

# Comparison of Maternal and Perinatal Outcomes of HELLP Syndrome and Severe Preeclampsia Cases

Selahattin Kumru, Mehmet Şimşek, Bilgin Gürateş, Ekrem Sıpmaz, Zeynep Özcan,  
Mehmet Nalbant, Denizmen Aygün

*Department of Gynecology and Obstetrics, Faculty of Medicine, Firat University, Elazığ*

## Abstract

**Objective:** To compare maternal and perinatal outcomes of women with HELLP (hemolysis, elevated liver enzymes and low platelets) syndrome and severe preeclampsia.

**Methods:** Between May-2001 and May-2004, the data's of women treated as HELLP syndrome and merely severe preeclampsia in Firat University Medical School Division of Obstetrics and Gynecology were retrospectively analyzed. Mortality, morbidities of pregnant, and their newborns were noted. Fisher's exact test and independent samples t-tests were used for statistical analyses of data. The level of significance was set at  $p<0.05$ .

**Results:** Twenty-two women with HELLP syndrome and 30 women with severe preeclampsia were enrolled in the study. Both groups had similar demographic characteristics. Although it was not statistically significant, mean gestational age of HELLP group ( $32.2\pm5.4$ ) was found to be 8.4% lesser than those of severe preeclamptic women ( $34.9\pm4.3$ ). It was found that HELLP group had a higher liver transaminase and lactic dehydrogenase levels. In addition, HELLP group had a more transfusion of blood, platelets, and cryoprecipitate than those of severe preeclamptic group. HELLP syndrome group had significantly higher intrauterine dead cases than severe preeclamptic group (27.3% vs. 3.3%,  $p<0.05$ ). Neonatal intensive care unit requirement and neonatal mortalities of HELLP and severe preeclampsia groups were found to be 37.5% and 13.8% and 18.8% and 3.3%, respectively. However, this difference was not statistically significant.

**Conclusion:** The HELLP syndrome cases seem had an increased transfusion requirement together with tendency to increased perinatal mortality and morbidity. Therefore, treatments of such cases should be planned in the advanced centers.

**Keywords:** HELLP syndrome, severe preeclampsia, mortality, morbidity.

## *HELLP sendromu ve ağır preeklampsi olgularında maternal ve fetal sonuçların karşılaştırılması*

**Amaç:** HELLP (hemoliz, yükselmiş karaciğer enzimleri, düşük trombosit sayısı) sendromu ve ağır preeklampsi olgularında maternal ve perinatal sonuçların karşılaştırılması.

**Yöntem:** Mayıs 2001 – Mayıs 2004 tarihleri arasında Firat Üniversitesi Tıp Fakültesi Kadın Hastalıkları ve Doğum Kliniği'nde tedavi edilen HELLP sendromu tanısı alan gebeler ile HELLP sendromu olmadan sadece ağır preeklampsi tanısı alan gebelerin dosyaları retrospektif olarak incelendi. Her iki gruptaki gebeler ve bunların yenidoğanlarındaki morbidite ve mortaliteler not edildi. Verilerin istatistiksel değerlendirmesi Fisher kesin ki-kare testi ile bağımsız örnekler t testi kullanılarak yapıldı.  $P<0.05$  değeri anlamlı kabul edildi.

**Bulgular:** Çalışma dönemi boyunca 22 HELLP sendromu ve 30 ağır preeklampsi olgusunun tedavi edildiği görüldü. Her iki gruptaki gebeler demografik yönden benzerdi. İstatistiksel olarak anlamlı olmamakla birlikte HELLP grubunda doğumda ortalama gebelik haftası ( $32.2 \pm 5.4$ ) ağır preeklampsi grubuna göre ( $34.9 \pm 4.3$ ) %8.4 daha azdı. HELLP grubunun ağır preeklampsi grubundan daha yüksek serum karaciğer transaminaz ve laktat dehidrogenaz düzeylerine sahip oldukları saptandı. İlave olarak, HELLP grubundaki gebelere daha fazla kan, trombosit ve dondurulmuş plazma transfüzyonu yapıldığı tespit edildi. HELLP sendromlu gebelerde istatistiksel anlamlı olarak daha fazla intrauterin ölüm olgusuna rastlandı (%27.3'e karşılık %3.3,  $p < 0.05$ ). HELLP ve ağır preeklampsi gruplarında yeni doğan yoğun bakım ünitesi ihtiyacı sırasıyla %37.5 ve 13.8; neonatal mortalite %18.8 ve %3.3 bulundu, ancak bu fark istatistiksel olarak anlamlı değildi.

