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CLINICAL STUDY

OUTCOME OF PREGNANCIES WITH HELLP SYNDROME COMPlicated BY ACUTE RENAL FAILURE (1989–1999)

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ABSTRACT

HELLP syndrome, a syndrome of hemolysis, elevated liver enzymes and low platelets may occur in pregnancy with pre-eclampsia/eclampsia, and its a significant complication is acute renal failure (ARF).

The aim of study was to determine frequency and outcome of HELLP syndrome complicated by ARF.

Thirty-nine patients with pregnancy-related ARF were treated between Jan 1, 1989 and Jan 1, 1999. In these patients, the most frequent causes were HELLP syndrome (n = 14; 36%), postpartum hemorrhage (n = 10; 26%), pre-eclampsia/eclampsia (n = 6; 15%) and abruptio placenta (n = 4; 10%). Seven of the patients with HELLP syndrome had impairment of consciousness during hospitalization. Of these patients, coma in 5, stupor in 1, confusion in 1 were diagnosed. Twelve of the patients with HELLP syndrome and 14 of the other patients were treated by dialysis. Mann-Whitney U test and χ² test(corrected by Yates and Fisher exact) were used for statistical analysis.

Although serious clinical findings, with supportive treatment, 12 patients with HELLP syndrome and 21 other patients were fully recovered. One patient both with and without HELLP syndrome could not recovered due to diffus cortical necrosis. Moreover, one patient with
HELLP syndrome and 3 other patients were died. Mortality rate of the patients with HELLP syndrome was not found different from those of the other patients ($p = 0.544$). The causes of death were cerebral hemorrhage in patient with HELLP syndrome and disseminated intravascular coagulation ($n=1$), cerebral emboli ($n=1$), adult respiratory distress syndrome ($n=1$). Fetal death occurred in 4 patients with HELLP syndrome (28.5%) and 7 other patients (28%), and rates were similar ($p > 0.5$).

Finally, HELLP syndrome was the most frequent cause leading to ARF in pregnancy and their prognosis was not different from those of the other patients.

*Key Words:* Acute renal failure, HELLP syndrome, Pregnancy, Prognosis.

### INTRODUCTION

HELLP syndrome, a syndrome of hemolysis, elevated liver enzymes and low platelets occurs generally as complications of pre-eclampsia and eclampsia in pregnancy, but it may be also occurred without pre-eclampsia/eclampsia (1,2). Incidence of HELLP syndrome was 19.3% in patients with pre-eclampsia and eclampsia (3). HELLP syndrome is seen before or after delivery. In nearly one third of cases, it had been seen after delivery (4). In before and after delivery, laboratory findings of HELLP syndrome were not found different. However, patients with postpartum HELLP syndrome had higher incidences of pulmonary edema and renal failure. In patients with HELLP syndrome, serious complications had been diagnosed as disseminated intravascular coagulation, abruptio placenta, acute renal failure, pulmonary edema, subcapsular liver hematoma and retinal detachment (5). Acute renal failure (ARF) was a complication in 7.7-19.6% of patients with HELLP syndrome (5-7). It can be not established literature knowledge about prevalence of HELLP syndrome in etiology of ARF in pregnancy.

The purpose of this study is to establish prevalence of patients with HELLP syndrome among patients with ARF in pregnancy, and to compare outcomes of patients with or without HELLP syndrome.

### PATIENTS AND METHODS

This study included 39 patients with ARF in pregnancy between Jan 1, 1989 and Jan 1, 1999. All of the patients were admitted to our clinic after treatment (delivery, curetage, caesarean etc.) in gynecology and obstetric clinics.

Acute renal failure was considered in the presence of oliguria-anuria of >3 days in association with progressive elevation in serum creatinine level.
To diagnose ARF, medical history was obtained, and physical examination, including evaluation of hemodynamic status was performed. Urinalysis, including careful sediment examination and simultaneous chemical analysis of blood and urine (Osmolality, urea, creatinine, sodium, potassium, uric acid) were done. Fractional sodium excretion and renal failure index, are the most sensitive indices, were determined. Ultrasonography was performed to establish renal structure and other complications (abdominal hematoma, subcapsular hematoma etc.). Unconsciousness patients were examined by neurology specialist, and were investigated by cerebral computed tomographic (CT) scan when indicated. Bilateral cortical necrosis was diagnosed by selective renal angiography.

