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Original Research

Adverse Outcomes of Preeclampsia in Previous and Subsequent Pregnancies and the Risk of Recurrence

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Abstract

Objectives: We evaluated the fetal and maternal outcomes of pregnant women with preeclampsia who gave birth in our hospital; we also evaluated preeclampsia recurrence rates in these patients and their fetal and maternal outcomes in their subsequent pregnancy.

Methods: In this retrospective cohort study, 126 patients whose medical records were accessed completely and who got pregnant again and gave birth in our hospital were analyzed. The primary aim was to show the recurrence rate of preeclampsia, while the secondary aim was to evaluate the maternal and fetal results of the first pregnancy in which preeclampsia developed and the subsequent pregnancy.

Results: The incidence of preeclampsia was found to be 2.1% in our clinic. The first pregnancy in which preeclampsia developed; 111 (80.2%) pregnancies resulted in a live birth, 7 (5.6%) resulted in termination, and 8 (6.3%) resulted in stillbirth. Neonatal death occurred in 10 (7.9%) pregnancies. While 105 of the subsequent pregnancies resulted in a live birth, 10 (7.9%) resulted in abortion, 9 (7.1%) resulted in stillbirth, and 2 (1.6%) resulted in termination due to preeclampsia. Neonatal death developed in 3 (2.6%) pregnancies. In the subsequent pregnancy, preeclampsia developed in 70 (55.5%) patients and 39 (55.7%) of these had preeclampsia with severe features.

Conclusion: The present study guides us on the risk factors related to preeclampsia and the rate of fetomaternal adverse outcomes and emphasizes the need for strict and regular antenatal follow-up in the subsequent pregnancies of women who have a history preeclampsia. Improvement of maternal and fetal morbidity and mortality in this way is the utmost goal.

Keywords: Preeclampsia; pregnancy outcomes; pregnancy; recurrence risk.

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Introduction

Hypertensive disorders of pregnancy are a common health problem and they are the second most common causes of maternal death worldwide.[1] Despite showing regional differences, these occur in approximately 2–8% of all pregnancies.[2] Hypertensive disorders of pregnancy can be classified as chronic hypertension, gestational hypertension, preeclampsia, and preeclampsia superimposed on chronic hypertension.[3] Preeclampsia is a multisystemic progressive

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pregnancy complication characterized by target organ damage with or without proteinuria accompanying new onset hypertension after the 20th week of pregnancy or during the postpartum period. Preeclampsia is responsible for 70% of hypertensive disorders of pregnancy and is one of the main causes of fetomaternal morbidity and mortality in pregnancy.[4] Although maternal mortality is very rare in preeclampsia patients, perinatal mortality is between 5% and 14%. These rates increase significantly when patients develop eclampsia (seizures). The gestational week in which preeclampsia begins, the severity of the disease and other accompanying medical problems are associated with the frequency of complications.[5] Maternal morbidity includes cerebrovascular damage, placental abruption, pulmonary edema, renal failure, hepatic dysfunction, recurrent seizures and Hemolysis, and Elevated Liver Enzymes and Low Platelets (HELLP) syndrome. Short-term fetal outcomes are preterm delivery and intrauterine growth retardation seen in almost 25% of cases.[6]

Maternal and fetoplacental factors that cause systemic endothelial functional disorder play a role in the pathogenesis of preeclampsia. The most important risk factor known for the development of preeclampsia is a history of preeclampsia in a previous pregnancy.[7] Apart from this, nulliparity, pregnancy at an age younger than 18 or older than 40, history of preeclampsia in the family, multiple pregnancy, molar pregnancy, ablatio placenta, chronic hypertension, obesity, renal disease, diabetes mellitus, hereditary thrombophilia, prolonged birth interval, and black race are other risk factors.[8,9] Although a large number of studies are available in the literature for early diagnosis before the clinical findings of the disease appear, the efficiency of individualized risk estimation models that try to demonstrate the significance of these risk factors has been limited because preeclampsia has heterogeneous pathophysiological mechanisms.[10]

Preeclampsia recurrence rates range between 5% and 65% in the literature.[11] This wide recurrence range results from variable sample sizes, study populations and differences in diagnostic criteria. The potential recurrence of preeclampsia is an important concern for patients, their families and health-care service providers. Revealing the risk of recurrence in women who have preeclampsia history in their previous pregnancy is important both in the clinical management of a subsequent pregnancy and in counseling patients about their future reproductive capacity.

