Clinical Findings and Maternal-Neonatal Outcomes of Eclampsia According to Time of Onset

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ABSTRACT Objective: To evaluate the impact of gestational age on clinical, laboratory findings and maternal-perinatal outcomes in eclamptic patients. Material and Methods: A retrospective review of 37 patients with eclampsia between January 2007 and January 2010 was performed. Data were separated into two groups by gestational age at the onset of disease: Group 1 (<34 weeks) and Group 2 (≥34 weeks). Clinical signs and symptoms, laboratory findings, the timing of the convulsions, maternal and perinatal outcomes were evaluated. Results: No differences were observed between the two groups for the clinical and laboratory characteristics except gravidity, need of intravenous antihypertensives and hospitalization time. Neonatal mortality was 24.3% for all patients, 42.1% for Group 1. In our study, the timing of convulsions were antepartum (81.1%), intrapartum (10.8%), and postpartum (8.1%). Intrapartum and postpartum eclampsia occurred significantly higher in late onset group. No maternal deaths occurred during this study and all women recovered with no long term sequelae. Conclusion: This study demonstrated that gestational age at admission was strongly associated with neonatal outcomes but no association observed with maternal outcomes, laboratory findings and clinical course of eclampsia. These results should be supported by systematic quantitative reviews.

Key Words: Eclampsia; pre-eclampsia; pregnancy outcome


Anahtar Kelimeler: Eklampsi; pre-eklampsi; gebelik sonucu

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Eclampsia refers to the event of generalized convulsions in secure presence of the preeclampsia and in the absence of other neurologic conditions. Convulsions should be considered only one of several
clinical manifestations of preeclampsia, rather than a separate disease. Despite advances in detection and management of preeclampsia, complications of severe preeclampsia such as eclampsia remain a common cause of maternal death. An eclamptic seizure occurs in approximately 0.5 percent of mild preeclamptic women and 2 to 3 percent of severe preeclamptic women. The incidence of eclampsia has been 6 to 100 cases per 10,000 live births in developing countries. The reported incidence is frequently higher in tertiary reference centers, and in population with no prenatal care.

The terminology of early and late onset preeclampsia according to gestational age at the onset of preeclampsia is used largely, as a reflection of the severity of the disease and different etiopathogenesis. Gestational age plays an important role in disease management and also impacts the perinatal morbidity and mortality. Unfortunately, there is insufficient data regarding the impact of gestational age on clinical course and maternal outcome in eclampsia. It has been demonstrated that some clinical and laboratory parameters predict the severity of disease, but it remains as an ongoing debate and controversy. Disease complications can be predicted by using patients’ characteristics, symptoms, physical signs and investigations and these can be used for the basis of management and clinical care. Therefore, there is a need for guidance about the best testing strategies to predict the development of complications in preeclampsia and eclampsia. The onset time of disease is important for perinatal outcomes, and the effect on maternal outcomes and management should be demonstrated. When eclampsia is diagnosed at an early gestational age, management options are stabilization of maternal disease and delivery after corticosteroid administration for fetal lung maturity. More temporizing approaches, allowing delivery to be delayed until the maternal or fetal condition shows deterioration was not demonstrated enough for eclampsia management yet. Once the diagnosis of eclampsia is established, timely management is essential to avoid or minimize mortality and morbidity.

The purpose of our study was to discuss the impact of gestational age on maternal outcome, clinical findings and laboratory parameters.

**MATERIAL AND METHODS**

A retrospective data review of eclamptic patients who were diagnosed and managed in Cukurova University, School of Medicine, Department of Obstetrics and Gynecology between January 2007 and January 2010 was conducted. The study was approved by the local ethical committee. As our center is a tertiary unit, most of the patients were referred from other centers. The patients were divided into two groups according to the onset of eclampsia. Group 1 (n=19) consisted of patients with early onset disease (<34 weeks of gestation) and Group 2 (n=18) consisted of patients with late onset disease (≥34 weeks of gestation). Clinical and laboratory findings, and maternal-perinatal outcomes were compared.

