Prepartum and Postpartum Hellp Syndrome Course of the Characteristic Laboratory Parametres in Peripartum Period*

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ÖZET

PREPARTUM VE POSTPARTUM HELLP SENDROMU : PERİPARTUM DÖNEMDE TİPİK LABORATUVAR VERİLERİN SEYRİ

Amaç: Prepartum ve postpartum HELLP olgularında laboratuvar parametrelerinin değişimini incelemek.
Yöntem: 1995-1998 yılları arasında izlenen 59 HELLP olgusu retrospektif olarak incelendi. Gebeler prepartum (n:37) ve postpartum (n:22) olarak iki gruba ayrıldı. Prepartum son 48 saat ile postpartum 0-48 ve 48-96. saatlerde trombosit, AST, LDH ve total bilirubin değerlerinin değişimlerini karşılaştırdık.
Bulgular: Postpartum HELLP olgularında, doğum öncesi trombosit sayısı hariç, tüm laboratuvar verileri anormal düzeylerde idi. Bu tip olgularda trombosit düzeyleri doğumdan hemen sonra düştü. Prepartum olgularda AST, LDH ve bilirubin ortalama düzeyleri normal düzeylerine daha erken dönemde dönme eğilimindeydiler. Postpartum olgularda ise aynı parametreler ilk iki günde pik yaparken, iki ile dördüncü günler arasında hala yüksek düzeylerde seyretmekte idiler. Laboratuvar bulgularının düzelme şekli her iki grupta da 48-96. saatlerde benzer özellikte idi.
Sonuç: Başlangıç zamanı ve anormal laboratuvar bulgularının düzelmesi dikkate alındığında, HELLP olguları arasında belirgin farklılıklar vardır. Postpartum HELLP olgularının büyük bir bölümü doğumdan önce eksik HELLP tanımına uymaktadır. Doğum, eksik HELLP'i tipik HELLP şekline dönüştüren bir tetikleme olarak karşımıza çıkmaktadır. Anormal laboratuvar bulgularında düzelme prepartum olgularda postpartum olgulardan daha erken dönemde görülür. Bu sendromda tam düzelmeyi gözlemlemek için hastaların 96 saatten daha uzun süre izlenmesi gereklidir.
Anahtar kelimeler: HELLP sendromu, laboratuvar parametreler, iyileşme.

SUMMARY

PREPARTUM AND POSTPARTUM HELLP SYNDROME COURSE OF THE CHARACTERISTIC LABORATORY PARAMETERS IN PERIPARTUM PERIOD

Objective: Our purpose was to evaluate the course of laboratory parameters in prepartum and postpartum HELLP cases.
Methods: Fifty-nine women with HELLP syndrome were reviewed between 1995 and 1998 retprospectively. Women were divided into two groups: prepartum (n=37) and postpartum (n=22) HELLP syndrome. We compared the trends of platelet count AST, LDH and total bilirubin in prepartum 48, postpartum 0-48 and postpartum 48-96 hours.
Results: Except platelet count, all laboratory values were at abnormal ranges in the postpartum HELLP cases even before delivery. Platelets decreased significantly just after delivery in postpartum cases. AST, LDH and bilirubin mean values tended to return to the normal levels earlier in prepartum HELLP cases. In postpartum HELLP cases they peaked to abnormal levels in the first 2 days and were found still high at 48-96 hours postpartum. The reversal patterns of each parameter at the 48-96 hours were similar.
Conclusions: Regarding the time of onset and improvement of laboratory abnormalities, there are considerable differences in HELLP cases. A significant percentage of patients in postpartum HELLP fit the incomplete HELLP syndrome before delivery. Parturition seems to be a trigger mechanism to worsen that incomplete syndrome to the complete HELLP syndrome. Reversals of the pathologic laboratory values occur earlier in prepartum than postpartum group. It needs to follow patients more than 96 hours to detect complete reversal of this syndrome.
Key Words: HELLP syndrome, laboratory parameters, improvement.

Hemolysis, abnormal liver function tests, and thrombocytopenia have been recognized as complications of preeclampsia-eclampsia for many years (1-3). In 1982 Weinstein invented the term HELLP

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Table 1. Demographic and Clinical Findings of Prepartum and Postpartum HELLP Groups

	Prepartum HELLP n=22	Postpartum HELLP n=22	p
Mean maternal age (years)	28.4±7.6	26±6.7	NS
Mean gestational age (weeks)	34.7±4.5	36.4±2.7	NS
Parity	3.5±3,2	2.9±3.0	NS
Chronic hypertension	1 (8%)	1(4.5%)	NS
Eclampsia	24 (64.9%)	10 (45.5%)	NS
Severe Preeclampsia	8 (21.6%)	5 (22.7%)	NS
Stillbirth	8 (21.6%)	4 (18.1%)	NS
Antihypertensive therapy	31 (83.8%)	21 (95.5%)	NS
Mg SO4 therapy	33 (89.2%)	16 (72.8%)	NS
Corticosteroid therapy	10 (27.0%)	3 (13.6%)	NS
Blood Transfusion	17 (45.9%)	10 (45.5%)	NS
Mean gestational weight (g)	1870±883	1860±826	NS
Twin	3 (8.1%)	1 (4.5%)	NS
APGAR 5th minute	4.7±2.8	5.6±3.1	NS
Perinatal mortality	17 (45.9%)	17 (77.3%)	S
Maternal mortality	4 (10.8%)	2 (9.1%)	NS
Delivery-discharge (day)	4.6±2.0	5.1±3.0	NS

NS: Not significant, S: Significant

syndrome, to describe a separate form of preeclamptic and eclamptic women who had thrombocytopenia, abnormal peripheral smear, and abnormal liver function test results (4). HELLP syndrome affects approximately 4% to 12% of patients with severe preeclampsia (5-7). There is much variety and conclusion about the management of HELLP syndrome. The indication and timing of different form of therapy including pla--telet transfusion, infusion of plasma and use of packed red blood cells are still controversial (4,5,8).

Sibai et al (5), proposed strict criteria for the diagnosis of the "true HELLP" syndrome. While many women with preeclampsia and eclampsia may have isolated thrombocytopenia or elevated liver enzymes without the complete HELLP syndrome, these patients may be considered partial or incomplete HELLP syndrome (9). There is little or no information regarding the influence of the time of onset of HELLP syndrome (prepartum and postpartum) on maternal morbidity.

The purpose of this report is to evaluate the course of typical laboratory parameters and their reversal patterns to the normal levels in prepartum and postpartum HELLP cases.

METHODS

The Obstetric clinic at Dicle University Research Hospital serves as a tertiary care facility for the southeastern part of Turkey. This retrospective study involved pregnancies complicated by complete HELLP syndrome between 1995 and 1998. Group I consisted of prepartum and group II of postpartum cases. Diagnosis of HELLP syndrome was based on all the following laboratory abnormalities: characteristic peripheral blood smear, serum lactate dehydrogenase (LDH) 600 IU/L, serum total bilirubin 1.2 mg/dL, serum aspartate aminotransferase (AST) 70 U/L, and platelet count <100.000/ml.

Patients with HELLP syndrome representing hypertension and classical prodromal signs of eclampsia received a magnesium sulfate protocol to prevent and control convulsions at a loading dose of 3g IV + 9g IM, followed by 4.5g every 4-6 hour and stopped in the postpartum 24th hour. Blood pressure, patellar reflex, urine output and respiratory function were observed during therapy. Nifedipine lOmg, when diastolic blood pressures exceed 110mm Hg and alpha-methyldopa (tid 250-500mg) routinely were administered to control severe hypertension. We obtained daily from prepartum period, routine laboratory tests such as liver function and complete blood cell count. After delivery, patients were monitored very closely in an in-

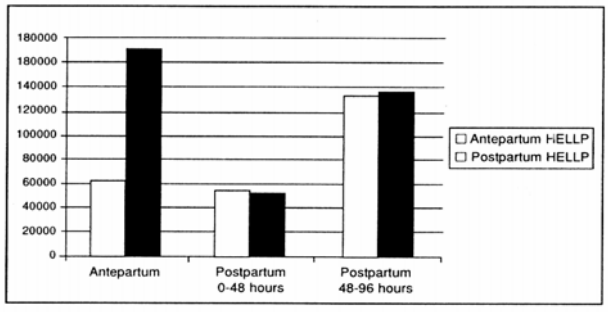

Figure 1. Mean platelet count at 48 hour intervalin prepartum and postpartum HELLP

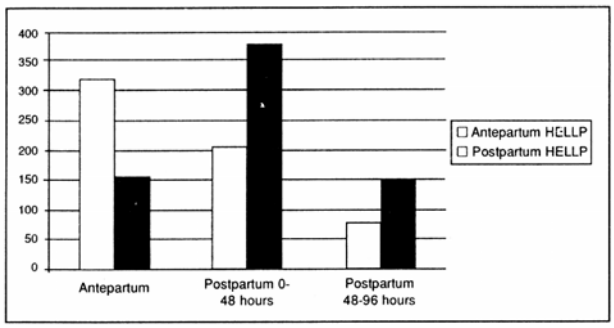

Figure 2. Mean aspartate aminotransferase at 48 hour interval in prepartum and postpartum HELLP.