In the present study, we evaluated the fetal and maternal outcomes of pregnant women with preeclampsia who gave birth in our hospital; we also evaluated preeclampsia recurrence rates in these patients and their fetal and maternal outcomes in their subsequent pregnancy.

Methods

The data from patients who gave birth at Kanuni Sultan Süleyman Training and Research Hospital between January 2010 and February 2015 were reviewed retrospectively from computer record systems and patient files. It was found that a total of 78485 deliveries occurred in our clinic within this period of time and that there were 1660 patients who gave birth with a diagnosis of preeclampsia. The records of these patients were examined, and it was found that there were 166 patients who got pregnant again and who gave birth in our hospital. Of these 166 patients, 126 patients whose medical records were accessed completely and who got pregnant again and gave birth in our hospital were included in the study. The patients whose pregnancies were terminated due to chronic hypertension, multiple pregnancies, and for non-preeclampsia reasons were excluded from the study. The study protocol was approved by the ethics committee of Kanuni Sultan Süleyman Training and Research Hospital (11424-2015).

Patient demographic data, obstetric history, and gestational week in which preeclampsia developed, pregnancy outcome (live birth, stillbirth, neonatal death, abortion, and termination), delivery type, fetal birth weight and gender, Apgar score, preeclampsia severity and in addition to these eclampsia, HELLP syndrome, preterm birth, the presence of intrauterine growth restriction, and maternal intensive care need data were recorded for the first pregnancy in which preeclampsia developed and for the subsequent pregnancy. The primary aim was to show the recurrence rate of preeclampsia, while the secondary aim was to evaluate the maternal and fetal results of the first pregnancy in which preeclampsia developed and the subsequent pregnancy.

Preeclampsia diagnosis was made with blood pressure ≥140/90 mmHg measured at least 2 times with an interval of 4 h or blood pressure ≥160/110 mmHg measured with an short interval (minutes) after the 20th week of pregnancy in pregnant women who were normotensive previously and with a comorbidity of proteinuria (≥300 mg/24 h urine collection or random urine sample protein/creatinine ratio ≥0.3 or protein ≥2+ in spot urine). In the absence of proteinuria, preeclampsia was defined as new-onset hypertension with the new onset of any of the following: (i) Thrombocytopenia (<100000/μL), (ii) elevated liver enzymes (at least 2 times the laboratory threshold reference value), (iii) pulmonary edema, (iv) new onset persistent headache or visual symptoms, and (v) renal

insufficiency (serum creatinine >1.1 mg/dL). The diagnosis of preeclampsia with severe features was made with ≥160/110 mmHg blood pressure in at least two measurements with an interval of 4 h and in addition to this with the coexistence of one or a few of the following conditions in patients: (i) Thrombocytopenia (<100000/μL), (ii) elevated liver enzymes (at least 2 times the laboratory threshold reference value) or by severe persistent right upper quadrant or epigastric pain, (iii) pulmonary edema, (iv) new onset persistent headache or visual symptoms, and (v) renal insufficiency (serum creatinine >1.1 mg/dL). Tonic-clonic focal or multifocal seizures after a preeclampsia diagnosis in a patient who did not have any previous neurological problem were evaluated as eclampsia. In the diagnosis of HELLP syndrome, the criteria of ≥600 IU/L lactate dehydrogenase, at least a two-fold increase in liver function tests and thrombocyte count <100000 μL were used.[12]

Statistical Analysis

Descriptive statistical methods were used in the statistical evaluation of the study data. The data are expressed in mean±standard deviation and number (percentage). Pregnancy complications and the distribution of some of the data were expressed using percentages. Statistical analysis was conducted using SPSS Version 20.0 (SPSS Inc. Chicago, USA).

Results

A total of 78485 births occurred in our hospital between January 2010 and February 2015 and preeclampsia occurred in 1660 of these pregnancies. The incidence of preeclampsia was found to be 2.1% in our clinic. The average age of the 126 patients in the pregnancy in which preeclampsia developed was found to be 27.17±5.57 years and the nulliparous patient rate was 65.9% (83 patients). Average gestational week of preeclampsia diagnosis was 33.16±4.6 and preeclampsia with severe features was found to develop in 105 (83.3%) patients. In addition, eclampsia developed in 3 (2.4%) and HELLP syndrome developed in 13 (10.3%) patients in the study group, while maternal intensive care needs developed in 5 (3.9%) patients. No maternal mortality was observed. Although 111 (80.2%) pregnancies resulted in a live birth, 7 (5.6%) resulted in termination and 8 (6.3%) resulted in stillbirth. It was found that 38 (30.2%) of the patients delivered vaginally, while 88 (69.8%) delivered by cesarean delivery. Average fetal birth weight was 1795.48±848.24 gr. First minute and 5th min Apgar scores were recorded as 6±2.55 and 8±2.9, respectively. IUGG occurred in 62 (49.2%) of the pregnancies, while preterm

