

## Severe Preeclampsia versus HELLP Syndrome: Maternal and Perinatal Outcomes at <34 and ≥34 Weeks' Gestation

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**Background:** Preeclampsia and Hemolysis, Elevated Liver enzymes, Low Platelet (HELLP) syndrome are important disorders affecting the health of both the mother and fetus. Prediction of the maternal and perinatal outcomes at early and late gestational age is important for the management of both disorders.

**Aims:** The purpose of the study was to investigate adverse maternal and perinatal outcomes in severe preeclampsia and HELLP syndrome cases according to gestational age.

**Study Design:** Retrospective cross-sectional study.

**Methods:** One hundred and ninety-seven pregnancies with severe preeclampsia and 56 pregnancies with HELLP syndrome were included the study. Clinical characteristics and adverse maternal and perinatal outcomes were noted from medical records. Participants were divided into two groups at <34 and ≥34 weeks' gestation: the severe preeclampsia group and the HELLP syndrome group. The differences between the outcomes in the groups were investigated. Statistical

analysis was performed using the Student t test, Fisher Exact test and Yates' Chi-square test.

**Results:** Eclampsia was more common in HELLP syndrome cases at <34 weeks' gestation (p 0.028). However, eclampsia rates were statistically similar between groups at ≥34 weeks' gestation. The requirement for blood products transfusion was higher in the HELLP group at all gestational weeks. No statistical difference was found in perinatal outcomes between severe preeclampsia and HELLP groups at less than and more than 34 weeks' gestation.

**Conclusion:** Eclampsia risk increases in HELLP syndrome, especially at gestations less than 34 weeks. Perinatal morbidity at less than 34 weeks' gestation and mortality were similar in severe preeclampsia and HELLP syndrome cases at the same gestational age.

**Keywords:** Blood transfusion, eclampsia, gestational age, HELLP syndrome, preeclampsia

Preeclampsia is an important disease affecting maternal and fetal health worldwide (1). Hemolysis, Elevated Liver enzymes, Low Platelet (HELLP) Syndrome is considered a more severe form of preeclampsia (2). However, the relationship between the two disorders is controversial. HELLP syndrome is assumed to be a separate disorder by some authorities due

to the lack of hypertension or proteinuria in fifteen to twenty percent of women with HELLP syndrome (3-4). Some studies have also shown that maternal morbidity risk is higher in HELLP syndrome cases than in severe preeclampsia (5-6). In other studies, no significant difference was found for the maternal and perinatal outcomes between the two disorders (7-8).

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The purpose of expectant management is to reduce problems due to prematurity in severe preeclampsia. However, maternal risks and perinatal benefits of expectant management are unclear (1). In this study, adverse maternal and perinatal outcomes were investigated in HELLP syndrome and severe preeclampsia cases, at <34 and  $\geq$ 34 weeks' gestation.

## MATERIALS AND METHODS

Severe preeclampsia and HELLP syndrome cases, treated in a tertiary education hospital, between January 2007 and January 2013, were included in this retrospective study. The local institutional review board approved the study. Written informed consent was obtained from women participating in the study.

Diagnostic criteria of severe preeclampsia were systolic blood pressure  $\geq$ 160 mmHg or diastolic blood pressure  $\geq$ 110mmHg in two separate readings more than four hours apart, new onset cerebral or visual disturbance, elevated liver enzymes, epigastric pain, pulmonary edema, low platelet count, progressive renal insufficiency (9). The presence of the following three criteria was required for the diagnosis of HELLP: (1) hemolysis (serum lactate dehydrogenase level of higher than 600IU/L or total bilirubin level of higher than 1.2mg/dL or decreased hemoglobin and hematocrit levels); (2) low platelet count (lower than 150000 cells/mm<sup>3</sup>); and (3) elevated liver enzymes (aspartate aminotransferase level of higher than 40IU/L and/or alanine aminotransferase level of higher than 40 IU/L) (5,10).

Last menstrual period and ultrasonographic findings at less than 20 weeks' gestation were used to detect gestational age. Maternal age, gravidity, parity, mean arterial blood pressure, previous preeclampsia and chronic hypertension history, gestational age at delivery, epigastric pain, headache, and visual disturbance were variables included in the study. Hemogram, liver and renal function tests, and coagulation profile results were recorded. Eclampsia, the requirement for blood products transfusion, pulmonary edema, placental abruption, cesarean delivery, disseminated intravascular coagulopathy (DIC), acute renal failure and death were the adverse maternal outcomes studied. Oliguria or anuria with serum creatinine level of higher than 2 mg/dL was defined as acute renal failure.

Adverse perinatal outcomes studied included preterm birth, low birth weight, the presence of fetal distress, low Apgar scores at 5 minutes and intrauterine death. Less than 37 weeks of gestation, birth weight of 2500 grams or below and an Apgar score of 7 or less at 5 minutes were defined preterm birth, low birth weight and low Apgar score, respectively. Fetal well-being was assessed with continuous electronic fetal

heart rate monitoring (Avalon FM 20 Fetal Monitor, Philips, Amsterdam, Netherlands), biophysical profile and umbilical artery Doppler measurement (Logiq P5, General Electric Healthcare, Wauwatosa, WI, USA).

