Maternal and Perinatal Mortality and Morbidity in Pregnant Women with Partial and Complete HELLP Syndrome

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OBJECTIVE: To detect maternal-perinatal mortality and morbidity in pregnant women with partial and complete (classical) HELLP syndrome.
STUDY DESIGN: Forty-two pregnant women having classical triad of HELLP syndrome (i.e., H: hemolysis, EL: elevated liver enzymes, LP: low platelet), 189 pregnant women having one or two criteria of HELLP syndrome (i.e. partial HELLP syndrome) and 34 preeclamptic pregnant women without HELLP syndrome were evaluated prospectively. Cases with partial HELLP syndrome were divided in to three subgroups according to the existing criteria (H, HEL, HLP).
RESULTS: The rates of abnormal clinical, laboratory findings, need for administration of corticosteroids, need for neonatal intensive care unite were found to be increased in relationship with the increasing number of HELLP criteria.
CONCLUSION: Maternal-perinatal mortality and morbidity were found to be lower in cases with partial HELLP syndrome than cases with complete HELLP syndrome, but to be higher than the cases without criteria of the syndrome. Low platelet count was found to be the most significant factor related with maternal-perinatal mortality. It may be possible to decrease maternal-perinatal mortality and morbidity by timely interference adjusted before the formation of HELLP criteria.
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Key Words: HELLP, Partial HELLP, Maternal, Perinatal, Mortality and morbidity

HELLP syndrome was defined first in 1982 by Weinstein as microangiopathic hemolytic anemia (Haptoglobulin <1.0g/dl, LDH >600 IU/l), increased liver enzymes (ALT and AST >70 U/l) and trombocytopenia (platelet count <100.000/mm^3).[1]

Audibert et al defined the patients carrying only one or two criteria of HELLP syndrome as "partial HELLP syndrome".[2] The most consistent finding of HELLP syndrome is trombocytopenia.[2,3] HELLP syndrome occurs in 10 percent of the cases of serious preeclampsia and eclampsia.[4]

We aimed to evaluate the rates of maternal-perinatal mortality and morbidity in the cases with complete and partial HELLP syndrome.

Material and Methods

This study was performed prospectively on randomly selected 265 preeclamptic pregnant women admitted in the department of high risk pregnancy between April 2001 and January 2002.

Gestational age was determined by last menstrual period and ultrasonographical biometrical measurements taken before 20 weeks of pregnancy.

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Preeclampsia was diagnosed by development of hypertension plus proteinuria, edema later than 20 weeks of pregnancy. Cases with preeclampsia were followed up continuously by hourly blood pressure determinations and higher values were noted down during follow up. Complaints of headache, nausea-vomiting, visual blurring, epigastric pain were paid attention as prodromal findings of eclampsia. Routine laboratory analyses included complete blood count, complete urinalysis, liver enzymes, kidney function tests.

HELLP syndrome was defined by three criteria: hemolysis (H; LDH> 600IU/l), elevated liver enzymes (EL; AST and/or ALT>70 IU/l), low platelet (LP; platelet count <150.000/mm^3).[1] Of 265 cases, 42 had three criteria of HELLP syndrome (complete HELLP), 189 had one or two of HELLP criteria (partial HELLP) and 34 cases had no criteria of HELLP syndrome (preeclampsia group). Cases with partial HELLP syndrome were divided into three subgroups according the existing criteria (H, HEL, HLP).

Cases with complete HELLP syndrome were divided into three classes (Class 1, 2 and 3) according to Martin classification based on platelet count.[3] Class1 is associated with platelet count <50000/m^3, class 2 is associated with platelet count between 50000-100000/m^3 and class3 is associated with platelet count between 100000-150000/m^3.[3]

Maternal complications (eclampsia, abruptio placenta, operative delivery, organ insufficiency, haemorrhagic diathesis, pulmonary oedema, exitus) and fetal-neonatal complications were noted down. Need for $MgSO_4$, corticosteroids, route of delivery, time of hospitalization were noted down.