**Sonuç:** HELLP sendromu olguları ağır preeklampsi olgularına göre artmış maternal transfüzyon ihtiyacı ile yüksek perinatal mortalite ve morbidite eğilimi göstermektedirler. Bu nedenle bu tür olguların mutlaka ileri merkezlerde tedavileri planlanmalıdır.

**Anahtar kelimeler:** HELLP sendromu, ağır preeklampsi, mortalite, morbidite.

## Introduction

HELLP (hemolysis, elevated liver enzymes, and low platelets) syndrome was first defined by Weinstein in 1982.<sup>1</sup> As understood from its definition, the syndrome is together with disorder of liver functions, increased maternal and fetal morbidity and mortality due to thrombocytopenia and hemolytic anemia.<sup>2</sup> In addition, pregnant with HELLP syndrome have increased risk for renal failure, consumption coagulopathy, ablatio placenta, lung and brain edemas, liver haematoma and hypovolemic shock.<sup>3</sup>

Maternal mortality is reported in between 0% and 24% in patients with HELLP.<sup>4</sup> Perinatal mortality is reported in between 85% and 37% in babies of these pregnant.<sup>4</sup> Absolute treatment of this syndrome is to bear the fetus and it is reported that perinatal results may be better by means of applying antepartum corticosteroid for providing fetal lung maturation and transferring fetus or newborn to centers having full equipped intensive care units.<sup>2</sup>

Heavy preeclampsia is a situation which contains HELLP syndrome and having increased risk of maternal and perinatal mortality and morbidity and which is treated by terminating the pregnancy without concerning the gestational age.<sup>6</sup> Although HELLP syndrome takes place within heavy preeclampsia group, it is reported that they have increased maternal problem risk when they are compared with heavy preeclampsia cases which do

not have HELLP syndrome.<sup>7,8</sup> However, there is no consensus about whether cases with HELLP syndrome have different maternal and fetal problem risk than heavy preeclampsia cases or not.<sup>9</sup>

Current study is planned to compare HELLP syndrome cases treated in our clinic and maternal-perinatal mortality and morbidity seen in only heavy preeclampsia cases which do not have HELLP syndrome.

## Method

The study was performed by retrospectively researching the files of patients treated with diagnoses of HELLP syndrome or only heavy preeclampsia in Clinic of Obstetrics and Gynecology of Firat Medical Center of Firat University in between May 2001 – May 2004. HELLP syndrome was defined as hemolysis (typical hemolysis diagnoses in peripheral spreading, being 600 U/I or upper of serum lactate dehydrogenase level, being 1.2 mg/ml or upper of total serum bilirubin level), elevated liver enzymes in serum and decrease of thrombocyte count.<sup>10</sup> Heavy preeclampsia diagnosis was done as to criteria of 2002 of American College of Obstetric and Gynecology (ACOG).<sup>6</sup> Hematological and biochemical examinations were performed as applied routinely to other patients and intravenous magnesium sulfate (Magnesium Sulfate, Galen Ilac Sanayi Ticaret AS, Istanbul) was given. Transfusion of blood and

blood products were performed when required. Also, dexamethasone (Dexamet ampule, Biosel Ilac San. ve Tic. AS, Beykoz/Istanbul) was applied to the cases with HELLP syndrome as steroid. Cases which have chronic liver, kidney or any other illness were excluded. Pregnants within two groups were treated by bearing without considering conservative treatment.

Gestational age was determined as to last menstruation date and early (<20<sup>th</sup> week) ultrasonography evaluations if possible. Two groups were compared as to their maternal and perinatal results. Maternal state comparison was made as to hematological and biochemical examination results, time for staying in hospital, maternal mortality, ablation of placenta, disseminated intravascular coagulation (DIC) liver failure, and requirement for transfusion of blood and blood products. DIC diagnosis was made in the existence of 3 or more of parameters of low fibrinogen (<300 mg/dl), low thrombocyte (<100.000 cell/ $\mu$ l), d-dimer positivity (>40 mg/dl), prolonged prothrombin time (>14 seconds) and partial thromboplastin time (>14 seconds). Being 2 mg/dl or upper of serum creatinin level together with oliguria or anuria and/or being 20 ml/minute or below of creatinin clearance were determined as kidney failure.

In order to compare perinatal results, neonatal death, hypoglycemia of newborn, respiratory distress syndrome (RDS), low birth weight (SGA), hyperbilirubinemia, bronchopulmonary dysplasia, intraventricular bleeding (IVC), necrotizing enterocolitis (NEC), intensive care requirement of newborn were checked from records of patients and their durations were noted if any.

