

Comparison of maternal and neonatal outcomes in women with HELLP syndrome and women with severe preeclampsia without HELLP syndrome

Abdulkadir Turgut
Oya Demirci
Elif Demirci
Mehmet Uludoğan

Zeynep Kamil Gynecologic and Pediatric Training and Research Hospital, Department of Obstetrics and Gynecology, Istanbul, Turkey

Corresponding author:

Oya Demirci
Zeynep Kamil Gynecologic and Pediatric Training and Research Hospital,
Department of Obstetrics and Gynecology,
Istanbul, Turkey, 34668
E-mail: demircioya@gmail.com

Summary

Objective: To examine and to compare postpartum maternal and neonatal complications and morbidities in women with HELLP syndrome (HELLP group) and women with severe preeclampsia without HELLP syndrome (severe preeclamptic group).

Methods: In this retrospective study, 111 patients in the HELLP group were matched with 467 patients in the severe preeclamptic group according to maternal and neonatal complications and morbidities. **Results:** The rate of transfusion of blood products and acute renal failure was significantly greater in women with HELLP syndrome. One maternal mortality (0.9 %) was found in women with HELLP syndrome, and no maternal mortality in women in severe preeclamptic group. There were significant differences between the HELLP group and the severe preeclamptic group in neonatal mortality and morbidity. It was found that HELLP syndrome cases had significantly lower gestational age and fetal bodyweight. The simultaneous presence of HELLP syndrome and preeclampsia, along with oliguria, ascites, thrombocytopenia, elevated liver enzymes and caesarean delivery, was associated with post-partum complications.

Conclusion: This study shows that maternal and neonatal morbidity and mortality are increased in pregnancies complicated by severe preeclampsia with HELLP syndrome. Neonatal mortality and morbidity appear to be influenced primarily by gestational age at delivery.

Key Words: HELLP syndrome, pre-eclampsia, neonatal outcome, maternal mortality.

Introduction

HELLP syndrome, considered to be an atypical form of severe preeclampsia, is characterized by the triad of hemolysis, elevated liver function test, and low platelet count (1). Since Weinstein's (2) initial description of the HELLP syndrome, many publications have focused on the diagnosis, management, and associated complications of this syndrome. The incidence of this syndrome among patients with severe preeclampsia is reported to be 4-18.9%, with 70% during the antenatal period and 30% during the post-partum period (3).

Pregnancy complicated by severe preeclampsia with HELLP syndrome is associated with an increased risk of maternal and perinatal morbidity and mortality (1,4). The reported maternal mortality and perinatal mortality rate of HELLP syndrome ranges from 0-24% and 6.6-60%, respectively (2,5). Maternal mortality appears related to renal failure, consumption coagulopathy, ablatio placenta, lung and brain edemas, liver hematoma, and hypovolemic shock (6). Perinatal mortality appears to be related primarily to gestational age at delivery (7-10). According to general opinion, HELLP syndrome presents a higher risk for mother and child than does severe preeclampsia without HELLP syndrome. The definitive therapy for severe preeclampsia, with or without HELLP syndrome, is removal of all gestational products from the uterus, although some investigators have advocated temporizing management (3, 11-13).

The purpose of this study is to examine and to compare postpartum maternal and neonatal complications and morbidities in women with HELLP syndrome (HELLP group) and in women with severe preeclampsia without HELLP syndrome (severe preeclamptic group).

Materials and Methods

The study was performed using the medical records of patients with a diagnosis of severe preeclampsia with HELLP syndrome (HELLP group) or severe preeclampsia without HELLP (severe preeclampsia group) in the Zeynep Kamil Gynecologic and Pediatric Training and Research Hospital between January 2005 and January 2008. Women with a history of hematological, liver, and renal illnesses or any other illness were excluded from the study.

HELLP syndrome was defined by using the strict criteria of Sibai (14). The diagnosis was made by determining that all 3 of the following criteria were present: hemolysis (characteristic peripheral blood smear and serum lactate dehydrogenase >600 u/l or serum total bilirubin \geq 1.2 mg/dl), elevated liver enzymes (serum aspartate aminotransferase \geq 70u/l), and low platelet counts (<100,000 cells/ μ l). Women were considered to have

severe preeclampsia if they met one or more of the following criteria of the National High Blood Pressure Education Program 2000 (15): systolic arterial BP \geq 160 mmHg or diastolic arterial BP \geq 110 mmHg on two or more consecutive occasions, at least 6 h apart, while the patient is at bed rest; cerebral or visual disturbances; epigastric or right upper-quadrant pain, ascites, or pulmonary edema; or proteinuria \geq 2 g/l and oliguria of less than 400 ml/24 h or 30 ml/h. All women routinely received intravenous magnesium sulfate to prevent and control convulsions and oral nifedipine to maintain diastolic blood pressure below 110 mgHg. Oral antihypertensive medications with methyl dopa or nifedipine were then used to maintain the diastolic pressure between 90-100mgHg. Blood products were used to correct severe anemia or coagulation abnormalities, as needed. Also, dexamethasone as a steroid was applied to the cases with HELLP syndrome.