Fetal outcome were evaluated by 1 and 5 min Apgar scores, perinatal mortality, need for NICU.

Table 1. Demographic clinical and laboratory characteristics of three groups.

	Preeclampsia n=34	Partial HELLP n=189	Complete HELLP n=42
Mean age (years) ±SD	27.76±6.11	27.94±6.55	27.98±6.38
Mean gravidity±SD	3.23±2.31	2.51±2.18	3.09±2.92
Mean parity±SD	1.81±2.08	1.18±1.69	1.94±2.58
Mean gestational age (weeks)±SD	37.29±3.09	33.9±4.06	34.29±3.62 *
Headache (n. %)	2 (5.8%)	40 (21.1%)	6 (14.2%)
Visual blurring (n. %)	1 (2.9%)	4 (2.1%)	1 (2.3%)
Epigastric pain (n. %)	0	3 (1.6%)	3 (6.9%)
Nausea/vomiting (n. %)	0	5 (2.6%)	2 (4.7%)
Previous preeclampsia in history (n. %)	3 (8.8%)	18 (9.5%)	4 (9.5%)
Need for antihypertensive agent (n. %)			
One agent	2 (5.9%)	35 (18.5%)	6 (14.3%)
Two agent	0	4 (2.1%)	6 (14.3%)
Mean systolic blood pressure (mmHg) ±SD	149.1±3.78	167.8±19.81	173.6±29.7 *
Mean diastolic blood pressure (mmHg))±SD	115.6±9.27	127.6±7.88	134.8±6.33 *
Need for $MgSO_4$(n. %)	14 (33.3%)	151 (79.8%)	39 (92.8%) *
Mean duration of $MgSO_4$ infusion (hrs)±SD	30.5±10.12	34.77±8.27	37.64±8.25
Need for corticosteroids (n. %)	3 (8.9%)	31 (16.5%)	39 (92.9%) *
Betamethasone	3 (8.8%)	20 (10.6%)	1 (2.4%)
Dexamethasone	0	11 (5.8%)	38 (90.5%)
Route of delivery			
Vaginal delivery	20 (14.0%)	82 (43.4%)	3 (7.1%) **
C/S	14 (41.2%)	107 (56.6%)	39 (92.9%)
Mean duration of hospital stay (days)±SD	3.8±2.0	4.4±1.8	6.2±1.8 *
Eclampsia (n. %)	0	12 (6.3%)	5 (14.7%)
Acute renal failure (n. %)	0	1 (0.5%)	2 (5.8%)
Haemorrhage due to uterine atony (n. %)	1 (2.9%)	-	0
Need for blood transfusion (n. %)	0	8 (4.2%)	16 (47.0%)
Pulmonary eodema (n. %)	0	2 (1.0%)	0
Wound infection (n. %)	0	2 (1.0%))	0
Maternal exitus (n. %)	0	1 (0.5%)	0
Mean haemoglobin (g/dl) ±SD	10.75±2.10	11.71±1.34	12.33±1.79 *
Mean haematocrit (%)±SD	33.03±3.48	33.15±6.31	36.29±5.64 **
Mean platelet count/ mm^3 ±SD	245.2±89.45	250.2±96.8	172.7±96.8 *
Mean AST (IU/l) ±SD	24.91±9.02	56.60±53.77	266.7±252.3 *
Mean ALT (IU/l) ±SD	13.59±10.46	31.06±27.48	184.4±133.7 *
Mean LDH (IU/l) ±SD	512.7±82.01	1187±431.3	2007±852.7 *
Mean total bilirubin (mg/dl) ±SD	0.51±0.20	0.65±0.18	1.33±0.97 *
Mean BUN (mg/dl) ±SD	10.79±3.21	10.38±1.78	15.93±6.7 *
Mean creatinine (mg/dl) ±SD	0.77±0.10	0.8±0.10	0.85±0.21 **
Mean uric acid (mg/dl) ±SD	5.58±1.39	6.5±0.63	6.76±0.89
Mean total protein (g/dl) ±SD	6.07±0.69	5.89±2.99	5.67±0.97
Mean albumin (g/dl) ±SD	3.09±0.48	3.17±3.76	2.69±0.59
Mean proteinuria (mg/l) ±SD	223.2±222.8	301.4±230.8	422.5±323.8 **

