Gynaecol Obstet, 2022. 159(2): p. 392-397.
10. Melchiorre, K., V. Giorgione, and B. Thilaganathan, The placenta and preeclampsia: villain or victim? Am J Obstet Gynecol, 2022. 226(2s): p. S954-s962.
11. Saftlas, A.F., et al., Abortion, changed paternity, and risk of preeclampsia in nulliparous women. Am J Epidemiol, 2003. 157(12): p. 1108-14.
12. Backes, C.H., et al., Maternal preeclampsia and neonatal outcomes. J Pregnancy, 2011. 2011: p. 214365.
13. Büyükeren, M., et al., Neonatal outcomes of early- and late-onset preeclampsia. Turk J Pediatr, 2020. 62(5): p. 812-819.
14. Magro-Malosso, E.R. and G. Saccone, Exercise during pregnancy and risk of gestational hypertensive disorders: a systematic review and meta-analysis. 2017. 96(8): p. 921-931.
15. August, P., et al., A prediction model for superimposed preeclampsia in women with chronic hypertension during pregnancy. Am J Obstet Gynecol, 2004. 191(5): p. 1666-72.
16. Sacks, G.P., et al., Maternal C-reactive protein levels are raised at 4 weeks gestation. Hum Reprod, 2004. 19(4): p. 1025-30.
17. Zhou, W. and H. Wang, Trophoblast Cell Subtypes and Dysfunction in the Placenta of Individuals with Preeclampsia Revealed by Single-Cell RNA Sequencing. 2022. 45(5): p. 317-328.