Obstetrics; *Maternal-Fetal Medicine and Perinatology*

Evaluation of Hypertension and Renal Function in Preeclamptic Women: A Follow-Up Study at 6th Week of Postpartum

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ABSTRACT

OBJECTIVES: Chronic hypertension stands as the primary contributing factor for cardiovascular ailments among women who have experienced preeclampsia. The purpose of this research is to examine how often preeclamptic symptoms persist at the postpartum 6th week.

STUDY DESIGN: This prospective cohort study included 50 singleton pregnant women in the third trimester who were diagnosed with preeclampsia according to ACOG criteria, were older than 18 years, had no known hypertension before the 20th gestational week, had no additional systemic disease, did not use medication, had no fetal chromosomal or structural abnormalities and delivered within 24-48 hours of hospitalization.

RESULTS: The mean age of preeclamptic pregnant patients was 29.26±7.15 years, the mean gestational week was 35.6±2.8, and the mean BMI was 31.3±4.9. Twenty (40%) of 50 preeclamptic patients had severe preeclampsia. The mean decrease in systolic blood pressure was 34.6±15.2 mmHg, while the mean decrease in diastolic blood pressure was 22.88±11.68 mmHg (p<0.001). The decrease in systolic and diastolic blood pressure at postpartum 6th week was statistically significant. The mean change in 24-hour urine protein value at postpartum 6th week was 2313.52 ± 2696.48 and the difference was statistically significant (p<0.001). There were 14 patients (28%) with persistent hypertension and 19 patients (38%) with persistent proteinuria.

CONCLUSIONS: Although preeclampsia is considered a complication of pregnancy, persistent hypertension, and proteinuria after delivery show us that preeclampsia is a disease that threatens maternal health even after delivery. These women should be followed up long-term period.

Keywords: Hypertension, Preeclampsia, Proteinuria, Renal function

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Introduction

Preeclampsia is one of the most important and common diseases in obstetrics. Although many studies have been conducted on it, its pathogenesis has not yet been sufficiently elucidated. Since it can lead to mortality and significant morbidities, clinical studies are ongoing to better understand its pathogenesis. The fact that preeclampsia may involve all body systems, especially the cardiovascular and renal systems, to varying degrees, that it is not yet adequately predicted, and that the success rate of clinical treatment varies from person to person make the management of preeclamptic cases difficult. Preeclampsia is a serious pregnancy complication characterized by high blood pressure and damage to multiple organs, most commonly the cardiovascular and renal systems (1,2). It occurs in about 5-8% of pregnancies and can be life-threatening if not promptly diagnosed and managed (3).

Preeclampsia can damage the kidneys (4,5). The kidneys play a crucial role in maintaining fluid and electrolyte balance in the body, as well as filtering waste products from the blood. Preeclampsia can impair renal function by reducing blood flow to the kidneys and causing damage to the small blood vessels in the kidneys. One of the hallmark features of preeclampsia is proteinuria, which is the presence of excess protein in the urine (6,7) This is a result of damage to the glomeruli, which are the tiny blood vessels in the kidneys responsible for filtering the blood. The damage to the glomeruli

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can lead to a decrease in their filtration capacity and cause proteins to leak into the urine (7,8). In addition to proteinuria, preeclampsia can also cause a decrease in glomerular filtration rate (GFR), which is a measure of how well the kidneys are functioning. This reduction in GFR is thought to be a result of decreased blood flow to the kidneys and damage to the glomeruli (7). In severe cases of preeclampsia, the renal function can be severely compromised, leading to acute kidney injury (9,10). This can result in a buildup of waste products in the blood, electrolyte imbalances, and fluid overload.

Preeclampsia can also have long-term effects on the mother's health (11,12). Women who have had preeclampsia during pregnancy have a higher risk of developing cardiovascular disease later in life (13,14). The American Heart Association has recognized that a history of preeclampsia is considered a sex-specific risk factor for cardiovascular disease. Cardiovascular disease is the leading cause of mortality in women irrespective of age and ethnicity (15,16). Women with a pregnancy complicated by pre-eclampsia experience a two- to eightfold increase in the long-term risk of chronic hypertension compared with women whose pregnancy remains normotensive (17,18). Among cardiovascular risk factors, chronic hypertension is one of the most important. This suggestion emphasizes that pregnancy could provide an excellent chance to identify cardiovascular risk factors and prevent the development of cardiovascular disease in the future. They may also be at increased risk for chronic kidney disease and other health problems. In severe cases, hospitalization and delivery may be necessary to protect the mother and fetus from further harm (19). Women who have had preeclampsia during pregnancy should be closely monitored by their healthcare providers after delivery and in the years to come to detect any long-term health problems (20,21). In conclusion, preeclampsia is a serious pregnancy complication that can have significant effects on the cardiovascular and renal systems. Recently, there has been a growing awareness of the importance of short-medium-long term effects of preeclampsia in the pathophysiology of cardiovascular and renal diseases in non-pregnant adults. In the literature, the continuing effects of preeclampsia on cardiovascular and renal systems are not investigated after the postpartum period to improve its long-term management. In this study, we aimed to evaluate the changes in hypertension and kidney functions, which have a significant role in the pathophysiology and complications of preeclampsia, during the early postpartum period when the transition from pregnancy physiology to normal physiology occurs.