Patients were classified as having hypertension, severe preeclampsia, and eclampsia according to the criteria of the American College of Obstetricians and Gynecologist. Patients with gestational age ≤24 weeks and patients with epilepsy and other neurologic disease and a systemic illness such as hepatic/renal diseases were excluded. Hematocrit, hemoglobin, platelet count, liver enzymes, lactic dehydrogenase (LDH), uric acid, spot urinary proteinuria were identified and coagulation tests (prothrombin time, partial thromboplastin time, bleeding time), renal function tests (blood urea nitrogen, creatinine) were performed. The patients were strictly monitored for blood pressure and urine output measurement and frequent assessment of symptoms. Gestational age was determined according to the last menstrual period or first or early second trimester ultrasonography. Laboratory assessments of platelet count, liver and renal function tests, LDH and uric acid values were made every 6 hours until delivery. Blood products were administered for patients with existing severe anemia or coagulation abnormalities. Nifedipine and/or, alpha methyl dopa and/or beta-blocker drugs were administered to control severe hypertension (diastolic blood pressure ≥110 mmHg). Intravenous
antihypertensives such as beta-blockers, nitroprusside or nitroglycerin were administered in the intensive care unit (ICU) if severe diastolic hypertension was not controlled with peroral medication. All patients with eclampsia routinely received magnesium sulfate as a 4.5 g intravenous loading dose before a 2 g maintenance dose per hour in our clinic. We don’t use diazepam, fentanyl and another drug for prevention of convulsions. Magnesium sulphate was generally applied for 24 hours postpartum period or after last convulsion. Women who do not improve rapidly following control of convulsion and hypertension, or those who develop localized neurologic signs evaluated further. If cerebral imaging was indicated, magnetic resonance imaging (MRI) or computed tomography (CT) were performed.

Demographics of the patients, such as maternal age, parity, gestational age, complains at admission, clinical findings including systolic and diastolic blood pressure at admission, prodromal symptoms (such as nausea, vomiting, headache, epigastric pain, visual change), laboratory results, mode of delivery, and postpartum eclampsia, timing and number of convulsion, presence of convulsion despite magnesium sulphate administration, hospitalization time were evaluated. Adverse maternal outcomes including HELLP syndrome, abruptio placenta, disseminated intravascular coagulation (DIC), requirement of transfusion, requirement of ICU, requirement IV antihypertensive drugs, retinal detachment were recorded. Perinatal complications including intrauterine growth restriction (IUGR), oligohydramnios, stillbirth, requirement of neonatal intensive care unit (NICU), low APGAR score and neonatal death were also assessed.

Statistical analysis was carried out using the Statistical Package for Social Sciences (SPSS version 16.0; SPSS Inc., Chicago, IL, USA). Data was shown as mean± SD, min-max value or n, percent. Student-T test and Mann Whitney U tests were used to determine the differences to compare the groups with parametric and nonparametric data. Chi-square test was used to compare the groups with categorical data. Statistical significance was set to p<0.05.

A total of 7422 deliveries occurred during the study period, and 38 of these deliveries were complicated by eclampsia (0.51%). Thirty-seven of these patients were included in this study, because atypical presentation and sinus vein thrombosis were diagnosed in one patient. Twenty patients (54%) had severe preeclampsia, five patients with mild preeclampsia (13.5%), 4 patients (10.8%) had superimposed preeclampsia, and 7 patients (18.9%) had HELLP syndrome complicated with eclampsia and there was no statistically significant difference between groups (p=0.472) for associated pathology. We compared the clinical and laboratory characteristics of the patients with eclampsia according to onset of disease (Table 1). The gravidity of the patients in the Group 1 were statistically higher than the patients in the Group 2 (Table 1). The ratio of nulliparous patients was 31% in Group 1 and 44.4% in Group 2 and was not significantly different between the groups. Clinical and laboratory findings of the patients in both groups were similar.

Outcomes and complications are shown in Table 2 and 3 for mothers and neonates respectively. There was no statistically significant difference in the maternal outcomes between the groups except need of intravenous antihypertensive drug and hospitalization time. Contrary to expectations, oligohydramnios and IUGR were higher in Group 2. Neonatal mortality rate was 42.1% in the Group 1. The perinatal mortality rate was 24.3% (n=9) in totally. There were 4 stillbirths in all patients.

The main maternal complications were DIC (10.8%), abruptio placenta (2.7%), HELLP syndrome (18.9%), requirement of intensive care unit (ICU, 59.5%), requirement of blood transfusion (13.5%), and retinal detachment (2.7%). Five patients required transfusion of blood products (platelet suspension, erythrocyte suspension and fresh frozen plasma). No intracerebral hemorrhage, subcapsular liver hematoma or bleeding, acute renal failure, adult respiratory distress syndrome, neurologic sequel or maternal deaths occurred during this study period. Groups were
compared according to timing of convulsions demonstrated at Table 4. All postpartum cases occurred within 48 hours of delivery. Late postpartum eclampsia, which occurs after 48 hours postpartum, was not seen in this study period. Thirty patients (81%) had convulsions before admitted to our clinic. Intrapartum and postpartum convulsions occurred significantly higher in late onset group and all convulsions occurred in antepartum period in the early onset group. All woman recovered with no long term sequelae.