*:p<0.0001, **:p<0.01

Statistical analyses were performed by Graphpad Prisma V3 Packet programme. One way anova, Tukey multiple comparison tests, chi square were used

Results

Table 1 shows the comparison of demographic and clinical and laboratory characteristics of three groups. There was no statistical difference between three groups for mean age, gravidity and parity. Gestational age was higher in preeclampsia group than complete and partial HELLP groups. The most frequent complaint in complete and partial HELLP groups was headache. None patient was admitted with epigastric pain. Requirement and duration of $MgSO_4$ therapy, need of corticosteroids, rates of cesarean delivery were found to be higher in complete and partial HELLP groups than preeclampsia group. Duration of maternal hospital stay was most longest in complete HELLP group. Systolic and diastolic blood pressures were found to be lower in preeclampsia group significantly than other two groups. Maternal

Table 2. Indications of cesarean sectio

	Preeclampsia n=34	Partial HELLP n=189	Complete HELLP n=42
Fetal distress	5 (35.7%)	50 (46.0%)	10 (25.6%)
Intrauterine growth restriction	0	10 (9.3%)	5 (12.8%)
Prior C/S	1 (7.1%)	4 (3.7%)	2 (5.1%)
Prolonged labor	0	0	0
Cephalo pelvic disproportion	1 (7.1%)	5 (4.6%)	0
Presentation abnormality	0	0	1(2.5%)
Abruptio placentae	0	20 (18.6%)	3 (7.6%)
HELLP syndrome alone	0	0	15 (38.4%)
Severe preeclampsia	3 (21.4%)	12 (11.2%)	1 (2.5%)
Eclampsia	3 (21.4%)	4 (3.7%)	2 (5.1%)
Multiple pregnancy	1 (7.1%)	2 (1.8%)	0

Table 3. Fetal outcome in three groups

	Preeclampsia n=34	Partial HELLP n=189	Complete HELLP n=42
Mean fetal weight (g) ±SD	2949±784	2227±1083	1986±787 *
Mean 1min Apgar Score±SD	7.23±1.68	5.79±2.82	5.61±2.42
Mean 5 min. Apgar Score±SD	8.64±1.61	7.35±2.86	7.38±2.65
Need for NICU (n. %)	4 (11.7%)	68 (35.9%)	28 (66.7%) *
Mean stay at NICU (day)s±SD	11±8.48	13.85±10.45	13.48±8.82
İn utero mort fetal (n. %)	1 (3.0%)	14 (7.0%)	2(4.7%)
Deaths in NICU (n. %)	0	18 (26.5%)	4 (14.3%)
Birth of premature baby (n. %)	2 (5.8%)	61 (32.0%)	22 (52.3%)
RDS (n. %)	0	33 (17.4%)	4 (11.7%)
IUGR (n. %)	4 (11.6%)	31 (16.4%)	7 (16.6%)
Hyperbilirubinemia (n. %)	0	5 (2.6%)	2 (5.0%)
Sepsis (n. %)	0	11 (5.8%)	2 (5.0%)
Fetal anomalia (n. %)	0	3 (1.5%)	1 (2.5%)
Hypoglycemia (n. %)	0	0	1 (2.5%)
Polycytemia (n. %)	0	1 (0.5%)	0
Albinism (n. %)	1 (2.9%)	-	-
Meconium aspiration Syndrome MAS (n. %)	1 (2.9%)	2 (1.0%)	-
Neonatal Exitus (n. %)	-	15 (7.9%)	-
Hidrops fetalis (n. %)	-	2 (1.0%)	-
Necrotizan enterocolitis (n. %)	-	2 (1.0%)	-
Metabolic disorder (n. %)	-	1 (0.5%)	-
Trombocytopenia (n. %)	-	-	1 (2.5%)

*: p<0.0001

haemoglobine, haematocrit, AST, ALT, LDH, bilirubin, BUN, creatinine, uric acid levels were found to be higher in complete HELLP than other two groups whereas, platelet count to be lower.