Table 1. Maternal and fetal characteristics of pregnancies in which preeclampsia developed

Variables	*n*=126
Maternal age (years)	27.17±5.57
Nulliparity	83 (65.9%)
Gestational week of onset of preeclampsia	33.16±4.6
Fetal birth weight (gr)	1795.48±848.24
1. min Apgar score	6±2.55
5. min Apgar score	8±2.9
Preeclampsia with severe features	105 (83.3%)
Eclampsia	3 (2.4%)
HELLP	13 (10.3%)
IUGR	62 (49.2%)
Need for maternal intensive care	5 (3.9%)
Preterm birth	98 (77.8%)
Pregnancy outcome	
Live birth	111 (80.2%)
Termination	7 (5.6%)
Still birth	8 (6.3%)
Neonatal death	10 (7.9%)
Type of delivery	
NSD	38 (30.2%)
C/S	88 (69.8%)
Female gender	66 (52.4%)

The values were expressed as average±standard deviation and number (percentage). HELLP: Hemolysis, elevated liver enzymes and low platelets; IUGR: Intrauterine growth restriction.

Table 2. Maternal and fetal characteristics of subsequent pregnancy

Variables	*n*=114
Birth Weight	2397.85±997.32
1. min Apgar score	7±2.64
5. min Apgar score	8±2.7
Need for maternal intensive care	5 (4.3%)
IUGR	34 (29.8%)
preterm birth	54 (47.3%)
Neonatal death	3 (2.6%)
Type of delivery	
NSD	23 (20.1%)
C/S	91 (79.8%)
Female gender	54 (47.3%)

The values were expressed as average±standard deviation and number (percentage). IUGR: Intrauterine growth restriction.

Table 3. The data of patients who developed preeclampsia in subsequent pregnancy

Variables	*n*=70
Gestational week of onset of preeclampsia	35.27±4.67
Preeclampsia	31 (44.2%)
Preeclampsia with severe features	39 (55.7%)
Eclampsia	3 (4.2%)
HELLP	3 (4.2%)

The values were expressed as average±standard deviation and number (percentage). HELLP: Hemolysis, elevated liver enzymes and low platelets.

birth occurred in 98 (77.8%). Neonatal death occurred in 10 (7.9%) pregnancies (Table 1).

While 105 of the subsequent pregnancies resulted in a live birth, 10 (7.9%) resulted in abortion, 9 (7.1%) resulted in stillbirth, and 2 (1.6%) resulted in termination due to preeclampsia. Table 2 shows the subsequent pregnancy characteristics, and the maternal and fetal results of the patients included in the study excluding pregnancies that resulted in abortion and termination. In the subsequent pregnancy, the vaginal birth rate was 20.1% (23 patients) and the cesarean birth rate was 79.8% (91 patients). Average fetal birth weight was 2397.85±997.32 gr. First minute and 5th min Apgar scores were recorded as 7±2.64 and 8±2.7, respectively. 54 (47.3%) of these births were preterm and 5 (4.3%) patients developed maternal intensive care needs. The IUGG rate was found to be 29.8% (34 patients). Neonatal death developed in 3 (2.6%) pregnancies.

The results of 70 patients who developed preeclampsia in a subsequent pregnancy are given in Table 3. In the subsequent pregnancy, preeclampsia developed in 70 (55.5%) patients and 39 (55.7%) of these had preeclampsia with severe features. Gestational week at which preeclampsia diagnosed was found as 35.27±4.67. The eclampsia rate was 4.2% (3 patients) and HELLP syndrome rate was found in 4.2% (3 patients). No maternal mortality occurred.