Material and Method

The study included 50 singleton pregnant women who were admitted to the Obstetrics and Gynecology Service of our University Hospital between September 2017 and September 2018, who were diagnosed with preeclampsia according to ACOG criteria, were older than 18 years of age, had no known hypertension before the 20th gestational week, had no additional systemic disease, did not use medication, had no fetal chromosomal or structural abnormalities, were in the third trimester and delivered within 24-48 hours of hospitalization. After the approval of the Human Research Ethics Committee of our institution, all patients participating in the study were informed in detail and informed consent was obtained (09.2017.332 on 05.05.2017) and all procedures were performed according to the Declaration of Helsinki.

After admission to the hospital, obstetric, medical, surgical, and gynecological histories were evaluated. Physical examinations were performed. Systolic and diastolic blood pressure values and body-mass index were evaluated. Body mass index (BMI) was calculated using the formula body weight (kg)/height (m^2). Blood pressure was measured from the brachial artery with an Omron M^2 digital fully automatic sphygmomanometer (Omron Healthcare; Kyoto, Japan) by placing a cuff on the right arm in a sitting position while the patient was at rest. Complete blood count, liver and renal function tests, 24-hour urine tests, routine fetal well-being assessments, and ultrasonographic fetal biometry measurements were performed in preeclamptic pregnant patients. At 6^{th} week of postpartum, during routine postpartum controls of preeclamptic patients, blood pressure was evaluated for hypertension and the results of routine blood and urine tests were compared with the prenatal results. Persistent hypertension was defined as blood pressure above 140/90 mmHg or the need to use antihypertensive agents to maintain blood pressure below 140/90 mmHg. Persistence of ≥300 mg/day proteinuria in 24-hour urine was considered persistent proteinuria.

Venous blood was drawn from the forearm of all pregnant women between 08.00 and 10.00 in the morning following a 12-hour fasting period and hemoglobin level, liver, and renal function tests were measured spectrophotometrically (Roche Diagnostic Gmbh, D-68298). 24-hour urine protein and creatinine were measured and creatinine clearance was evaluated (Cobas Integra 400/400 plus, Roche Diagnostics).

During routine postpartum follow-up of preeclamptic patients in the 6th week after delivery, blood pressure was evaluated for hypertension, and routine blood and urine tests were performed.

For statistical analysis of data, the IBM SPSS 22 program (IBM, USA) was used. The distribution of the data was analyzed by the Kolmogorov-Smirnov test. Data were expressed as mean ± standard deviation and number with percentage. A dependent sample t-test was used to compare the findings of preeclamptic patients before and 6 weeks after delivery. $p<0.05$ was considered statistically significant.

Results

In our study, 50 pregnant women with preeclampsia were

evaluated prenatally and at the 6th week of postpartum. The average age of preeclamptic patients was 29.3±7.2 years. The average gestation was 35.6 ± 2.8 weeks and average BMI was 31.3 ± 4.9. Severe preeclampsia occurred in 20 (40%) of the 50 preeclamptic patients. The statistically significant decline in both systolic and diastolic blood pressure was observed at postpartum 6th week. The average reduction in systolic blood pressure was 34.6±15.2 mmHg and the average reduction in diastolic blood pressure was 22.9±11.7 mmHg (p<0.001) (Figure 1). Additionally, there was a statistically significant elevation in platelet values (p<0.001). AST and LDH values exhibited a statistically significant decrease while no significant difference was observed in ALT values. Total protein and albumin values demonstrated a statistically significant increase (p<0.001). There was a significant decrease in BUN and uric acid values during the 6th week postpartum (p<0.001) (Table I). Also, no significant difference was observed in 24-hour urine creatine clearance calculated by the Cockroft-Gault formula (Table II). The average change in 24-hour urine protein value at the 6th week postpartum was 2313.5±2696.5 and this difference was statistically significant (p<0.001) (Figure 2). At the 6th week of postpartum, 14 patients (28%) remained hypertensive while proteinuria persisted in 19 patients (38%).