Table 2 shows indications of cesarean section. In three groups, rates of cesarean delivery for fetal distress were 35.7% (5 cases), 46.0% (50 cases) and 25.6% (10 cases), respectively.

Table 3 shows fetal outcomes in three groups. Gestational age at delivery and birth weight, were found to be higher in preeclampsia group than other two groups, whereas need for NICU was found to be higher in complete and partial HELLP groups than preeclampsia group. There was no statistically significant difference between three groups for intrauterine and neonatal death rates.

Fifteen (35.7%), eighteen (42.8%) and nine (21.4%) of 42 cases with HELLP syndrome were classified as Class 1, 2 and 3, respectively. Table 4 shows the distribution of 42 HELLP cases into three classes, maternal outcomes in these groups. The most frequent fetal problem was delivery of premature baby in all classes of HELLP. All of the 3 neonatal exitus were due to RDS in class 1. There was no fetal loss in classes 2 and 3.

Of 189 partial HELLP syndrome, 122 (64.5%) had hemolysis (H), 30 (15.8%) of them had hemolysis and elevated liver enzymes (HEL) and 37 (19.7%) had hemolysis and low platelet (HLP). All of the patients had elevated LDH levels. Table 5 shows maternal and fetal outcomes in three classes of 189 partial HELLP cases

Table 4. Maternal and fetal outcomes in three classes of 42 HELLP cases

	Class 1 n=15	Class 2 n=18	Class 3 n=9
Cesarean delivery (n. %)	14 (93.3%)	16 (88.8%)	9 (100.0%)
Abruptio placentae (n. %)	1 (6.0%)	3 (16.6%)	0
Eclampsia (n. %)	2 (12.0%)	2 (11.1%)	1 (11.1%)
Need for blood transfusion (n. %)	7 (46.6%)	9 (50.0%)	0
Acute renal failure (n. %)	1 (6.0%)	1 (5.5%)	0
Intrauterine growth restriction (n. %)	2 (12.0%)	3 (16.6%)	2 (22.2%)
Small for gestational age (n. %)	0	2 (%11.1)	1 (11.1%)
Prematurity (n. %)	8 (48.0%)	10 (%55.5)	4 (44.4%)
Respiratory Distress Syndrome (n. %)	4 (24.0 %)	0	0
Sepsis (n. %)	2 (12.0%)	0	0
Hyperbilirubinemia (n. %)	1 (6.0%)	1 (5.5%)	0
Fetal anomaly (n. %)	0	0	1 (11.1%)
Neonatal exitus (n. %)	3 (20.0%)	0	0
Trombocytopenia (n. %)	1 (6.0%)	0	0
Hypoglycemia (n. %)	0	1 (5.5%)	0

