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Risk factors for maternal mortality in eclampsia: analysis of 167 eclamptic cases

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Abstract. – BACKGROUND: The aim of this study was to evaluate risk factors associated with maternal mortality in patients with eclampsia.

METHODS: The probable risk factors of maternal mortality including maternal age, length of hospital stay, gestational age, systolic and diastolic blood pressures; hematocrit, hemoglobin, platelet count, levels of alanine aminotransferase (ALT), aspartate aminotransferase (AST), lactate dehydrogenase were determined from patients' charts and Odds ratios (OR) of these factors were detected using by logistic regression analysis.

RESULTS: According to logistic regression model, AST [OR, (95% Confidence Interval, CI): 7.39 (2.71-20.13)]; ALT [6.45 (2.42-17.16)]; postpartum diastolic blood pressure [4.58 (1.80-11.62)]; hematocrit [3.52 (1.86-6.65)]; hemoglobin [2.67 (2.01-3.55)] were found to be significant risk factors for maternal mortality.

CONCLUSIONS: In eclamptic patients, close monitoring of particular laboratory values and blood pressure, and early intervention to alterations of certain variables will provide possibility for prevention against potential complications and subsequently decreasing mortality.

Key Words:
Eclampsia, Maternal mortality, Risk factors.

Introduction

Eclampsia is the most important reason for maternal mortality in high-low income countries (1). It has been reported that 0.5-10% cases of maternal mortality usually required high quality intensive care (2). Eclampsia is defined as the occurrence of seizures in a woman with preeclampsia that cannot be attributed to other causes (3). It takes years to collect the data needed to be able to draw valid conclusions from analyzing cases of maternal mortality. Although many publications related to eclampsia are available in the literature, articles discussing risks for eclampsia that associated with higher mortality, especially in selected cases, are scarce. In this study, we have investigated the etiologic factors which may be related with increasing risk of mortality in our reference hospital in Southeast Anatolian Region of Turkey.

We evaluated probable risk factors associated with maternal mortality in patients with eclampsia using by logistic regression models to determine the Odds ratios (OR).

Materials and Methods

Study Design

In this retrospective study patients diagnosed as eclampsia between September 2005 and September 2010 in the Department of Gynecology, and Obstetrics, Dicle University Faculty of Medicine which is a reference Hospital in Southeast Anatolian Region of Turkey were examined. The study protocol was approved by Local Ethics Committee. Patients' information was obtained from hospital records. The exclusion criteria were hypertension and proteinuria diagnosed before 20th gestational weeks; renal, hematologic and cardiac diseases causing proteinuria, and hypertension, multiparous women, and patients with hematologic or other diseases with increased hepatic enzyme levels.

Hypertensive patients (blood pressure over 140/90 mmHg) with proteinuria (more than 300 mg/24 h after 20 weeks of gestation) were defined as preeclampsia. Eclampsia is defined as the occurrence of seizures in a woman with preeclampsia that cannot be attributed to other causes. The HELLP syndrome was defined as

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hemolysis (peripheral blood smear findings and lactate dehydrogenase (LDH) > 600 U/L, or serum total bilirubin level > 1.2 mg/dL), decreased platelet count (< 100,000 cells/L), and elevated liver enzymes [alanine aminotransferase (ALT) > 70 U/L[3].

Gestational weeks of the patients were determined according to the last date of menstruation and/or ultrasonographic measurements. All patients included in the study were monitored in the intensive care unit (ICU). Vital signs of all patients were monitored, and magnesium therapy was initiated. Loading dose of magnesium (6 g) was administered in 20 minutes, and maintenance dose was given at a rate of 2 g per hour. On the first admission, variables such as blood pressure, whole blood counts, ALT, AST, and LDH were evaluated. The decision to deliver was determined based on obstetric anamnesis, maternal and fetal status, and Bishop Scores. Vaginal delivery was preferred, however in the presence of unsuitable cervix, fetal distress, and in patients with previous caesarian delivery, Cesarian section was performed. The deceased patients were evaluated in Group 1 (GR1) and survived patients in Group 2 (GR2). The association between maternal age, length of hospital stay, gestational age, systolic and diastolic blood pressure, hematocrit, hemoglobin, platelet count, levels of ALT, AST, LDH parameters were evaluated for use as risk factors of the maternal mortality.

Statistical Analysis

Means and standard deviations (SD) were calculated for continuous variables. Subject characteristics and demographics were analyzed descriptively. The normal distribution of the variables was analyzed by the Kolmogorov-Smirnov test. The Chi-square test and the Student's t test were used to evaluate differences between the categorical and continuous variables. Logarithmic transformation (log10) was performed to correct the variance of platelet count, ALT, AST, and LDH, as the range of those distributions was very large. The logistic regression analysis was used to find the risk factors for preeclamptic patients by including all variables in the model and to calculate the odds ratios. All variables were included in the backward stepwise procedure. Two-sided p values were considered statistically significant at $p < 0.05$. Statistical analyses were carried out using the statistical package SPSS 15.0 for Windows (SPSS Inc., Chicago, IL, USA).