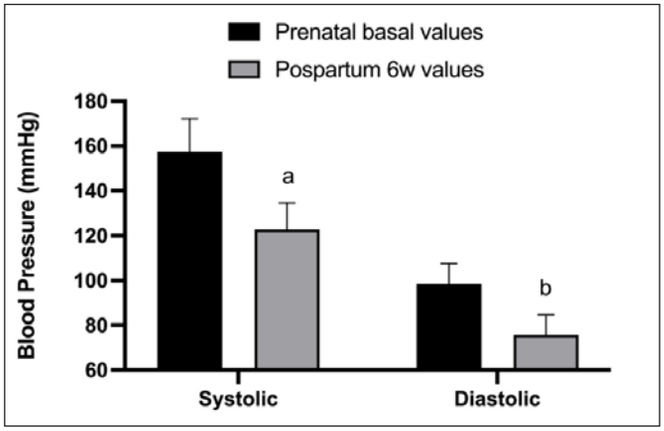

Figure 1: *Systolic and diastolic blood pressure values of the study population measured during the prenatal period and postpartum 6 weeks. a,b p<0.001 vs. prenatal baseline measurements.*

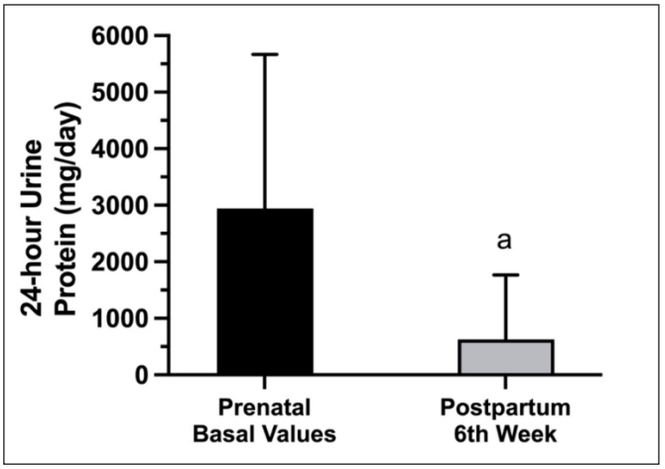

Figure 2. *24-hour urine protein values of the study population measured during the prenatal period and postpartum 6 weeks. ap<0.001 vs. prenatal baseline measurements.*

Discussion

Persistent hypertension and proteinuria after preeclampsia and eclampsia have been shown in different studies. Both may persist months or even years after delivery (22,23). Despite this, deterioration in renal function is not expected even after a short period, but data suggest that these patients are more likely to develop chronic kidney disease in their later years (24-26). In a similar study, 54 pregnant women were prospectively followed up with postpartum 1st day, 6th week, 3rd

Table I: *Selected biochemical changes in preeclamptic patients at 6 weeks postpartum.*

	Prenatal basal values	Postpartum 6-week values	p
AST (U/L)	46.1±65.1	21.5±9.3	0.012[a]
ALT (U/L)	36.4±68.5	22.3±13.3	0.173
LDH (U/L)	337.6±223.2	209.5±38.7	<0.001[b]
BUN (mg/dL)	22.3±13.3	10.1±2.9	<0.001[b]
Creatinine (mg/dL)	0.7±0.2	0.6±0.1	0.142
Uric acid (mg/dL)	6.3±1.67	5.0±1.31	<0.001[b]
Total protein (g/dL)	5.4±0.64	7.3±0.6	<0.001[b]
Albumin (g/dL)	2.6±0.4	4.2±0.4	<0.001[b]
Platelets (/µl)	193640±66545.6	298300±88089.8	<0.001[b]

Table II. *Protein and creatinine clearance in 24-hour urine at 6 weeks postpartum in preeclamptic patients.*

	Prenatal basal values	Postpartum 6-week values	p
Creatinine clearance, (mL/min) (24-hour urine)	138.9±75.7	137.2±53.7	0.889
Creatinine clearance, (mL/min) (24-hour urine) (Cockroft-Gault formula)	169.3±54.2	174.7±54.2	0.377

month, and 6th month parameters and it was shown that hypertension persisted in 42.6% (23/54) and proteinuria in 48.1% (26/54) of the patients at 6th week (9). The fact that these rates are higher than in our study may be because all of the patients included in this study had severe preeclampsia findings. Indeed, in both studies, proteinuria persisted more than hypertension at week 6. In addition, in this study, a limit value of 200 mg/day was taken for persistent proteinuria, which was estimated from the urine protein/creatine ratio. In our study, proteinuria values were measured from 24-hour urine, and a limit value of 300 mg/day was taken. In this study, hypertension was found to persist in 27.8% (23/54), 14.8% (8/54), and proteinuria in 31% (17/54) and 1.8% (1/54) at the 3rd and 6th-month follow-up. Here, it was shown that proteinuria decreased tragically by the 6th month, but hypertension persisted at a relatively higher rate.