HELLP syndrome was diagnosed by physical examination (icter, arterial hypertension etc.) and laboratory tests including peripheral smear, total and conjugated (direct) bilirubin in serum, reticulocyte count, urobilinogen in urine, lactate dehydrogenase (LDH), aspartate aminotransferase, alanine aminotransferase in serum and platelet count in blood. Complications of HELLP syndrome were diagnosed by fibrinogen, fibrin degradation products, prothrombin and partial thromboplastin time, the chest radiography, retinal examination and cerebral CT scan.

The patients with ARF were treated by isotonic fluids (0.9% NaCl, 5% Dextrose etc.) or blood in volume depletion, high dose furosemide (120-240mg) or mannitol (12-20g) in oligo-anuria. Dialysis was performed early’prophylactic’ or in severe complications due to uremic state (coma, hyperkalemia, metabolic acidosis, hypervolemia etc.). Nutritional therapy, including adequate calories was given by oral or parenteral route. Sepsis or local infections were treated by non-nephrotoxic antibiotics. For antihypertensive treatment, drugs, uneffective on renal hemodynamic parameters, were selected. Blood, platelet or fresh freezed plasma were given to patients with severe haemorrhage (vaginal, gastrointestinal, cerebral etc.).

Pregnancies of the patients with HELLP syndrome and ARF were finished by caesarean section in 4 and induction of labour in 5. However, in other patients, pregnancy was finished by induction of labour in 3 patients and caesarean section in 4 patients; in addition, hysterectomy was performed due to persistent hemorrhage in 2 patients.

Median values of various findings of groups were found, and data were analysed statistically by Mann-Whitney U, $\chi^2$ test corrected by Yates and Fisher exact $\chi^2$ test. Statistically, significant difference was accepted as $p < 0.05$.

RESULTS

In 39 patients with pregnancy-related ARF, etiological causes were summarized in Table 1.
As seen, HELLP syndrome was the most frequent cause. In 9 (64%) of these patients, pre-eclampsia or eclampsia was diagnosed together with HELLP syndrome. HELLP syndrome was complete in 12 patients (86%) and partial in 2 (14%) patients. Hemolysis was not seen in cases with partial HELLP syndrome. HELLP syndrome occurred in postpartum period in 10 patients (71%) and antepartum period in 4 patients (29%).

All of the patients were distinguished two groups with respect to existence of HELLP syndrome. Then, they were compared with respect to various findings and prognosis. Some findings of the patients were shown in table 2.

The patients with HELLP syndrome had higher blood pressures, but their age and pregnancy number were not different from those of the other patients.

Clinical findings of the patients with HELLP syndrome were summarized in Table 3.

The most patients with hemorrhage improved by suitable treatment. One patient, has cerebral hemorrhage, died; other patient improved, but she had hemiplegia as remnant.

Laboratory findings were summarized in patients with HELLP syndrome in Table 4.
Prognosis of the patients with and without HELLP syndrome were summarized in Table 5.

In patients with complete renal recovery, oligo-anuria duration (median) was 8.5 days (4-16) in patients with HELLP syndrome and 6 days (3-15) in the other patients \( p < 0.02 \); in addition, renal recovery duration (median) was 13 days (8-23) in patients with HELLP syndrome and 11 days (7-40) in the other patients \( p < 0.13 \). In patients with HELLP syndrome, oligo-anuria duration was longer but renal recovery duration was not different from those of the other patients. The patients, who have never recovery renal function, had bilateral renal cortical necrosis. Irreversible renal damage was seen in 7% of patients with HELLP syndrome and in 4% of other patients, and rates were similar \( p = 0.47 \). Maternal and fetal mortality rates were not different in patients with and without