To prevent and control seizures, intravenous magnesium sulfate (Magnesium sulfate 15%, Osel, Istanbul, Turkey) was administered routinely (6 g loading dose and 2 g/h maintenance dose, continued postpartum for 24 hours). To accelerate fetal lung maturity, 2 doses of 12 mg betamethasone (Celestone Chronodose, Merck Sharp Dohme, Cook County, IL, USA) intramuscularly every 24 hours were administered at <34 weeks' gestation. Women were divided into two groups at <34 and  $\geq$ 34 weeks' gestation: the severe preeclampsia group and the HELLP syndrome group. The differences between the maternal and perinatal outcomes in the two groups were investigated.

SPSS version 21 (SPSS Inc., Chicago, IL, USA) was used for statistical analysis. The Kolmogorov-Smirnov test was used to check the normal distribution of continuous variables. Descriptive statistics presented were mean values and standard deviation. When data were not sufficient quality to satisfy the assumptions of parametric tests, the Mann-Whitney U test was used. Differences between groups for categorical variables were examined with Fisher Exact tests or Yates' Chi-square test. A p value <0.05 was considered statistically significant.

## RESULTS

Two hundred and fifty three severe preeclampsia and HELLP syndrome cases were included the study. There were 116 (46%) pregnancies at less than 34 weeks' gestation and 137 (54%) pregnancies at more than 34 weeks' gestation. Eighty-six (74%) women had severe preeclampsia and 30 (26%) women had HELLP syndrome at <34 weeks' gestation. One hundred and eleven (81%) women had severe preeclampsia and 26 (19%) women had HELLP syndrome at  $\geq$ 34 weeks' gestation. Details of clinical characteristics, symptoms and the mean value of the laboratory parameters are shown in Table 1. Maternal age, gestational age, gravidity, parity were not statistically different in two groups, at <34 and  $\geq$ 34 weeks' gestation ( $p>0.05$ ). The mean blood pressure was significantly higher in the severe preeclampsia group at  $\geq$ 34 weeks' gestation ( $134.10\pm 12.54$  mmHg versus  $126.73\pm 11.91$  mmHg;  $p 0.007$ ). Headache rate was higher in the severe preeclampsia group at <34 weeks' gestation (60.5% versus 33.3%;  $p 0.019$ ). Epigastric pain rate, peak serum aspartate aminotransferase (AST) level, and peak serum alanine aminotransferase (ALT) level were higher and mean platelet count was lower in the

**TABLE 1.** Demographic characteristics, clinical and laboratory findings

	<34 weeks' gestation		≥34 weeks' gestation	
	Severe preeclampsia N=86 (74%)	HELLP syndrome N=30 (26%)	Severe preeclampsia N=111 (81%)	HELLP syndrome N=26 (19%)
Maternal age (years, mean±SD)	29.01±6.12	29.53±5.50	28.21±6.22	28.62±5.75
Gravidity (mean±SD)	2.24±1.41	2.66±1.78	2.57±1.83	2.42±1.14
Parity (mean±SD)	1.80±0.98	2.05±1.70	1.96±0.99	1.59±0.71
Mean arterial blood pressure (mmHg, mean±SD)	156.13±117.07	140.53±15.91	134.10±12.54*	126.73±11.91*
Gestational age (weeks, mean±SD)	29.86±2.54	29.10±3.08	36.60±1.74	36.27±1.66
Headache (%)	52 (60.5%)*	10 (33.3%)*	49 (44.1%)	12 (46.2%)
Visual disturbance (%)	13 (15.1%)	5 (16.7%)	13 (11.7%)	3 (11.5%)
Epigastric pain (%)	5 (5.8%)*	14 (46.7%)*	6 (5.4%)*	7 (26.9%)*
Platelet count (cells/mm <sup>3</sup> , mean±SD)	204448±71044*	91667±62941*	211045±64576*	83154±41540*
AST (IU/L, mean±SD)	35.77±24.49*	372.13±425.91*	36.53±37.51*	306.00±266.22*
ALT (IU/L, mean±SD)	25.42±14.79*	223.77±207.25*	30.84±52.94*	185.46±144.99*
Creatinine (mg/dL, mean±SD)	0.72±0.19	0.95±0.58	0.76±0.22	0.70±0.18

AST: aspartate aminotransferase; ALT: alanine aminotransferase; HELLP: hemolysis - elevated liver enzymes - low platelet; SD: standard deviation

\*p<0.05

**TABLE 2.** Maternal outcomes

	<34 weeks' gestation			≥34 weeks' gestation		
	Severe preeclampsia N (%)	HELLP syndrome N (%)	p value	Severe preeclampsia N (%)	HELLP syndrome N (%)	p value
Eclampsia	4 (4.7)	6 (20.0)	0.028	-	1 (3.8)	0.190
Placental abruption	4 (4.7)	2 (6.7)	0.648	1 (0.9)	-	1.000
Transfusion of blood products	4 (4.7)	8 (26.7)	0.002	5 (4.5)	5 (19.2)	0.022
Acute renal failure	1 (1.2)	1 (3.3)	0.452	-	-	-
Cesarean delivery	75 (87.2)	28 (93.3)	0.510	88 (79.3)	23 (88.5)	0.407

HELLP: hemolysis - elevated liver enzymes - low platelet

HELLP syndrome cases at all stages of gestation (p<0.05). There was no difference between the mean creatinine values in either group.