Table 5. Maternal and fetal outcomes in three classes of 189 partial HELLP cases

	H n=122	HEL n=30	HLP n=37
Cesarean delivery (n. %)	59 (48.3%)	15 (50.0%)	33 (89.0%)
Abruptio placentae (n. %)	10 (8.0%)	0	6 (16.2%)
Eclampsia (n. %)	6 (4.8%)	1 (3.3%)	5 (13.5%)
Blood transfusion (n. %)	4 (3.2%)	1 (3.3%)	3 (8.1%)
Pulmonary oedema (n. %)	0	0	2 (5.4%)
Acute renal failure (n. %)	1 (0.8%)	0	0
Wound infection (n. %)	1 (0.8%)	1 (%3.3)	0
Haemorrhage due to uterine atony (n. %)	1 (0.8%)	0	0
Maternal exitus (n. %)	0	1 (%3.3)	0
İntrauterine growth restriction (n. %)	22 (18.0%)	5 (16.5%)	4 (10.8%)
Prematurity (n. %)	32 (26.2%)	13 (42.9%)	16 (43.2%)
Small for gestational age (n. %)	6 (4.8%)	1 (3.3%)	1 (2.7%)
Respiratory Distress Syndrome (n. %)	17 (13.9%)	6 (19.8%)	10 (27.0%)
Hyperbilirubinemia (n. %)	2 (1.6%)	1 (3.3%)	2 (5.4%)
Fetal Anomaly (n. %)	0	1 (3.3%)	2 (5.4%)
Meconium Aspiration Syndrome (n. %)	0	1 (3.3%)	1 (2.7%)
Hydrops fetalis (n. %)	0	2 (6.6%)	0
Sepsis (n. %)	6 (4.8%)	1 (3.3%)	4 (10.8%)
Necrotizan enterocolitis (n. %)	1 (0.8%)	0	1 (2.7%)
Metabolic disorders (n. %)	1 (0.8%)	0	0
Polycytemia (n. %)	1 (0.8%)	0	
Neonatal Exitus (n. %)	9 (7.2%)	2 (6.6%)	4 (10.8%)

Discussion

Weinstein[1] suggested that HELLP syndrome might be occur without clinical findings of preeclampsia. Although, the most considered component of HELLP syndrome is trombocytopenia, there are discussions about differential diagnosis of this pathologic condition.[1,5,6] It may be supposed that HELLP syndrome is a spectrum of laboratory findings of preeclampsia. Symptoms, signs and laboratory findings seen in HELLP syndrome may be explained by systemic microangiopathy, microangiopathic hemolysis and intravascular coagulopathy mentioned in the pathophysiology of preeclampsia.[5,7]

Audibert et al.[2] investigated relationship between maternal outcome and different treatment protocols on 316 patients, and could not find any difference for complications and prognosis between the cases with severe preeclampsia and partial HELLP syndrome, whereas rates of cesarean delivery, DIC, need for blood transfusion were higher in cases with HELLP. So, authors concluded that HELLP syndrome and partial HELLP must be evaluated separately.

Our rate of HELLP syndrome was 15%. In literature, rate of HELLP syndrome was reported as 4%-17%.[8,9] Rate of abruptio placenta was reported as 4%-21.7%.[10,11] Our rate were 2.9%, 8.4% and 11.7% in preeclampsia, partial HELL

and complete HELLP groups, respectively. Although, it is reported that HELLP syndrome occurs more frequently in white, multiparous and older (>35 years) women, we could not find statistically significant difference between three groups. The relative risk of occurrence of HELLP syndrome was reported to be higher in white and yellow women than Hispanic and Indian women (RR:2.3).[11,12]

We found AST, ALT, LDH and bilirubine levels to be higher in cases with complete HELLP syndrome. This can be explained by hemolytic component of disease process and hepatic injury.[12,13] Occurrence of epigastric pain was increased concordantly with increasing HELLP findings.

Although preeclampsia was reported as a first pregnancy disease, recurrent disease may be occured. Rate of recurrence was reported as 19.5-36%.[9,14,15] We found the rate of recurrences in group 1, 2 and 3 as 8.8%, 9.5% and 9.5%, respectively. These lower rates may be related poor surveillance in previous pregnancies.

In our study, corticosteroids were used in group 1 and 2 to accelerate fetal lung maturity whereas used in group 3 to correct abnormal laboratory findings. Corticosteroid therapy accelerates maternal stabilization, so, saves time for fetal lung maturity.[16-21]