Gestational age was determined by using the best obstetric criteria, including either last menstrual period or ultrasonography (where available) at $<$ 12 weeks' gestation, or both. Corticosteroids were used to accelerate fetal lung maturity in all cases when the gestational age was \geq 25, but less than 34 weeks. Intrauterine growth restriction was defined as a birth weight below the 5th percentile for that gestational age. The comparison of maternal conditions was made with regard to hematological and biochemical examination results, eclampsia, duration of hospital stay, maternal mortality, requirement for transfusion of blood and blood products, abruptio placentae, disseminated intravascular coagulopathy (DIC), acute renal failure, pulmonary edema, wound infection, thromboembolic complication, re-operation, atony, hematoma and neurological signs, requirement for intensive care unit, and requirement for mechanic ventilation. The DIC was defined as the presence of \geq 3 of the following criteria: low platelet count ($<$ 100,000 cells/ μ L), low fibrinogen level ($<$ 300 mg/dL), positive D-dimers (\geq 40 mg/dL), or prolonged prothrombin time (\geq 14 seconds) and partial thromboplastin times (\geq 40 seconds). Acute renal failure was diagnosed in the presence of oliguria or anuria in association with a creatinine clearance of \leq 20 mL/min and an elevated serum creatinine level of \geq 2 mg/dL. Pulmonary edema was assessed on the basis of clinical findings and radiography of the chest. The neonatal medical records were reviewed for the following outcomes as diagnosed by the attending pediatrician: fetal growth restriction (FGR), hypoglycemia of the newborn, hyperbilirubinemia, respiratory distress syndrome (RDS), bronchopulmonary dysplasia (BPD), intraventricular hemorrhage (IVH), necrotizing enterocolitis (NEC), duration of stay in an intensive care unit, sepsis, and neonatal death.

Data are presented as mean \pm SD, median and range, or frequency, as appropriate. Categorical data were compared by the Chi-2 test-square or the Fisher exact test. Continuous variables were analyzed by the Student t test. A multivariate A P value $<$.05 was considered significant. Analysis was performed with logistic regression analysis.

Results

During the study period, there were 40,908 deliveries at this tertiary medical center in Turkey, 578 of which were complicated by severe preeclampsia; and 467 severe

preeclamptic patients without HELLP syndrome (severe preeclamptic group) were compared with 111 patients with HELLP syndrome (HELLP group). A total of 35 intrauterine fetal deaths (29 fetuses in the severe preeclampsia group, and 6 fetuses in the HELLP group) were excluded from this study group when comparing neonatal outcomes. The demographic and clinical characteristics of these women are shown in Table I. Gestational age at diagnosis, gestational age at delivery, and the time interval between diagnosis and delivery were significantly lower in the HELLP group. Caesarean delivery was significantly higher and post-partum oliguria was significantly lower in the HELLP group. Rates of epigastric pain were also significantly higher in the women with HELLP syndrome. The comparison of presenting symptoms is shown in Table II. The pre-partum and post-partum hematological and biochemical characteristics of the women are shown in Table III. Post-partum blood urea nitrogen (BUN) and creatinine levels were significantly higher, and hemoglobin and hematocrit levels were significantly lower in the HELLP group than in the severe preeclamptic group when compared pre-partum. Table IV compares maternal complications and morbidities among severe preeclamptic women with or without HELLP syndrome. It was found that more blood transfusions, especially thrombocyte, erythrocyte, and fresh frozen plasma, were used for the HELLP group ($<$ 0.001). There was a significant association between acute renal failure and HELLP syndrome. The need for the intensive care unit and mechanical ventilation was significantly higher in the HELLP group. The occurrence of at least one complication was significantly higher in the HELLP group (16.8%) than in the severe preeclamptic group (11.8%). There was one maternal mortality (0.9%) in the HELLP group and no maternal mortality among the women in severe preeclamptic group a. The neonatal outcomes are presented in Table V. It was found that HELLP syndrome cases had significantly lower gestational age and fetal bodyweight. There were significant differences between the HELLP group and the severe preeclamptic group in neonatal mortality, NEC, requirement for mechanical ventilation and the intensive care unit, and the duration of stay in the newborn intensive care unit. Table 6 compares post-partum complications according to pathology, clinical signs, labor and delivery, and laboratory data between groups. The simultaneous presence of HELLP syndrome and preeclampsia was associated with post-partum complications (OR: 8.4, 95%; CI: 5.6-13, 4), whereas that was not the case when the two conditions were considered separately. Presence of acid and pre-partum oliguria, caesarean delivery, and the time interval between diagnosis and delivery were associated with post-partum complications. A shorter interval time between diagnosis and delivery appeared to be associated with post-partum complications. A thrombocyte count of $<$ 100,000 cells/ μ L and a level of AST \geq 70 U/L were found to be statistically associated with post-partum complications (OR:7.7; CI:4.6-12.9; OR:6; CI:3.1-11.5, respectively).

Discussion

The HELLP syndrome has been a subject of much controversy with regard to diagnosis, incidence, and outcome. The aforementioned criteria proposed by Sibai

Comparison of maternal and neonatal outcomes in women with HELLP syndrome and women with severe preeclampsia without HELLP syndrome

Table I - Demographic and clinical characteristics of HELLP group and severe preeclamptic group

	Severe preeclamptic group (n:467)	HELLP group (n:111)	p
Gravidity	2.3±1.8	2.4±1.6	NS
Parity(n)	0.9±1.3	1.1±1.3	NS
Gestational age at diagnosis	34.4±3.6	33.1±3.6	NS
Gestational age at delivery	34.6±3.6	33.2±3.6	<0.001
Ante-partum			
Systolic BP(mmHg)	174.6±16.6	172.8±21.6	NS
Diastolic BP(mmHg)	114.1±10.3	113.9±14.5	NS
Post-partum			
Systolic BP(mmHg)	153.1±16.6	155±15.7	NS
Diastolic BP(mmHg)	100±11.1	101.8±11.1	NS
Time interval between diagnosis and delivery	1.5±1.7	0.7±1.1	<0.001
Maternal age	27.6±5.7	27.7±5.4	NS
Vaginal delivery	134 (28.7)	21 (18.9)	0.037
Caesarean delivery	333 (71.3)	90 (81.1)	0.037
Parity			
Primigravida	219(46.9)	42(37.8)	NS
Parous	248(53.1)	63(56.8)	NS
At Caesarean Section			
Abdominal acid	60 (18.0)	22 (24.4)	NS
Amount of acid	400.8±570.8	484.1±699.7	NS
Feature of amnion liquid			
Clear	455 (97.4)	107 (96.4)	NS
Meconium	12 (2.6)	4 (3.6)	NS
Uterine contraction before Caesarean Section	57 (17.1)	16 (17.8)	NS
Oliguria(400ml/24h or30ml/h)			
Pre-partum	115 (24.6)	24 (21.6)	NS
Post-partum	85 (18.2)	37 (33.3)	<0.001
Eclampsia			
Pre-partum	18 (3.9)	6 (5.4)	NS
Post-partum	2 (0.4)	3 (2.7)	NS
Preterm rupture of membrane	10 (2.1)	-	NS
Chorioamnionitis	1 (0.2)	-	NS

Table II - Presenting symptoms in women

Symptoms	Severe preeclamptic group (n:467)	HELLP group (n:111)	Odds ratio (GA %95)	p
Headache	280 (60.0)	58 (52.3)	1.39 (0.90-2.07)	NS
Visual change	132 (28.3)	40 (36.0)	0.70 (0.45-1.08)	NS
Epigastric pain	26 (5.6)	36 (32.4)	0.12(0.07-0.21)	<0.001
Nausea and vomiting	38 (8.1)	7 (6.3)	1.32(0.57-3.03)	NS
Dizziness	12 (2.6)	1 (0.9)	2.90 (0.37-22.55)	NS
At least 1 symptom	162 (34.7)	32 (28.8)	1.31 (0.83-2.06)	NS

Table III - Hematological and biochemical characteristics of HELLP group and severe preeclamptic group

	Severe preeclamptic group (n:467)	HELLP group (n:111)	p
Pre-partum			
Hemoglobin(g/dl)	12.1±1.7	12.2±2	NS
Hematocrit(%)	35.6±4.7	35.5±6.3	NS
Platelet count (/mm ³)	222636.6±77574.5	93972.5±61236.6	<0.001
AST(U/L)	36.4±28.6	321.4±318.1	<0.001
ALT(U/L)	36±30.7	257.7±274.1	<0.001
LDH(U/L)	283.1±109.0	758±476.8	<0.001
BUN(mg/dl)	12.3±4.9	13.1±4.2	NS
Creatinine(mg/dl)	0.8±0.2	0.8±0.2	NS
Uric acid(mg/dl)	5.9±1.5	6.1±1.3	NS
Total protein(g/dl)	5.7±0.7	5.6±0.6	NS
Albumin(g/dl)	2.3±0.5	2.3±0.6	NS
Sodium(mmol/L)	135.9±3.7	134.7±3.6	NS
Potassium(mmol/L)	4.5±0.6	4.5±0.6	NS
Chlorine(mmol/L)	103.4±11.4	102.7±12.6	NS
Urine protein			
-dipstick testing			<0.001
.o or trace(%)	-	2(1.8)	
.+1.+2(%)	8(1.7)	21(18.9)	
.+3,+4(%)	459(98.3)	88(79.3)	
-proteinuria in a 24 h period(g/24h)	7.6±11.2	5.7±6.6	NS
LDH≥600(U/L)	5 (1.1)	54 (48.6)	<0.001
AST≥70(U/L)	31 (6.6)	93 (83.8)	<0.001
Uric acid≥5.5mg/dl	261 (55.9)	76 (68.5)	0.016
Post-partum			
Hemoglobin(g/dl)	10.7±1.7	10.1±2.1	0.002
Hematocrit(%)	31.7±5.1	29.1±6	<0.001
Platelet count (/mm ³)	225154.4±80336	102918.9±59266.3	<0.001
AST(U/L)	36.1±19.3	207.4±247.3	<0.001
ALT(U/L)	37±28.4	171.6±186.8	<0.001
LDH(U/L)	303.3±94.2	691.1±558.3	<0.001
BUN(mg/dl)	12±5.2	16±19.7	0.001
Creatinine(mg/dl)	0.8±0.2	0.9±0.7	0.002
Uric acid(mg/dl)	5.9±1.6	6±1.5	NS
Total protein(g/dl)	5.2±0.7	5.1±0.7	NS
Albumin(g/dl)	2±0.5	2.1±0.4	NS
Sodium(mmol/L)	135.6±4.1	135.6±5	NS
Potassium(mmol/L)	4.6±0.6	4.5±0.6	NS
Chlorine(mmol/L)	103.5±4.1	103.4±3.6	NS
LDH≥600(U/L)	3 (0.6)	43 (38.7)	<0.001
AST≥70(U/L)	21 (4.5)	71 (64.0)	<0.001
Uric acid≥5.5mg/dl	209 (44.8)	72 (64.9)	<0.001

AST(aspartate aminotransferase), ALT(alanine aminotransferase), LDH(lactate dehydrogenase), BUN(blood urea nitrogen),

et al., which are the more stringent, were used in this study (14). The HELLP syndrome occurs in 0.17-0.85% of all pregnancies (16). Consistently, we found that the HELLP syndrome occurs in an average of 0.27% of all pregnancies. Consistent with the literature (3), the HELLP syndrome rate among patients in the severe

preeclamptic group was 18% in our data. Our rate comes from tertiary care center data, and we do not have yet a rate for the overall population in our country. But Liu et al. reported a higher proportion than this rate (25%). The study's authors explained that this difference may arise from the possibility of underestimat-

Comparison of maternal and neonatal outcomes in women with HELLP syndrome and women with severe preeclampsia without HELLP syndrome

Table IV - Maternal complications in the HELLP group and severe preeclamptic group

	Severe preeclamptic group (n:467)	HELLP group (n:111)	p
Post-partum complications			
Fever $\geq 38.5^{\circ}\text{C}$	18 (3.9)	3 (2.7)	NS
Re-operation	6 (1.3)	2 (1.8)	NS
Thromboembolic complication	-	-	-
Wound infection	11 (2.4)	3 (2.7)	NS
Post-partum eclampsia	2 (0.4)	3 (2.7)	NS
Blood transfusion			
Thrombocyte transfusion	4 (0.9)	55 (49.5)	<0.001
Erythrocyte transfusion	24 (5.1)	34 (30.6)	<0.001
Whole blood transfusion	1 (0.2)	2 (1.8)	NS
Fresh frozen plasma transfusion	15 (3.2)	33 (29.7)	<0.001
DIC	-	1 (0.9)	NS
ARF	11 (2.4)	9 (8.1)	NS
Pulmonary edema	1 (0.2)	-	NS
Maternal death	-	1 (0.9)	NS
Boon curettage	6 (1.3)	1 (0.9)	NS
Atony	2 (0.4)	1 (0.9)	NS
Hematoma	1 (0.2)	4 (3.6)	0.006
Retinal detachment	1 (0.2)	1 (0.9)	NS
Visual disturbance	3 (0.6)	-	NS
Occipital infarction and visual problems	1 (0.2)	-	NS
Hemodialysis	-	1 (0.9)	NS
Intracerebral hemorrhage	-	1 (0.9)	NS
Brain edema	-	1 (0.9)	NS
Abruptio placentae	21 (4.5)	7 (6.3)	NS
At least one complication	50 (10.7)	18 (16.2)	<0.001
Intensive care unit	-	4 (3.6)	0.001
Mechanical ventilation	-	2 (1.8)	0.037
The length of stay after delivery	11.2 \pm 17.9	13.6 \pm 16.3	NS