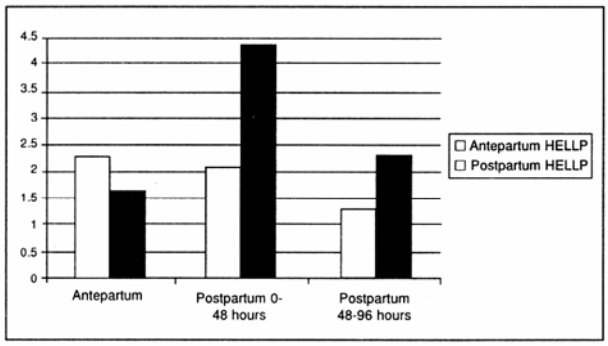

Figure 3. Mean total bilirubin at 48 hour interval in prepartum and postpartum HELLP.

tensive care facility for at least 96 hours. Blood and blood products were used to correct coagulation abnormalities and anemia as needed. All patiens received close monitoring of fluid intake and output.

After excluding cases with maternal mortality (n=6), we compared the trends of platelet count, AST, LDH and total bilirubin in prepartum 48 hours, 0 to 48 hours and 48 to 96 hours in postpartum period at 52 women. Statistical analyses were performed by Student's t and Chi square tests. A p value of < 0.05 was considered significant.

RESULTS

Inclusion criteria for this report were composed of 59 gravid women including primigravid (34%) and multiparous (66%) women. Thirty-seven women have had the syndrome before giving birth, whereas 22 women have been developed the syndrome after delivery. Six women, 4 in prepartum, 2 in postpartum group, died because of: pulmonary embolism (n:l), diffuses hypoxic encephalopathy (n:2), acute renal failure (n:2) and disseminated intravascular coagulopathy (n:l). Mean maternal age, gestational age, parity, preexisting chronic hypertension, eclampsia, severe preeclampsia, stillbirth, magnesium sulfate (MgSO4), antihypertensive and corticosteroid therapy, blood transfusions, maternal mortality and delivery-discharge period were similar in both group's (p>0.05). Perinatal mortality was higher in postpartum HELLP group (p<0.02) (Table I).

The time between hospital admission and delivery ranged between 8 to 32 hours in both group with a mean interval of 24 + 4 hours.

In prepartum HELLP group (group I), the differences between the last and two previous measurements were significant for platelets (p< 0.001; p< 0.001), for AST (p< 0.001; p< 0.001), for total bilirubin (p< 0.001; p< 0.01) and for LDH (p< 0.001; p< 0.001) (Table II).

In postpartum HELLP group (group II), the differences between the second and the other measurements (first and last) were significant for platelets (p< 0.001; p< 0.001), for AST (p< 0.05; p< 0.001) and for total biliaibin (p< 0.01; p< 0.01). For LDH, only the difference between the second and the third measurements was significant (p< 0.001). Furthermore the last platelet count was significantly different from the first measurement (p<0.02) (Table III). High levels of bilirubin in 80%, of AST in 50%, of LDH in 50% of the cases were observed in group II before delivery.

The courses of platelets, aspartate transaminase, lactic dehydrogenase and total bilirubin levels were shown in figures' 1-4 in both groups.

DISCUSSION

Some patients with HELLP syndrome have the abnormalities in prepartum period, while others have them in postpartum period. The pattern of disease progression and regression occur at different time intervals. How rapidly a patient recovers from HELLP syndrome depends on a number of factors, mainly the termination of pregnancy.

In 1976 Pritchard et al (10), reported that the low platelet counts of eclamptic patients rose to the normal range within 5 days of delivery and then frequently became supranormal. In a prospective study reporting patients with thrombocytopenia and transaminase elevation associated with preeclampsia, the platelet count nadir occurred at an average of 23 hours postpartum, and platelet counts approached to normal levels within 72-120 hours postpartum (11). Neiger at

Table 2. Laboratory Parameters of Prepartum HELLP Group

	Before delivery	Postpartum 48 hours	Postpartum 96 hours
Platelets	63.000±24.063	54575±22199	133727±52032
Aspartate aminotransferase	322±252	202±187	71±49
Total bilirubin	2.3±2.1	2.0±1.6	1.2±0.9
Lactate dehydrogenase	1103±633	893±517	492±149

Table 3. Laboratory Parameters of Postpartum HELLP Group

	Before delivery	Postpartum 48 hours	Postpartum 96 hours
Platelets	164600±47089	50750±21829	136500±43425
Aspartate aminotransferase	220±160	378±320	141±143
Total bilirubin	1.7±2.1	4.3±4.8	2.1±2.6
Lactate dehydrogenase	925±604	1039±656	661±321

al (12), prospectively followed up 20 patients with HELLP syndrome. The average time from delivery to platelet count recovery 100000/mm^3, was 82 hours. Eighteen patients out of 20, required to recover the platelet counts by the fifth postpartum day.