Adverse maternal outcomes are shown in Table 2. Eclampsia was more common in HELLP syndrome cases at <34 weeks' gestation (20% versus 4.7%; or 5.1; 95% confidence interval 1.3 -19.6; p 0.028). There were statistically similar eclampsia rates between groups at ≥34 weeks' gestation. The requirement for blood products transfusion was more common in HELLP syndrome cases than in severe preeclampsia cases in both gestational age groups (26.7% versus 4.7%, p 0.002 at <34 weeks' gestation; 19.2% versus 4.5%, p 0.022 at ≥34 weeks' gestation). Placental abruption, cesarean delivery, and acute renal failure rates in two groups were statistically similar at <34 and ≥34 weeks' gestation (p>0.05). DIC, pulmonary edema, or maternal death did not occur in any individuals.

Adverse perinatal outcomes are shown in Table 3. Perinatal outcomes were similar in the two groups at <34 and ≥34 weeks' gestation.

## DISCUSSION

In our study, clinical findings, maternal and perinatal outcomes were investigated in severe preeclampsia and HELLP syndrome cases at less and more than 34 weeks' gestation. Maternal age, gravidity, parity, gestational age at delivery, and mean arterial blood pressure were similar in both disorders. However, Haddad et al. (8) showed that severe preeclampsia cases were younger than HELLP syndrome cases and another study found lower gestational age at delivery in HELLP syndrome cases (7).

Analogous with previous reports, we found a higher epigastric pain rate in HELLP syndrome cases at less and more than 34 weeks' gestation and a higher headache rate in severe preeclampsia cases at less than 34 weeks' gestation (5).

We found that eclampsia rate was higher only at <34 weeks' gestation and the requirement for transfusion of blood products was higher at both <34 and ≥34 weeks' gestation in HELLP syndrome cases than in severe preeclampsia cases. Other adverse maternal outcome rates were similar in both disorders

TABLE 3. Perinatal outcomes

	<34 weeks' gestation		≥34 weeks' gestation	
	Severe preeclampsia N (%)	HELLP syndrome N (%)	Severe preeclampsia N (%)	HELLP syndrome N (%)
Preterm birth	86 (100)	30 (100)	49 (44.1)	13 (50.0)
Fetal distress	36 (42.4)	11 (37.9)	23 (20.7)	3 (11.5)
Low Apgar scores	44 (51.2)	18 (60.0)	4 (3.6)	2 (7.7)
Low birth weight	85 (98.8)	29 (96.7)	51 (45.9)	12 (46.2)
Intrauterine death	12 (14.0)	5 (16.7)	3 (2.7)	0 (0)

HELLP: hemolysis - elevated liver enzymes - low platelet

and gestational age groups. There are other studies presenting similar and different findings in the literature. Martin et al. (11) showed that the eclampsia rate was higher in HELLP syndrome cases than in severe preeclampsia between 24 and 32 weeks of gestation. However, another study found similar eclampsia rates in both groups and the requirement for blood products transfusions was higher in HELLP syndrome than in severe preeclampsia in cases at <28 weeks' gestation (8).

There are several studies showing that HELLP syndrome and severe preeclampsia increase perinatal morbidity and mortality (12-14). However, it is unclear whether perinatal morbidity and mortality is dependent on the prematurity or nature of disease. Some studies have shown that perinatal morbidity was higher in patients with HELLP syndrome than in those with hypertension alone (15,16). However, there are further studies showing that gestational age was more effective than maternal disease for perinatal outcomes (7,17-19). In two studies, neonatal death rates were not different between HELLP syndrome and severe preeclampsia at the same stage of gestation (7,20). In our study, women were divided into two gestational age groups and perinatal outcomes were evaluated separately in these two groups. We found that perinatal mortality and morbidity rates were statistically similar for the two disorders. In contrast to our findings, Abramovici et al. (7) suggested that low birth weight, low Apgar scores and intrauterine death rates were higher in HELLP syndrome cases than severe preeclampsia at <36 weeks' gestation.

In conclusion, the aim of treatment in HELLP syndrome and severe preeclampsia is to decrease maternal and perinatal morbidity and mortality. Our study showed that perinatal morbidity and mortality were similar in HELLP syndrome cases and severe preeclampsia cases at the same gestational age. However, some maternal adverse outcomes were more frequent in HELLP syndrome cases. Eclampsia risk was higher in HELLP syndrome, especially at <34 weeks of gestation. Therefore, labor induction might be considered earlier in HELLP syndrome cases than in severe preeclampsia at <34 weeks' gestation.

**Ethics Committee Approval:** Ethics committee approval was received for this study from the Institutional Review Board.

**Informed Consent:** Written informed consent was obtained from patients who participated in this study.

**Peer-review:** Externally peer-reviewed.

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