DIC (disseminated intravascular coagulation), ARF (acute renal failure)

ing the incidence of severe preeclampsia cases (17). We found that the mean interval time between diagnosis and delivery is 0.7 days and 1.5 days for all pregnancies and 0.9 days and 2.2 days in pregnancies before a gestational age of 32 weeks for the HELLP group and the severe preeclamptic group, respectively. We opted for expeditious delivery when maternal conditions progressed adversely. Traditionally, women with severe preeclampsia, even if remote from term, are delivered expeditiously, regardless of gestational age. Haddad et al. reported several retrospective, case-control, observational, prospective, or randomized trials in which expectant management in women with severe preeclampsia was feasible in well-selected patients without prejudicing maternal safety (18). In our study this short interval between diagnosis and delivery is due to the high rate of complicated cases referred to our institution and also because the condition was not recognized as promptly in medical centers already visited by the women as it was in ours.

The overall rate of adverse maternal complications observed in the HELLP group (16.2%) was higher than in the severe preeclamptic group (11.8%). It was found that the HELLP group cases required a statistically significant greater amount of thrombocyte, erythrocyte, and fresh frozen plasma transfusion. Similar to our study, several studies state that HELLP syndrome cases require a greater amount of blood products (8,9,19-21). We also found that acute renal failure was significantly higher in the HELLP syndrome group. Similarly, Liu et al. and Martin et al. found significantly higher acute renal failure in the HELLP group compared with the severe preeclamptic group (17,22). In this study, we found a significantly higher requirement for mechanical ventilation and the intensive care unit in the HELLP group, although only one maternal mortality was observed (0.9%) in the HELLP group and no maternal mortality in the severe preeclamptic group. Liu et al. reported that the maternal mortality rate with the HELLP syndrome was no different than the maternal mortality rate for se-

Table V - Neonatal outcomes in the HELLP group and severe preeclamptic group

	Severe preeclampsia (n:467)	HELLP Syndrome (n:111)	p
Sex			NS
female	232(49.7)	60(54.1)	
male	235(50.3)	51(45.9)	
FGR 124(26.6)	28(25.2)	NS	
Apgar score ≤ 6 at 5 min*	31(7.1)	13(12.4)	NS
Neonatal mortality *	23(5.3)	15(14.3)	0.001
RDS *	40(9.1)	14(13.3)	NS
IVH *	9(2.1)	3(2.9)	NS
NEC *	0(0)	3(2.9)	0.007
BPD *	5(1.1)	0(0)	NS
Hypoglycemia *	41(9.4)	15(14.3)	NS
Hyperbilirubinemia *	174(39.7)	49(46.7)	NS
Sepsis *	47(10.7)	15(14.3)	NS
ROP *	8(1.8)	3(2.9)	NS
Perinatal asphyxia *	5(1.1)	2(1.9)	NS
Glucocorticoid therapy <34 hafta	205(43.9)	65(58.6)	0.005
IUFD 29(6.2)	6(5.4)	NS	
Mechanical ventilation *	62(14.2)	33(31.4)	<0.001
Intensive care *	233(53.2)	73(69.5)	0.002
Fetal body weight (g)	2282.6 \pm 868.1	1971.2 \pm 735.5	<0.001
Apgar score 1.min *	6.5 \pm 1.7	6.0 \pm 1.8	0.004
Apgar score 5.min*	8.3 \pm 1.2	8.0 \pm 1.2	0.012
Gestational age at delivery	35.3 \pm 4.2	34.3 \pm 3.3	0.008
Period for staying in neonatal intensive care unit(d) *	5.2 \pm 14.3	13.1 \pm 18.5	<0.001