Cesarean delivery rate in HELLP syndrome was reported as 63.4-96%.[22,23] Our cesarean delivery rates in cases with partial and complete HELLP were 56.6% and 92.9%, respectively. Between the three classes of HELLP syndrome, although the rate of cesarean delivery was higher in Class 3 HELLP syndrome (9 cases, 100%) than Class 1 (14 cases, 93.3%) and 2 (16 cases, 88.8%), the differences were found to be statistically insignificant. Between the subgroups of partial HELLP, rate of cesarean delivery was higher in subgroup characterized by hemolysis and low platelet count (HLP). Low platelet count may be promoting factor to decide delivery. Vaginal delivery is the best route of delivery to reduce morbidity. Vaginal labor trial must be first choice, provided presentation abnormality, placenta previa, unriped cervix, extreme prematurity, fetal distress exist. Increased rates of cesarean delivery may be explained by decreased uteroplacental perfusion leading to fetal distress and IUGR. Before 34 weeks of gestation, unriped cervix unfavorable to oxytocin induction may also be related with increased cesarean rates. Sibai et al[24] reported the rates of cesarean delivery for fetal distress as 37%-47%. Our cesarean rates in group 1, 2 and 3 were 35.7%, 46% and 25.6%, respectively.

In our study, there was one maternal death in partial HELLP group due to sepsis. Maternal death rate was reported as 0-13000/100.000.[5]

We found the rates of eclampsia in three groups as 0% 6.3% and 14.7%, respectively. Only one of the cases of eclampsia occured during postpartum period. Sibai et al[9] reported the rate of eclampsia as 10%.

Incidence of pulmonary eodema was 1% in our study. Sibai et al[9] reported this rate as 3%.

In our study, although gestational ages at delivery were different between three groups, there was no difference between neonatal NICU stays. Need for NICU was increased paralelly to deteriorating laboratory findings. In these cases, lower gestational age at delivery may also increase the need for NICU. Dötch et al[25] suggested that need for resussitation was higher in babies of mothers with HELLP sydrome, so, these women must be delivered in tertiary centers with NICU.

Our intrauterine fetal loss rates in three groups were 3%, 7% and 4.7%, respectively. There was no fetal loss in Chari et al's study[26] performed on severe preeclamptic women. They explained this result by close antenatal surveillance and suggested that to prevent intrauterine fetal loss, it must be known how frequently the antenatal test must be applied. In spite of the pathological finding in antenatal surveillance tests, clinician's choice of expectant management due to fear of delivery of LBW infant may cause most of the fetal loss. Eeltink et al[27] reported the rates of fetal loss and early neonatal death as 9.9% and 9.9%, respectively whereas Sibai et al's rates were 19.3% and 17.4%. The difference between these two studies was explained by the higher number of black women who were socially deprived, in Sibai et al's study.

In our study neonatal sepsis rates in in complete and partial HELLP groups were 5.0% and 5.8%, respectively. The neonates of women with hypertensive disorders or HELLP syndrome, are at increased risk due to neutropenia. The risk is reported to be higher especially if gestational ages is less than 30 week and fetal weight less than 1500.[28]

It was suggested that low platelet count in babies of women with HELLP syndrome might be caused by suppression of trombopoesis due to placental insufficiency.[29] In our study, only one baby of a woman with complete HELLP had trombocytopenia, and there was no correlation between neonatal and maternal trombocytopenia.

Buga et al[30] reported the rates of stillbirth and prematurity as 11.2% and 34.0%. To decrease the perinatal mortality, close antenatal surveillance, fetal monitorization, early detection of fetal distress and opportunity of NICU are necessary. Poor neonatal care opportunities may be responsible for higher rates of perinatal mortality.

Diagnosis and treatment of HELLP syndrome and its variants are still a dilemma for obstetricians. Because of nonspecific symptoms and signs early diagnosis and treatment may delay. Partial HELLP syndrome may be a bridge between preeclampsia and HELLP syndrome. It must be kept in mind that the rates of maternal- perinatal mortality and morbidity is higher in partial HELLP syndrome than preeclampsia without HELLP criteria, but lower than HELLP syndrome. Severity of the clinical picture correlates with the number of pathological laboratory test. Although poor maternal

and perinatal outcome occur in cases with HELLP, partial HELLP syndrome may cause serious maternal and perinatal outcome too.

The most higher rates of intrauterine and neonatal fetal loss and need for NICU occur in women with HELLP syndrome. In the lights of these findings, it may be concluded that, to decrease the rates of maternal and perinatal mortality and morbidity, early diagnosis and timely intervention is mandatory before all of the three criteria of HELLP occur.

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