<table>
<thead>
<tr>
<th>Clinical finding</th>
<th>Patient number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Consciousness</td>
<td></td>
</tr>
<tr>
<td>Confusion</td>
<td>1</td>
</tr>
<tr>
<td>Stupor</td>
<td>1</td>
</tr>
<tr>
<td>Coma</td>
<td>5</td>
</tr>
<tr>
<td>Icter</td>
<td>5</td>
</tr>
<tr>
<td>Subicter</td>
<td>3</td>
</tr>
<tr>
<td>Hemorrhage</td>
<td></td>
</tr>
<tr>
<td>Vaginal</td>
<td>4</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>2</td>
</tr>
<tr>
<td>Cerebral</td>
<td>2</td>
</tr>
<tr>
<td>Subcutaneous</td>
<td>1</td>
</tr>
<tr>
<td>Hypertension</td>
<td>10</td>
</tr>
<tr>
<td>Convulsion</td>
<td>4</td>
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</table>

<table>
<thead>
<tr>
<th>Laboratory finding</th>
<th>Median</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fibrin degredation products (mg/L)</td>
<td>5.0</td>
<td>3-14</td>
</tr>
<tr>
<td>BUN (mmol/L)</td>
<td>23.7</td>
<td>15-42.8</td>
</tr>
<tr>
<td>Serum Creatinine (µmol/L)</td>
<td>496</td>
<td>372-762</td>
</tr>
<tr>
<td>Platelet count (x10^9/L)</td>
<td>67.5</td>
<td>15-142</td>
</tr>
<tr>
<td>Total bilirubin (µmol/L)</td>
<td>118</td>
<td>15.3-819.4</td>
</tr>
<tr>
<td>Conjugated bilirubin (µmol/L)</td>
<td>49.3</td>
<td>0.2-241.4</td>
</tr>
<tr>
<td>Aspartat aminotransferase (U/L)</td>
<td>375</td>
<td>110-1663</td>
</tr>
<tr>
<td>Alanine aminotransferase (U/L)</td>
<td>308</td>
<td>103-1251</td>
</tr>
<tr>
<td>Lactate dehydrogenase (U/L)</td>
<td>1976.5</td>
<td>1002-3010</td>
</tr>
</tbody>
</table>
HELLP syndrome \( (p = 0.544, \ p = 0.519, \ \text{respectively}) \). The causes of maternal mortality were cerebral hemorrhage in one patient with HELLP syndrome, and disseminated intravascular coagulation \( (n = 1) \), cerebral emboli \( (n = 1) \), adult respiratory distress syndrome \( (n = 1) \) in the other patients.

**DISCUSSION**

The main causes of ARF in pregnancy were reported as toxemia of pregnancy and sepsis (8), uterine hemorrhage and pre-eclampsia/eclampsia (9), septic abortion (10), abortion (11), spontaneous and septic abortion (12), and abortion, hemorrhage and pre-eclampsia (13). As seen, main causes were generally abortion and pre-eclampsia/eclampsia.

In present series, HELLP syndrome was the most frequent cause. The cause of this may be the increased frequency of pre-eclampsia/eclampsia. In previous our series, abortion was main cause, but the frequency of abortion decreased due to legalization of medical abortion in the period of 10 week-gestation (12). Therefore, HELLP syndrome replaced abortion in the present series.

In one third of cases, the onset of HELLP syndrome was generally within 48 hours of postpartum period (4). In addition, complications were more frequency in these cases (5). One of them is ARF. As similar to this report, in the most cases of the present series, HELLP syndrome was in postpartum period. The patients with only elevated liver enzymes or low platelets (14) or ELLP syndrome (no hemolysis) (15) had been defined as patients with partial HELLP syndrome (14,15). There was not found clear difference in the clinical features and complications between partial and complete HELLP syndrome (14). In the present series, complete HELLP syndrome was high frequency. Hemolysis was not found in patients with partial HELLP syndrome.
Maternal and perinatal complications are shown high frequency in patients with HELLP syndrome. Therefore, such patients should be referred to a tertiary care center, where maternal and neonatal intensive care facilities are available (16). Likewise, patients series with ARF and HELLP syndrome had been treated in intensive care units (7,17,18). