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## CLINICAL ARTICLE

## Incidence of eclampsia with HELLP syndrome and associated mortality in Latin America

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## ABSTRACT

**Objective:** To describe the maternal outcome among women with eclampsia with and without HELLP syndrome (hemolysis, elevated liver enzymes, and low platelet count). **Methods:** A cross-sectional study of women with eclampsia was undertaken in 14 maternity units in Latin America between January 1 and December 31, 2012. Outcomes were compared between women with and without concomitant HELLP syndrome. Logistic regression analysis was performed to identify independent risk factors of maternal mortality. **Results:** There were 196 eclampsia cases among 115 038 deliveries; 142 (72.4%) women had eclampsia alone and 54 (27.6%) women had concomitant HELLP syndrome. Severe systolic hypertension ( $\geq 160$  mm Hg), severe diastolic hypertension ( $\geq 110$  mm Hg), and hypertensive encephalopathy were significantly more common among women with HELLP than among those with eclampsia alone ( $P = 0.01$  for all). There were 8 (4.1%) maternal deaths, all in the group with HELLP syndrome, and 18 (9.1%) perinatal deaths. In a multivariate regression model, maternal mortality was significantly associated with low platelet count and severe systolic hypertension ( $P < 0.05$ ). **Conclusion:** Eclampsia with HELLP syndrome is a dangerous complication associated with pregnancy. Low platelet count secondary to HELLP syndrome and severe systolic hypertension were independently associated with maternal mortality from eclampsia.

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## 1. Introduction

Eclampsia is defined as the occurrence of grand mal seizures during pregnancy or during/after delivery in a woman with pre-eclampsia, gestational hypertension, or superimposed pre-eclampsia [1,2]. Eclampsia increases the risks of morbidity and mortality for mother and child. The maternal mortality rate associated with eclampsia ranges from 0% in high-income countries to 15% in low-income countries [3].

The management of pre-eclampsia and eclampsia has changed considerably since the 1980s, with advances including early and accurate diagnosis, frequent use of magnesium for the management of

severe pre-eclampsia, and use of antihypertensives for the treatment of severe hypertension [1–4]. However, the information available on the incidence and risk factors of death associated with eclampsia is based on studies conducted several decades ago [1,5].

HELLP syndrome (hemolysis, elevated liver enzymes, and low platelet count) is a complication of pregnancy affecting 2%–30% of women with pre-eclampsia/eclampsia [3,6]. The clinical course of this syndrome can be characterized by a progressive and sometimes rapid deterioration in the health of mother and fetus [6]. The maternal outcomes of HELLP syndrome include complications such as subcapsular liver hematoma, renal failure, and retinal detachment; maternal and perinatal mortality are also increased [4,7]. Prompt recognition and precise diagnosis are necessary for adequate treatment.

Mortality among women with eclampsia and HELLP syndrome has been evaluated in a literature review [3]. However, no large prospective studies were found that investigated the risk of death in this population.

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The objective of the present study was to evaluate the maternal outcome of women with eclampsia with or without HELLP syndrome who were treated at one of 14 maternity units in Latin America during a 1-year period.

## 2. Materials and methods

The present cross-sectional study was conducted from January 1 to December 31, 2012, in 14 tertiary teaching hospitals with experience in the treatment of severe pre-eclampsia and eclampsia across Colombia, Ecuador, El Salvador, Panama, Peru, and Venezuela. All women diagnosed with eclampsia were included in the study. The ethics committees or institutional review boards of all participating hospitals approved the protocol. Oral informed consent was obtained from the women or a relative if the mother was of adolescent age.

Eclampsia was defined as the occurrence of generalized convulsions among women with pre-eclampsia, gestational hypertension, or superimposed pre-eclampsia not due to epilepsy or causes not related to pregnancy. It was diagnosed according to the clinical judgment of the treating physician during admission or hospital stay. Prepartum eclampsia was defined as the occurrence of convulsions before delivery; postpartum eclampsia was defined as the occurrence of convulsions after delivery.

Magnesium sulfate (4 g loading dose given over 10–20 minutes; maintenance dose of 1 g/hour) was administered to control seizures in women with severe pre-eclampsia or eclampsia. It was also administered for 24 hours post partum if eclampsia was diagnosed before or during delivery, and for 24 hours after a convulsion if eclampsia was diagnosed post partum. All women were admitted to hospital and carefully monitored. The management policy was prompt delivery in women with eclampsia or HELLP syndrome. Blood transfusion was used to treat anemia, and platelet transfusion was used if the platelet count was 50 000 per  $\mu\text{L}$  or less before delivery. The following medications were given as necessary to maintain the blood pressure at 160/110 mm Hg or lower: 5 mg hydralazine as an intravenous bolus every 20 minutes; labetalol as an intravenous bolus every 20 minutes at increasing doses (20 mg, 40 mg, 80 mg, 80 mg, and 80 mg); or 10 mg nifedipine given orally every 20 minutes.

Data for age, pregnancy duration, systolic and diastolic blood pressure, platelet count, admission to the intensive care unit, cesarean delivery, and maternal complications (pulmonary aspiration, hypertensive encephalopathy, death) were collected. The pregnancy duration was established using the date of last menstrual period or ultrasonography if the duration was less than 20 weeks.

The women were divided in two groups: women with eclampsia who did not have HELLP syndrome, and women with both eclampsia and HELLP syndrome. The cohort was also divided by whether patients survived or died.

The diagnosis of HELLP syndrome was made if a woman with eclampsia presented with hemolysis (lactate dehydrogenase  $\geq 600$  IU/L and elevated serum bilirubin levels), a platelet count of  $\leq 150$  000 per  $\mu\text{L}$ , and hepatic dysfunction (increased levels of aspartate aminotransferase, lactate dehydrogenase, and alanine transaminase). A systolic blood pressure of 160 mm Hg or more, or a diastolic blood pressure of 110 mm Hg or more was classified as severe hypertension. Hypertensive encephalopathy was defined by the presence of severe hypertension that was difficult to control, with accompanying central nervous system symptoms.

Statistical analysis was performed with Epi Info version 7 (Centers for Disease Control and Prevention, Atlanta, GA, USA). The  $\chi^2$  test was used to compare categorical variables. When appropriate, the Fisher exact test was used.  $P < 0.05$  was considered statistically significant. A logistic regression model was constructed with variables that were significantly different between women with and without HELLP syndrome to assess a possible association with maternal mortality. The following variables were entered into the model: severe systolic hypertension,

HELLP syndrome, platelet count, hypertensive encephalopathy, and pulmonary aspiration.

## 3. Results

The total number of deliveries in the 14 hospitals during the study period was 115 038. Overall, 196 women had eclampsia, giving an incidence of 1 in 587 deliveries. Among the study patients, 142 (72.4%) had eclampsia alone and 54 (27.6%) had eclampsia with HELLP syndrome. Patients with HELLP syndrome were significantly older than were those without this disorder ( $P = 0.02$ ), but they had a shorter pregnancy duration ( $P = 0.03$ ) (Table 1). In the entire cohort, 109 (55.6%) women were aged 20 years or younger.

More patients with HELLP than those with eclampsia alone had prepartum eclampsia ( $P = 0.05$ ) (Table 1). Severe systolic hypertension, severe diastolic hypertension, and hypertensive encephalopathy were significantly more common in the group with HELLP syndrome ( $P = 0.01$  for all) (Table 1). Platelet count was significantly lower among women with HELLP syndrome ( $P = 0.001$ ) (Table 1). In the entire cohort, 146 (74.5%) women were diagnosed with eclampsia before admission to hospital, with no difference in frequency between the groups (Table 1).

There were 8 (4.1%) deaths in the entire cohort (all in the HELLP group) and 18 (9.2%) perinatal deaths; both events were significantly more common in women with HELLP syndrome than in those with eclampsia alone ( $P = 0.01$  for both) (Table 1). Characteristics of the women who died are shown in Table 2. Six (3.1%) women had hypertensive encephalopathy.

Univariate analysis revealed five variables that were significantly associated with maternal mortality (Table 3): severe systolic hypertension ( $P = 0.04$ ), HELLP syndrome ( $P = 0.001$ ), low platelet count ( $P = 0.001$ ), hypertensive encephalopathy ( $P = 0.001$ ), and aspiration ( $P = 0.03$ ). These five variables were incorporated into a multiple regression model. In this model, severe systolic hypertension ( $P = 0.02$ ) and low platelet count ( $P = 0.047$ ) were independently associated with maternal mortality (Table 3).

**Table 1**  
Characteristics of women with eclampsia with/without concurrent HELLP syndrome (n = 196).<sup>a</sup>

Variable	Eclampsia (n = 142)	Eclampsia and HELLP syndrome (n = 54)	P value
Age, y	21.5 $\pm$ 6.5	24 $\pm$ 7.9	0.02
Pregnancy duration, wk	36.2 $\pm$ 3.7	34.9 $\pm$ 3.9	0.03
Prepartum eclampsia	96 (67.6)	44 (81.5)	0.05
Postpartum eclampsia	37 (26.1)	10 (18.5)	0.26
One seizure only	80 (56.3)	23 (42.6)	0.08
Eclampsia before hospital admission	103 (72.5)	43 (79.6)	0.34
Blood pressure			
Diastolic blood pressure, mm Hg	98.7 $\pm$ 14.0	103 $\pm$ 14.0	0.07
$\geq 110$ mm Hg	40 (28.2)	24 (44.4)	0.01
Systolic blood pressure, mm Hg	169 $\pm$ 25.0	154 $\pm$ 21.0	0.01
$\geq 160$ mm Hg	51 (35.9)	35 (64.8)	0.01
Urine protein, mg/24 h	941 $\pm$ 910	1362 $\pm$ 1164	0.28
Absence of albuminuria	23 (16.1)	10 (18.5)	0.80
Platelet count, cells/ $\mu\text{L}$	203 481 $\pm$ 72 000	75 005 $\pm$ 30 000	0.01
Hypertensive encephalopathy	31 (21.8)	23 (42.6)	0.01
Pulmonary aspiration	45 (31.7)	7 (13.0)	0.01
Cesarean delivery	113 (79.6)	40 (74.1)	0.53
Perinatal death	7 (4.9)	11 (20.4)	0.01
Birth weight, g	2612 $\pm$ 776	2338 $\pm$ 831	0.05
Maternal death	0	8 (14.8)	0.01

Abbreviation: HELLP, hemolysis, elevated liver enzymes, and low platelet count.

<sup>a</sup> Values are given as mean  $\pm$  SD or number (percentage), unless indicated otherwise.

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