FGR (fetal growth restriction), RDS (respiratory distress syndrome), IVH (intraventricular hemorrhage), NEC (necrotizing enterocolitis), BPD (bronchopulmonary dysplasia), ROP (), IUFD (intrauterine fetal death)

vere preeclampsia (17). We believe that the low maternal mortality rate in our study, especially for severe preeclampsia, can be explained by the aggressive approach to delivery—i.e., that the fetus is delivered when maternal conditions warrant, regardless of gestational age. In recent publications maternal mortality was reported as ranging from 0% to 4.3 % for the HELLP syndrome group (20,23,24). We also detected that post-partum hematoma was significantly higher in the HELLP group, although instances of re-operation, DIC, and thromboembolic complications were not found to be different between the HELLP group and the severe preeclamptic group. Similarly, Haddad et al. reported no difference in DIC between the HELLP syndrome and severe preeclampsia groups (8). Conversely, Liu et al., Martin et al., and Pampus et al. reported a strong association between HELLP syndrome and coagulation abnormalities (4,17,22). In addition, although, in agreement with Haddad et al (8), we found similar rates of eclampsia in the HELLP group and in the severe preeclamptic group, Liu et al., Martin et al, and Miles et al. found, on the contrary, that eclampsia was more frequent in women with HELLP syndrome (17,22,25). In the present study, the simultaneous presence of HELLP syndrome and preeclampsia was strongly associated with post-partum complications, whereas such

was not the case when the two conditions were considered separately. Deruelle et al. supported this conclusion (26). Additionally, the presence of ascites and oliguria and the shorter interval between diagnosis and delivery was found to be significantly associated with post-partum complications. Deruelle et al. supported our result regarding ascites. But, after multivariate analysis, they did not find an association linking post-partum complications with oliguria and the interval between diagnosis and delivery (26). Moreover, we determined that thrombocytopenia (<100.000 cells/ μ l) and elevated liver enzymes (serum aspartate aminotransferase ≥ 70 u/l) were indicators of post-partum complications. Deruelle et al. found an association between thrombocytopenia and post-partum complications, although they did not find an association between elevated liver enzymes and post-partum complications after multivariate analysis, as consistent with Martin et al. (22, 26).

There is general agreement that both perinatal and fetal morbidity and mortality rates are increased in pregnancies complicated by HELLP syndrome. In our study, as previously reported (7-10,27,28), overall neonatal mortality and morbidities (NEC and lower 1.5-min APGAR scores) was greater in infants of women with the HELLP syndrome, and there was a greater need for mechanical ventilation, neonatal intensive care, and longer

Comparison of maternal and neonatal outcomes in women with HELLP syndrome and women with severe preeclampsia without HELLP syndrome

Table VI - Post-partum complications in women with preeclampsia and/or HELLP syndrome according to pathology, clinical signs, labor and delivery, biological features

	n=578	Women with post-partum complications			
		n(%) ^a	p	OR	CI (%95)
Type of pathology					
Severe preeclampsia alone	467 (80.8)	80 (17.1)	<0.001	0.1	0.1 – 0.2
HELLP syndrome alone	9(1.6)	4(44.4)	NS	0.2	0.1-1.2
Severe preeclampsia and HELLP syndrome	102 (17.6)	65 (63.7)	<0.001	8.4	5.6-13.4
Clinical signs					
Systolic BP≥160 mmHg	531 (91.9)	135 (25.4)	NS	0.9	0.4 – 2.4
Diastolic BP≥110mmHg	472 (81.7)	115 (24.4)	NS	0.9	0.5 – 1.6
Headache	338 (58.5)	80 (23.7)	NS	0.8	0.5 – 1.2
Visual change	172 (29.8)	49 (28.5)	NS	1.0	0.6 – 1.8
Epigastric pain	62 (10.7)	27 (43.5)	NS	1.1	0.5 – 2.4
Nausea and vomiting	45 (7.8)	12 (26.7)	NS	1.2	0.5 – 2.9
Dizziness	13 (2.2)	5 (38.5)	NS	3.8	0.9 – 16.4
Ascites	82 (19.4)	40 (48.8)	<0.001	2.9	1.6 – 5.0
Oliguria (<400ml/24h or 30ml/h)	221 (38.2)	73 (33.0)	0.029	1.7	1.1 – 2.8
Delivery					
Vaginal	134 (28.7)	22 (16.4)	referans		
Caesarean	333 (71.3)	127 (38.1)	<0.001	2.6	1.2-3.8
Gestational age<32 hafta	135 (23.4)	48 (35.6)	NS	1.1	0.5 – 2.1
Caesarean					
Before labor	350 (82.7)	100 (28.6)	referans		
During labor	73 (17.3)	27 (38.0)	NS	1.3	0.7 – 2.5
Time interval between diagnosis and delivery	1.4±1.7	1.0±1.3	0.009	0.8	0.7 – 0.9
The length of stay after delivery	11.6±17.6	12.9±18.5	NS	1.0	0.9 – 1.0
Eclampsia	27 (4.7)	13 (48.1)	NS	1.4	0.5 – 4.2
Preterm membrane rupture	10 (1.7)	2 (20.0)	NS	0.6	0.1 – 3.1
Abruptio placenta	23 (4.8)	10 (35.7)	NS	1.2	0.4 – 3.5
Thrombocyte count <100.000/mm ³	124 (22.9)	73 (58.9)	<0.001	7.7	4.6 – 12.9
LDH≥600 U/L	80 (17.4)	49 (61.3)	NS	1.6	0.7 – 3.2
AST≥70 U/L	144 (30.4)	72 (50.0)	0.022	6.0	3.1 – 11.5
Serum uric acid ≥5.5mg/dl	331 (75.6)	102 (30.8)	NS	0.9	0.6 – 1.8

times in the neonatal intensive care unit. Kim et al., Haddad et al., Abramovici et al., and Magann et al. indicated that neonatal morbidity or mortality is directly related to gestational age at delivery (7-10). In the present study, mean gestational age at delivery and fetal body weight was significantly lower in the HELLP group, although the other factors affecting neonatal outcomes—such as age of the mother, fetal growth restriction, abruptio placentae, and eclampsia—were not different between the groups. In addition, all of the 15 neonatal mortalities in the HELLP syndrome group had <32 weeks' gestational age, and 13 of these 15 neonatal mortalities were <30 weeks' gestational age. While 38% of the HELLP group pregnancies were below 32 weeks' gestational age, the rate for the pregnancies in the severe preeclamptic group was 20%. Thus our result supports the literature showing an association between gestational age and neonatal morbidity and mortality.

This study supports the idea that HELLP syndrome is associated with increased maternal and neonatal morbidity and mortality. Neonatal outcomes appear to be influenced primarily by gestational age at delivery. Aggressive treatment for the pregnant women appears to decrease the maternal mortality rate. Also, this observation allows the clinician to be more attentive to clinical and biological disturbances, especially the simultaneous presence of HELLP syndrome and preeclampsia, along with oliguria, ascites, thrombocytopenia, and elevated liver enzymes.

Management and delivery of HELLP syndrome mothers and infants should be performed at tertiary centers, where highly trained neonatal and adult intensive care unit personnel and facilities are available, and a team approach with obstetricians and specialized pediatricians is essential to improve both the maternal and neonatal outcomes.