In our results, the timing of convulsions were antepartum (81.1%), intrapartum (10.8%), and postpartum (8.1%). Intrapartum and postpartum eclampsia occurred higher in late onset group than early onset group. In one large series, which was consisted 82 eclamptic patients, approximately one-half of all cases of eclampsia occurred antenatal period, 13 percent occurred intrapartum and 32 percent occurred postnatal period. Other studies reported that late postpartum eclampsia (eclamptic
seizures developing after than 48 hours, but less than four weeks postpartum) accounts 3 to 26 percent and represents as many as one-quarter of all postpartum cases.9,10 In general, tonic-clonic seizures are typical eclamptic seizures which do not have focal neurologic deficits or prolonged coma and do not require diagnostic evaluation with either electroen-
cephalographic or cerebral imaging studies. But there may be difficulty in differentiating neurological conditions clinically, then the presenting symptoms and signs are nonspecific. Investigation with cerebral CT and MRI may provide valuable diagnostic information and alter clinical management.11,12 In our study five patients (13.5%) underwent cerebral imaging by CT or MRI and cerebral imaging.

The definitive treatment of eclampsia is delivery, irrespective of gestational age, to reduce the risk of maternal morbidity and mortality from complications of the disease; however, this does not preclude induction of labor.13,14 After maternal stabilization determining the mode of delivery should be considered according to gestational age, Bishop score, presence of labor. In our study, C/S rate was too high as 91.9% and was not different between the groups. Nassar et al concluded that cesarean delivery is a reasonable option for patients with an unfavorable cervix and not in labor.15

Pritchard et al demonstrated that maternal complications occurred in up to 70 percent of women with eclampsia such as abruptio placenta, DIC, ARF, hepatocellular injury, liver rupture, intracerebral hemorrhage, transient blindness, cardiorespiratory arrest, aspiration pneumonitis, acute pulmonary edema, and postpartum hemorrhage.16 Brain damage from hemorrhage or ischemia may result in permanent neurologic sequelae and was found most common cause of death in eclamptic women.17 Maternal mortality and severe morbidity rates were reported lowest among women receiving regular prenatal care who are managed by experienced physicians in tertiary centers.18,19 Maternal mortality rate and related factors were identified by Moodley in South Africa and were determined related factors such as non-attendance for antenatal care, delay in seeking help, problem recognition, delay in referral and management at an inappropriate level of health care.19 In a large retrospective analysis of 990 cases of eclampsia in Mexico, the overall maternal mortality rate was 13.9 percent.20 The subgroup of women with eclampsia prior to 28 weeks of gestation had the highest risk of maternal death. Multiple seizures outside of the hospital setting was another common cause of death in this study. Conde-Agudelo and Kafury-Goeta demonstrated that maternal age above 26 years, multiparity, and no prenatal care were the maternal risk factors identified for the development of complicated eclampsia.21 It is important to note that maternal complications are significantly higher among women who develop antepartum eclampsia, particularly among those who develop eclampsia remote from term.5 In another study, the greatest risk of death was found among women with pregnancies at or before 28 weeks of gestation.18 In spite of these study results, we did not demonstrated higher maternal morbidity in the early onset group than late onset group. This condition may be explained by the fact that the number of patients is not enough to make definitive conclusions for maternal outcomes according to the onset of the disease. We compared clinical and laboratory findings of the time of the onset of eclampsia, found no difference between the two groups except gravidity. There was no difference in the maternal outcomes between the groups except the need of intravenous antihypertensive medication and hospitalization time. One interesting finding was that more than half of the women in early onset group needed intravenous antihypertensive agents. Hospitalization time was significantly longer in early onset group as it can expected.

Perinatal mortality and morbidities remain high in eclamptic pregnancies. Premature delivery, abruptio placenta, IUGR and intrauterine asphyxia are the primary causes of perinatal death in eclam-
tic pregnancies.\textsuperscript{22,23} Perinatal mortality ranges from 9 to 66 percent and is closely related to gestational age.\textsuperscript{24,25} The overall risk of perinatal mortality in this study was similar to these studies. Other studies reported that the rate of preterm delivery is approximately 50%, with approximately 25% of these occurring before 32 weeks of gestation.\textsuperscript{25}

This study demonstrated that gestational age at admission was strongly associated with neonatal outcomes but no association observed with maternal outcomes. Clinical presentation, symptoms, laboratory tests and onset of disease should be evaluated to predict the complications of eclampsia with systematic quantitative reviews such as preeclampsia.

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### REFERENCES