Results

During the study period a total of 23.507 deliveries were achieved, of whom 167 patients were eclamptic (0.7%). HELLP syndrome was associated with 74 (44.3%) patients. Nine patients died (GR1). Intracranial bleeding (n=3), and HELLP syndrome (n=5; hepatic rupture, 1; n=1; sepsis; n=2, renal failure secondary to DIC, n=1; cerebral bleeding, n=1) were found in the deceased group. In the survived group (GR2) median numbers of pregnancies, and parities were 5, and 3, while in Group 1, the corresponding numbers were 2, and 1, respectively. Comparative demographic, and clinical parameters of the patients in Groups 1, and 2, are shown in Table I.

No intergroup difference was detected for age, hospital stay, platelet (PLT) counts, gestational age, and birth weight of the fetus ($p > 0.059$), while a significant difference was found for hematocrit, hemoglobin, AST, ALT, LDH values, pre- and postpartum systolic and diastolic blood pressures, and Apgar scores of the fetus at 1. and 5. minutes ($p = 0.05$).

In Group 1, 33.3 (n=3), and 66.7% (n=6) of the patients experienced 2 and more than 2 seizure episodes, respectively, while in Group 2 the corresponding rates were % 79.0% (n=125), and 21.0% (n=33), respectively. In Fisher's exact test a significant difference was found between 2 groups ($p = 0.0006$).

Table II summarizes the risk variables for mortality in eclamptic patients by using Logistic Regression Model. According to the model, AST, ALT, postpartum diastolic blood pressure, hematocrit and hemoglobin levels were found to be significant risk factors for maternal mortality. The OR (95% CI) were 7.39 (2.71-20.13); 6.45 (2.42-17.16); 4.58 (1.80-11.62); 3.52 (1.86-6.65); and 2.67 (2.01-3.55) respectively.

Discussion

Eclampsia is one of the important causes of mortality in pregnant women (4). It takes years to collect the numbers needed to be able to draw valid conclusions from analyzing cases of maternal mortality from eclampsia. Literature reviews demonstrate an increased incidence of mortality especially in lower-income countries (5,6). However in higher-income countries, maternal mortality rates in eclamptic patients with HELLP syn-

Table I. Comparison of laboratory and clinical charecteristics of the survive or no survive eclamptic patients.

	Group	$\bar{x} \pm SD$	Test values*	p
Age (years)	GR1	31.12 ± 12.21	$t = 1.123$	= 0.632
	GR2	29.89 ± 11.92		
Length of hospital stay (day)	GR1	4.3 ± 3.03	$t = 1.770$	= 0.079
	GR2	6.3 ± 3.30		
Hematocrit (%)	GR1	27.51 ± 9.22	$t = 2.702$	= 0.008
	GR2	33.73 ± 6.27		
Hemoglobin (g/dL)	GR1	9.24 ± 2.81	$t = 2.631$	= 0.009
	GR2	11.41 ± 2.22		
LogPLT	GR1	1.73 ± 0.50	$t = 1.886$	= 0.061
	GR2	2.06 ± 0.39		
LogALT	GR1	2.14 ± .83	$t = 4.366$	= 0.001
	GR2	1.64 ±.522		
LogAST	GR1	2.52 ± 0.82	$t = 8.103$	= 0.001
	GR2	1.85 ± 0 .48		
LogLDH	GR1	3.25 ± 0.46	$t = 5.006$	= 0.001
	GR2	2.81± 0.32		
Prepartum sistolic blood pressure (mm/Hg)	GR1	172.50 ± 10.32	$t = 2.446$	= 0.015
	GR2	162.22 ± 11.51		
Prepartum diastolic blood pressure (mm/Hg)	GR1	110.01 ± 11.97	$t = 2.581$	= 0.011
	GR2	100.86 ± 9.78		
Postpartum sistolic blood pressure (mm/Hg)	GR1	148.78 ± 9.94	$t = 5.847$	= 0.001
	GR2	128.72 ± 9.41		
Postpartum diastolic blood pressure (mm/Hg)	GR1	93.79 ± 10.69	$t = 3.406$	= 0.001
	GR2	81.33 ± 10.03		
Gestational weeks (weeks)	GR1	32.15 ± 3.44	$t = 0.556$	= 0.579
	GR2	33.04 ± 4.51		
Fetal birth weight (g)	GR1	1680.02 ± 594.08	$t = 1.555$	= 0.122
	GR2	2126.36 ± 799.43		
Apgar score 1	GR1	1.35 ± 1.37	$t = 3.392$	= 0.001
	GR2	4.04 ± 2.23		
Apgar score 5	GR1	2.83 ± 2.48	$t = 2.791$	= 0.006
	GR2	5.6 ± 2.7		

$p \leq 0.05$ is accepted to be statistically significant. $\bar{x} \pm SD$: Mean and Standard Deviation; Log: Logarithmic transformation (Log_{10}); *Student's *t* test used to analyse two independent mean group.

drome are increasing. Early diagnosis and treatment of eclampsia and concomitant HELLP syndrome will decrease rates of maternal mortality.