References

1. American College of Obstetricians and Gynecologists. Hypertension in pregnancy. Washington: The College; 1996. Technical Bulletin No.: 219.
2. Weinstein L. Syndrome of hemolysis, elevated liver enzymes, and low platelet count: a severe consequence of hypertension in pregnancy. *Am J Obstet Gynecol.* 1982;142:159-67.
3. Vigil-De Gracia P. Pregnancy complicated by preeclampsia-eclampsia with HELLP syndrome. *Int J Gynecol Obstet.* 2001;72:17-23.
4. Van Pampus MG, Wolf H, Westenberg SM, van der Post JA, Bonsel GJ, Treffers PE. Maternal and perinatal outcome after expectant management of the HELLP syndrome compared with preeclampsia without HELLP syndrome. *Eur J Obstet Gynecol Reprod Biol.* 1998;76:31-6.
5. Sibai BM, Taslimi MM, El-Nazer A, Amon E, Mabie BC, Ryan GM. Maternal-perinatal outcome associated with the syndrome of hemolysis, elevated liver enzymes, and low platelets in severe preeclampsia-eclampsia. *Am J Obstet Gynecol.* 1986; 155: 501-509.
6. Vigil-de Gracia PE, Tenorio-Maranon FR, Cejudo-Carranza E, Helguera-Martinez A, Garcia-Caceres E. Difference between preeclampsia, HELLP syndrome and eclampsia, maternal evaluation. *Ginecol Obstet Mex.* 1996;64:377-82.
7. Kim HY, Sohn YS, Lim JH, Kim EH, Kwon JY, Park YW, Kim YH. Neonatal outcome after preterm delivery in HELLP syndrome. *Yonsei Med J.* 2006 Jun 30;47(3):393-8.
8. Haddad B, Barton JR, Livingston JC, Chahine R, Sibai BM. HELLP (hemolysis, elevated liver enzymes, and low platelet count) syndrome versus severe preeclampsia: onset at < or =28.0 weeks' gestation. *Am J Obstet Gynecol.* 2000(a); 183: 1475-9.
9. Abramovici D, Friedman SA, Mercer BM, Audibert F, Kao L, Sibai BM. Neonatal outcome in severe preeclampsia at 24-36 weeks' gestation: does the HELLP (hemolysis, elevated liver enzymes, and low platelet count) syndrome matter? *Am J Obstet Gynecol.* 1999; 180: 221-225.
10. Magann EF, Perry KG, Chauhan SP, Graves GR, Blake PG, Martin JN Jr. Neonatal salvage by weeks' gestation in pregnancies complicated by HELLP syndrome. *J Soc Gynecol Invest.* 1994;1:206-9.
11. Martin JN Jr, Perry KG Jr, Blake PG, MayWA, Moore A, Robinette L. Better maternal outcomes are achieved with dexamethasone therapy for postpartum HELLP (hemolysis, elevated liver enzymes, and thrombocytopenia) syndrome. *Am J Obstet Gynecol.* 1997;177: 1011-7.
12. Sibai BM. Diagnosis, controversies, and management of the syndrome of hemolysis, elevated liver enzymes, and low platelet count. *Obstet Gynecol.* 2004;103:981-91.
13. Clenney TL, Viera AJ. Corticosteroids for HELLP (haemolysis, elevated liver enzymes, low platelets) syndrome. *BMJ.* 2004; 329: 270-2.
14. Sibai BM. The HELLP syndrome (hemolysis, elevated liver enzyme levels, and low platelets): much ado about nothing? *Am J Obstet Gynecol.* 1990;162:311-6.
15. National High Blood Pressure Education Program Working Group on High Blood Pressure in Pregnancy. Report of the National High Blood Pressure Education Program Working Group on high blood pressure in pregnancy. *Am J Obstet Gynecol.* 2000;183:S1-S22.
16. Prichard JA, Weissman R, Ratnoff OD et al. Intravascular hemolysis, thrombocytopenia, and other hematologic abnormalities associated with severe toxemia of pregnancy. *N Engl J Med.* 1954;250:89-98.
17. Liu CM, Chang SD, Cheng PJ, Chao AS. Comparisons of maternal and perinatal outcomes in Taiwanese women with complete and partial HELLP syndrome and women with severe preeclampsia without HELLP. *J Obstet Gynaecol Res.* 2006 Dec;32(6):550-8.
18. Haddad B, Sibai BM. Expectant management in pregnancies with severe preeclampsia. *Semin Perinatol.* 2009 Jun;33(3):143-51.
19. Raval DS, Co S, Reid MA, Pildes R. Maternal and neonatal outcome of pregnancies complicated with maternal HELLP syndrome. *J Perinatol.* 1997;17:266-9.
20. Ertan AK, Wagner S, Hendrik HJ, Tanriverdi HA, Schmidt W. Clinical and biophysical aspects of HELLP-syndrome. *J Perinat Med.* 2002; 30: 483-9.
21. Van Pampus MG, Wolf H, Ilsen A, Treffers PE. Maternal outcome following temporizing management of the HELLP syndrome. *Hypertens Pregnancy.* 2000;19:211-20.
22. Martin JN Jr, Rinehart BK, May WL, Magann EF, Terrone DA, Blake PG. The spectrum of severe preeclampsia: comparative analysis by HELLP (hemolysis, elevated liver enzyme levels, and low platelet count) syndrome classification. *Am J Obstet Gynecol.* 1999;180:1373-84.
23. Lipstein H, Lee CC, Crupi RS. A current concept of eclampsia. *Am J Emerg Med.* 2003;21:223-226.
24. Isler CM, Rinehart BK, Terrone DA, Martin RK, Magann EF, Martin JN. Maternal mortality associated with HELLP (hemolysis, elevated liver enzymes, and low platelets) syndrome. *Am J Obstet Gynecol.* 1999;181: 924-928.
25. Miles JF Jr, Martin JN Jr, Blake PG, Perry KG Jr, Martin RW, Meeks GR. Postpartum eclampsia: a recurring perinatal dilemma. *Obstet Gynecol.* 1990;76:328-31.
26. Deruelle P, Coudoux E, Ego A, Houfflin-Debarge V, Codaccioni X, Subtil, D. Risk factors for postpartum complications occurring after preeclampsia and HELLP syndrome. *Eu J Obstet Gynecol Reprod Biol.* 2006;125: 59-65.
27. Witlin AG, Saade GR, Mattar F, Sibai BM. Predictors of neonatal outcome in women with severe preeclampsia or eclampsia between 24 and 33 weeks' gestation. *Am J Obstet Gynecol.* 2000 Mar;182(3):607-11.
28. Tompkins MJ, Thiagarajah S. HELLP (hemolysis, elevated liver enzymes, and low platelet count) syndrome: the benefit of corticosteroids. *Am J Obstet Gynecol.* 1999 Aug;181(2):304-9.