Obtained data were given as average  $\pm$  standard deviation or frequency (percentage). Discontinuous data were compared by Fisher absolute  $\chi^2$ -test and continual data were compared by free samples t-test.  $p < 0.05$  value was deemed as significant. All statistical analyzes were performed by using package program of SPSS 11.0 for Windows.

## Results

While 22 of pregnant who have criteria for being included into study during study period were diagnosed as HELLP syndrome, 30 pregnant who

have criteria for being included into study during study period were diagnosed as heavy preeclampsia without HELLP syndrome. Statistically not being significant, average gestational week at delivery of HELLP group ( $32.2 \pm 5.4$ ) was less than heavy preeclampsia group about 8.4% ( $34.9 \pm 4.3$ ). Pregnants in both groups were similar in terms of demographic qualities and clinic diagnoses (Table 1). It was found after the results of hematological and biochemical examinations that pregnant with HELLP syndrome had higher levels of serum aspartate transaminase ( $p < 0.003$ ), alanine transaminase ( $p < 0.001$ ) and lactate dehydrogenase (LDH) ( $p < 0.001$ ) and lower thrombocyte levels ( $p < 0.001$ ) than pregnant with heavy preeclampsia (Table 2). When pregnant were compared in terms of maternal complications, it was found that more intrauterine fetal death ( $p < 0.02$ ) was observed at pregnant within HELLP syndrome group and that more transfusions of blood ( $p < 0.01$ ), thrombocyte ( $p < 0.02$ ) and frozen plasma ( $p < 0.001$ ) was done to these pregnant (Table 3). Additionally, though no maternal death was observed in heavy preeclampsia group, one pregnant from HELLP syndrome group died due to disseminated intravascular coagulation and multiple organ failure. No significant difference was found between groups in terms of other maternal problems (Table 3). Although statistically results of compared newborns were not significant, perinatal mortality and morbidity increase tendency was found in HELLP syndrome group (Table 4).

## Discussion

Although medical care has been improved today, heavy preeclampsia cases have increased risk in terms of malign maternal and perinatal results with HELLP syndrome whether complicated or not.<sup>11,12,13</sup> It is not clearly understood whether cases with HELLP syndrome are different from cases with heavy preeclampsia or not. It was found in current study that there is no significant difference between HELLP syndrome and heavy preeclampsia cases when they are compared in terms of their demographic qualities. It was reported in the study of Haddad et al that HELLP syn-

**Table 1.** Demographic qualities and clinical diagnoses of patients.\*

Parameter	Heavy preeclampsia (n:30)	HELLP (n: 22)	p value
Gravida	2.6±1.9	3.6±2.6	NS
Parite	1.3±1.8	2.0±2.0	NS
Gestational week	34.9±4.3	32.2±5.4	NS
Systolic blood pressure (mm/Hg)	166.0±19.4	156.8±29.3	NS
Diastolic blood pressure (mm/Hg)	104.0±15.4	95.9±20.6	NS
Period for staying in hospital (day)	5.5±1.9	7.3±1	NS

\* Average ± Standard deviation, NS: Not significant

**Table 2.** Laboratory diagnoses of pregnant.\*

Parameter	Heavy preeclampsia (n:30)	HELLP (n: 22)	p value
Alanine transaminase (U/L)†	120.1±10.0	1106.5±121.1	<0.001
Lactate dehydrogenase (U/L)	729.4±213.1	1437.1±942.8	<0.001
Blood urea nitrogen (mg/dL)	25.6±8.0	30.1±13.3	NS
Creatinin (mg/dL)	0.9±0.2	0.9±0.2	NS
Hemoglobin (g/dL)	12.1±1.6	12.0±2.7	NS
Hematocrit (%)	35.3±4.8	35.6±7.2	NS
White sphere (10 <sup>3</sup> /uL)	12.7±4.1	12.7±6.7	NS
Thrombocyte (10 <sup>3</sup> /uL)	270.4±62.2	122.9±98.2	<0.001

\* Average ± Standard deviation, †: Proteinuria amount was determined by dipstick method as examining in positivity base, NS: Not significant

drome cases are younger only than heavy preeclampsia cases.<sup>9</sup> Abromovici et al reported that HELLP syndrome cases are not different from only heavy preeclampsia cases in terms of maternal age.<sup>14</sup> Limited data in literature are not enough to prove if HELLP syndrome cases have demographic risks different from heavy preeclampsia cases and our diagnoses support the idea that these two illness groups have similar demographic qualities.