Vigil-De Gracia et al[2] reported mortality rate of eclampsia in higher-income countries as 9.4%. The incidence of HELLP among deceased patients was given as 54 percent. In our study, mortality rate in patients with eclampsia, and concomitant HELLP syndrome was found to be increased. Vigil-De Gracia and Garcia Caceres[7] reported that; higher predictive value of thrombocytopenia in patients died of eclampsia was as-

Table II. The risk variables for mortality in eclamptic patients by using Logistic Regression Model.

	β	SE	Wald	Odds ratio	95% CI	p
AST	2.00	0.51	15.33	7.39	2.71-20.13	< 0.001
ALT	1.86	0.49	13.96	6.45	2.42-17.16	< 0.001
Postpartum diastolic blood pressure	1.52	0.47	10.26	4.58	1.80-11.62	< 0.001
Hemoglobin	1.26	0.32	15.12	3.52	1.86-6.65	< 0.001
Hematocrit	0.98	0.14	46.14	2.67	2.01-3.55	< 0.001

Correct classification: 96.20%. β: Regression coefficient; SE: Standard error; Wald: Test statistics; 95% CI: Confidence interval for 95%.

serted. However, in their study any potential association of HELLP syndrome with eclampsia was not evaluated. In our study contrary to thrombocytopenia, we have observed higher maternal mortality rates in HELLP syndrome associated with increased AST, ALT levels. Elevation of liver enzymes may reflect the haemolytic process as well as liver involvement. Haemolysis contributes substantially to the elevated levels of LDH, whereas enhanced AST and ALT levels are mostly due to liver injury[8].

Especially in lower-income countries due to inadequate pregnancy care, and lack of prenatal care up to delivery because of some cultural practices and other reasons, mortality rates are higher in eclampsia. Diagnosis of eclampsia and HELLP syndrome is challenging because of inadequate number of relevant specialists, unsatisfactory laboratory facilities, transportation problems, and wrong diagnoses[9].

Generally, HELLP syndrome is a multisystem disease affecting central nervous system[8,10-13], lungs[14], liver, and kidneys[10,11]. In some cases, single organ damage as cerebral bleeding or liver rupture might be the cause of death. However most of the cases are lost because of multiorgan failure. Cerebral bleeding (n=4), and hepatic rupture (n=1) were detected as causes of mortality in our patient population.

In addition to increased AST, and ALT levels associated with HELLP syndrome, systolic hypertension of eclampsia is an etiologic factors for increased risk of maternal mortality. Evaluation of previous literature findings has revealed that intracerebral bleeding due to hypertension was also linked with increased mortality[10,15,16]. In our study, also, intracranial bleeding was detected in 4 patients. Cerebrovascular events in eclampsia appear to constitute a continuum characterized by an initial, reversible phase of vasogenic edema and seizures caused by hypertension, along with endothelial dysfunction[13]. Still, hypertension associated with HELLP syndrome also disrupts blood-brain barrier secondary to endothelial dysfunction[17]. In our study, lower hematocrit, and hemoglobin values, and anemia were also among etiologic factors for increased mortality rates. The proportion of schistocytes and echinocytes was significantly greater than they become functionally defective in preeclamptic and eclamptic women compared to normally pregnant women[18]. Erythrocyte functions are also important for a healthy metabolism. Higher mortality risks in eclamptic patients can be explained with the presence of dysfunctional red blood cells, and lower hematocrit levels. Protection of eclamptic patients from development of multiple convulsions is very important for the prevention from occurrence of manifestations of cerebral bleeding, and HELLP syndrome. In our study, higher number of deceased patients exposed to more than 2 seizure episodes relative to survived patients.

As for our study, association of systolic and diastolic hypertension with HELLP syndrome, and anemia represented a deadly triad. Vigil-De Gracia et al[15], replaced convulsion instead of anemia in this triad. Previous studies reported higher rates of mortality in cases of eclampsia especially progressing with HELLP syndrome, and hypertension[15-17]. Martin et al[17] mentioned about 29 preeclamptic, and eclamptic patients who had experienced attacks of stroke in whom they detected HELLP syndrome (n= 18), and eclampsia (n=8). In their study 15 patients with baseline systolic hypertension (155-160 mmHg) died after an episode of stroke. Miguil et al[19] reported 23 patients who died of eclampsia in whom they detected cerebral bleeding, and ischemia (61%), systolic, and diastolic hypertension (> 50%). In an UK study[20], 18 deceased eclamptic patients were reported who had died of HELLP syndrome (44.4%), and eclampsia (33.3%).

Conclusions

According to our findings, increased AST, ALT secondary to HELLP syndrome, postpartum systolic hypertension, decreased hematocrit, and hemoglobin levels were important factors for increasing maternal mortality. Further prospective studies are necessary to evaluate the risk factors of maternal mortality with eclampsia.

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