In a study by Girsberger et al. involving the evaluation of 202 preeclampsia patients at the 6th postpartum month, it was shown that hypertension persisted in 20.3% (41/202) and proteinuria persisted in 33.1% (66/199) (21). The rate of severe preeclampsia in the trial was 67%. The persistence of proteinuria at such a high rate here is because proteinuria is defined as protein/creatine ratio >11 mg/mmol in spot urine; when the limit value was revised as 0.3 g/day, the rate of persistent proteinuria in the 6th month was 8%.

In another study by Berks et al. including 205 preeclamptic patients, it was found that hypertension persisted in 39%, 18%, and proteinuria in 14%, 2% in the 3rd month and 2nd year after delivery (23). In this study, the threshold value for proteinuria was accepted as 0.3 g/day. When we look at all these, it seems possible to say that while proteinuria tends to improve in the short term, hypertension persists for a longer period.

In terms of renal function, in our study, no significant difference was observed in GFR levels during pregnancy and at the 6th week of postpartum, it was found to be within the normal range. In the study Girsberger et al. GFR was found to be within the normal range (110 mL/min/1.73m^2) in the postpartum 6th month and was found to be low in only 1 patient (<60 mL/min/1.73m^2) (21). Thus, it can be said that a decrease in GFR in the early period after preeclampsia is rare. This coincides with the study by Vikse et al. who found the rate of end-stage renal failure to be 0.1% approximately 30 years after preeclampsia (24).

There are also some studies in the literature that examined the relationship between the amount of proteinuria in preeclamptic pregnant women and the development of chronic hypertension. In the study by Tanacan and colleagues, 126 preeclamptic pregnant women who gave birth after the 24th week of pregnancy were included in the study. They were divided into three groups based on the amount of proteinuria in a 24-hour urine collection: mild (<2g), severe (<5g), and massive (>5g) proteinuria. At postpartum week 12, the patients were reevaluated for persistent hypertension or worsening of preexisting chronic hypertension. The rates were found to be 87.5% (21/24) in the massive proteinuria group, 48.3% (14/30) in the severe proteinuria group, and 23.6% (17/72) in the mild proteinuria group (27). This study suggests that the severity of proteinuria should be considered a valuable marker for the risk of developing chronic hypertension after childbirth. Our study was limited to the 6th postnatal week, which limits our ability to comment on the extent to which hypertension becomes chronic and its relationship with proteinuria.

Generally, we obtained similar results with other studies in the literature in terms of showing that hypertension and proteinuria persisted in the early postpartum period. GFR did not differ significantly and was evaluated within normal limits in both periods. The higher rate of proteinuria compared to hypertension at 6 weeks postpartum is similar to other studies. However, the fact that hypertension persisted more and proteinuria showed a significant decrease in the following months after delivery, especially at the 6th month and beyond, as shown in most studies, limited us to make comments since our study was limited only to the 6th week.

This study supports the idea that preeclampsia should be considered a systemic disease, requiring continued monitoring and follow-up not only during pregnancy but also after delivery. Proteinuria emerges in cases where kidney functions are impaired, indicating glomerular damage. In preeclampsia, kidney functions are affected, and one of the indicative findings for diagnosis is proteinuria. In the pathophysiology of preeclampsia, hypertension is a major symptom and complication. Hypertension itself complicates vascular damage, which, in turn, affects kidney glomeruli due to capillary involvement. This intensifies glomerular damage and impairs kidney functions, making hypertension more unstable. Detecting and breaking this vicious cycle in the early stages will prevent long-term complications. Therefore, optimizing blood pressure levels in the postpartum period can have beneficial effects on the development of hypertension and improve long-term cardiovascular and renal health. Regular clinical follow-up should be recommended for these patients in the long term until the values are within normal limits.

Declarations

Ethics approval and consent to participate:

All participants signed informed written consent before being enrolled in the study The study was reviewed and approved by the ethics committee of Marmara University Clinical Research (Ethics approval reference number: 09.2017.332 date 05.05.2017). All participants were included in the study with written signed informed consent. All procedures were performed according to the Declaration of Helsinki.

Availability of data and materials

The data supporting this study can be obtained through the respective author upon a reasonable request. The datasets and

codes used and/or analyzed during the study can be obtained from the respective author upon a reasonable request.

Conflict of interest

The authors declare that there is no conflict of interest.

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Authors' contributions

Gokce Anık Ilhan and Ebru Ayguler conceived the idea and designed the study together. The data and Gokce Anık Ilhan conducted the analyses. Ebru Ayguler collected and prepared the first draft of the manuscript. All authors contributed to the writing of the article and read and approved the final version.

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