It was found that results of laboratory tests were similar in HELLP syndrome and only heavy preeclampsia cases except laboratory determinations which are diagnosis criteria of HELLP syndrome. However, it was observed that HELLP syndrome cases as statistically significant required more blood (%45.5), thrombocyte (18.1), and frozen plasma (40.9) transfusions. Additionally, it was found that HELLP syndrome cases as statistically significant had more intrauterine fetal death (27.3%). There are many reports which state that HELLP syndrome cases required higher blood and

blood products,<sup>9,14,15,16,17</sup> same results were obtained in this work. Reason of 4 cases of 6 intrauterine fetal death cases were ablatio placenta in our work. Though it was not statistically significant, it was found that ablatio placenta risk increased six times in HELLP syndrome cases (Table 3). We think that ablatio placenta risk contributes to increased perinatal death risk in HELLP syndrome cases according to both healthy pregnant<sup>18</sup> and only preeclampsia cases.<sup>13</sup>

Maternal death was seen at only one case (4.5%) within 22 HELLP syndrome cases that were treated during study period. Though no autopsy was performed, death reason was DIC and multiple organ failure. It is a well-known situation that pregnant with HELLP syndrome had increased maternal death risk. Maternal death frequency in our country changes between 0%<sup>11</sup> and 10.5%.<sup>12</sup> This risk is reported in developed country as between 0%<sup>19</sup> and 6.25%.<sup>20</sup> It is known that this risk was about 20% approximately 20 years ago.<sup>4</sup> Maternal deaths are

**Table 3.** Maternal complications seen at pregnant. .

Parameter	Heavy preeclampsia (n:30)	HELLP (n: 22) (%)	p value
DIC	0 (0)	1 (4.5)	AD
Hemodialysis	0 (0)	1 (4.5)	AD
Kidney failure	0 (0)	0 (0)	
Blood transfusion	2 (6.6)	10 (45.5)	<0.01
Thrombocyte transfusion	0 (0)	4 (18.1)	<0.02
Frozen plasma	0 (0)	9 (40.9)	<0.001
Ablatio placentae	1 (3.3)	4 (18.1)	AD
Intrauterine fetal death	1 (3.3)	6 (27.3)	<0.02
Cesarean requirement	21 (70)	13 (59.1)	AD
Maternal death	0 (0)	1 (4.5)	AD

DIC: Disseminated intravascular coagulation, AD: Not significant

**Table 4.** Clinical diagnoses of newborns.

Parameter	Heavy preeclampsia (n:29)	HELLP (n: 16) (%)	p value
NBICU requirement	4 (13.8)	6 (37.5)	AD
Period for staying in NBICU (day)*	21.5±18.2	19.1±17.6	AD
RDS	1 (3.4)	1 (6.3)	AD
Bronchopulmonary dysplasia	0 (0)	0 (0)	
Lower birth weight	0 (0)	0 (0)	
Intraventricular bleeding	0 (0)	0 (0)	
Necrotizing enterocolitis	0 (0)	0 (0)	
Hypoglycemia	4 (13.8)	2 (12.5)	AD
Hyperbilirubinemia	5 (17.3)	3 (18.8)	AD
Transient tachypnea	1 (3.4)	1 (6.3)	AD
Neonatal mortality	1 (3.3)	3 (18.8)	AD

NBICU: Newborn intensive care unit, RDS: Respiratory distress syndrome, \*: Average ± Standard deviation, AD: Not significant

generally occur due to multiple organ failures,<sup>20</sup> heart failure, cerebral bleeding, lung edema, spontaneous liver rupture.<sup>12,21</sup> As seen, HELLP syndrome cases continue to be an important reason of maternal mortality and morbidity.

When perinatal results are evaluated, it was found that HELLP syndrome cases had neonatal mortality risk six times more than only heavy preeclampsia cases even though it was statistically not significant. Additionally, it was observed that other perinatal problems tended to appear more in HELLP syndrome cases even though it was statistically not significant. It is known that neonatal results in HELLP syndrome cases are worse than in healthy pregnant.<sup>7,8</sup> Evidences were found which proves that prematurity is the reason of increased

mortality in limited number of works done in order to find out whether the reason arises from HELLP syndrome itself or being premature of newborns. For instance, Haddad et al<sup>9</sup> reported that HELLP syndrome and preeclamptic have similar neonatal mortality within newborns on similar gestational week. Gestational weeks were statistically similar in our work but HELLP syndrome cases were 8.4% less than heavy preeclampsia cases. We think that gestational age may contribute to perinatal morbidity and mortality increase tendency observed in HELLP syndrome.

## Conclusion

HELLP syndrome cases require more blood and blood product transfusion and perinatal mortality

increase exists. We believe that it is beneficial to treat these illnesses in centers with both adult and newborn intensive care unit by diagnosing early.

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