In our study we found that platelet count felt sharply after birth in both groups and persisted to be low in the first two days postpartum, but raised to the levels between 100000-150000/mm^3 at the third and fourth day in both groups. Six patients (18%) in group I, 3 patients (15%) in group II had platelet count less than 100000/mm^3 at 96 hours postpartum. Between 2nd to 4th days after delivery, platelet counts were above 100000/mm^3 in 84% of the cases.

Martin et al (13), analyzed the postpartum recoveiy of 70 preeclamptics whose platelet nadir was below 50000/mm^3 and 88 patients whose platelet nadir was between 50000-100000/mm^3. All patients in both groups exceded a platelet count of 100000/mm^3 at the 6th postpartum day. We found that patients with very low platelet count, reached a level above 100000/mm^3 in 75% of the group I and 70% of the group II, at the 96th postpartum hour.

Acceptance of HELLP syndrome as a developing entity in the mildly thrombocytopenic range of 100000 to 150000/mm^3 platelets should alert the physicians as maternal-fetal care and lead earlier recognition of disease and appropriate therapy (14). In fact, 40% of our postpartum HELLP cases showed a platelet count below 150000/mm^3 before delivery. Furthermore mean biochemical parameters were all high in postpartum group before delivery suggesting that there were incomplete HELLP cases.

Catanzarite et al (15), retrospectively reviewed the perinatal course of 79 women with HELLP syndrome and observed that the lowest platelet counts and mean aspartate aminotransferase and lactate dehydrogenase occurred within 72 hours of delivery in almost all cases. At 48th hours, we observed in postpartum HELLP group the lowest platelet count in 95%, the highest bilirubin level in 80%, the highest AST level in 65% and the highest LDH level in 50% of the cases. AST values became normal in 85% and LDH values in 76% of the cases at the 2nd to 4th days postpartum.

Roberts et al (l6), showed that a higher incidence of postpartum hemorrhagic complications occurred in lower platelet count in pregnancies with HELLP syndrome. The tendency to have postpartum incisional bleeding after abdominal or vaginal delivery was related to the degree of thrombocytopenia. We did not observe any incisional bleeding complication in our group because of using fresh blood products in early period. Especially in patients with advanced cases, high-dose corticosteroid therapy appears to significantly hasten recovery and lessen the severity of the disease postpartum (17).

Julius et al (18), showed that the AST was the first parameter to peak and the first to normalize. According to this study the laboratory values normalized in the following order: AST, platelets and LDH. Platelets and total serum LDH are the best tests to reflect the severity of HELLP syndrome (18,19). We showed that all the laboratory parameters except platelets, used in the surveillance of HELLP syndrome remained at pathologic levels even at the end of fourth day especially in postpartum group.

Perinatal mortality was high in both groups. We comment this result on the high proportion of referral cases and our policy to intervene aggressively in HELLP syndrome. Late admission to our center had increased the perinatal mortality rate especially in postpartum cases.

Martin et al (13), reported that the natural history of HELLP syndrome is a deteriorating postpartum process with a disease nadir at 24 to 36 hours postpartum followed by a gradual recovery. Our study pointed out that delivery is a trigger mechanism in incomplete HELLP cases. It is suggested that the causative episodes reach maximal levels at or around the time of delivery. Probably platelet comsumption in delivery aggravate the incomplete disease and complete the classical description of HELLP. We observed that, laboratory findings of the disease process related to HELLP syndrome became aggravated in 24 to 48 hours after delivery and improved thereafter. The earliest parame-

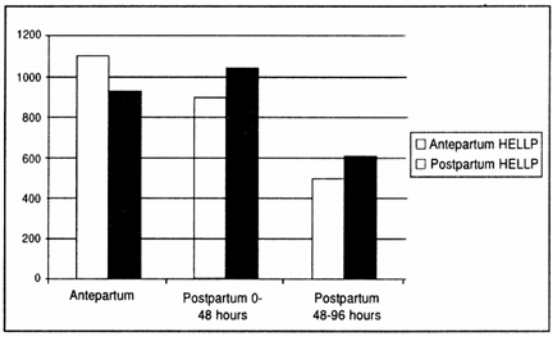

Figure 4. Mean lactate dehydrogenase at 48 hour interval in prepartum and postpartum HELLP

ter normalizing during the surveillance period was the platelet count. Biochemical parameters persisted to be high even at the 4th day.

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