Discussion

In this large retrospective cohort study, the incidence of preeclampsia was found to be 2.1% in İstanbul between the years 2010 and 2015. This rate was the same as the 2.1% reported in a global, multicentered study with 313,000 diseases published in 2014.[13] The incidence of preeclampsia in Turkey reported by the World Health Organization is 5.2%.[1]

Although there are a large number of studies on preeclampsia in the literature, there are not enough studies on recurrent preeclampsia. There are serious differences between the results of existing studies. Studies conducted worldwide have reported a recurrence rate between 5% and 65%.[11] In their single-centered study conducted on a young patient group, Sibai *et al*. reported a preeclampsia recurrence rate of approximately 40%.[14] However, a preeclampsia recurrence rate of 13.8% was found in a recent meta-analysis.[15] In a multi-centered study conducted in Tanzania, the absolute preeclampsia recurrence risk was found to be 25% in women who had a history of preeclampsia in a previous pregnancy; this rate is similar to the rates reported in the USA.[16] Recurrence risk was found to be between 13% and 15% in Scandinavian countries.[7,17] In our study, the recurrence rate of preeclampsia was 55.5%. One of the potential reasons for this high recurrence rate can be the fact that the center in which the study was conducted is a tertiary reference hospital. High risky pregnancy follow-up rates and referral rates can cause sample selection bias. The possible causes for the differences in recurrence rates may be related to differences between the prevalence of risk factors for preeclampsia and the examined factors (such as chronic hypertension and diabetes), differences in population characteristics or differences in diagnostic criteria. In addition, differences in inclusion and exclusion criteria and the methodology of studies and preeclampsia recurrence calculation criteria (absolute risk and relative risk) can cause variable results. These recurrence rates emphasize the need to have data obtained from local populations.

Nulliparity is an important risk factor for the development of preeclampsia. In their review, Duckitt and Harrington found that the risk of developing preeclampsia is 2–3 times higher in the nulliparous population when compared with the multiparous population.[18] In a study conducted in Turkey including 623 preeclamptic pregnant women, the nulliparity rate was reported to be 63%.[19] In parallel with the literature, 65.9% of the pregnant women who developed preeclampsia were nulliparous in our study. In a prospective cohort study conducted by Hernández-Díaz *et al*., the risk of developing preeclampsia in the first pregnancy was 4.1%, while this was 1.7% in multiparous pregnant women who did not have a history of preeclampsia. In addition, while the risk of developing preeclampsia in the next pregnancy was found as 14.7% in nulliparous preeclamptic women, this rate was found to increase to 30% in the second subsequent pregnancy.[7]

Complications that develop due to preeclampsia have negative effects on both the mother and the baby. In a recent review conducted in Ethiopia, remarkable maternal and fetal results were found. The rate of eclampsia seizures was found to be between 24% and 34% in patients who developed gestational hypertension, while the HELLP syndrome rate was 13% and the maternal mortality rate was

4%. Perinatal mortality was found to occur in one fourth of pregnancies included in the study. While the low birth rate was 37%, the preterm birth rate was found to be between 31 and 65%.[20] In a study conducted in Norway, perinatal mortality was found to be 9.2%.[21] In a study conducted in India, the most frequent fetal morbidities were prematurity (23.6%), low birth weight (7.5%), and IUGG (9.6%).[22] In our study, when the data of the first pregnancy in which pre-eclampsia developed were examined, preeclampsia with severe features was found in 83.3%; the eclampsia rate was 2.4%, HELLP syndrome occurred in 10.3%, and maternal intensive care was required in 3.9%. When the perinatal results were examined, preterm birth was found in 77.8%, IUGG was found in 49.2%, and perinatal mortality was found in 14.2% of pregnancies.

The strongest aspect of this study was the fact that it was conducted with a large patient series and that it was the first study in which preeclampsia recurrence was examined in Turkey. However, our study also has some limitations such as being a single-centered study and its retrospective design.

Preeclampsia is a clinical situation that is one of the leading causes of maternal and fetal morbidity and mortality in Turkey and throughout the world. The present study guides us on the risk factors related to preeclampsia and the rate of fetomaternal adverse outcomes and emphasizes the need for strict and regular antenatal follow-up in the subsequent pregnancies of women who have a history preeclampsia. Improvement of maternal and fetal morbidity and mortality in this way is the utmost goal.

Disclosures

Ethics Committee Approval: Ethics Committee of Kanuni Sultan Süleyman Training and Research Hospital (11424-2015).

Peer-review: Externally peer-reviewed.

Conflict of Interest: None declared.

Authorship Contributions: Concept – U.C.; Design – U.C., O.D.U.; Supervision – U.C.; Materials – U.C.; Data collection &/or processing – O.D.U., S.O.; Analysis and/or interpretation – T.T., O.D.U.; Literature search – T.T.; Writing – U.C., T.T.; Critical review – T.T.

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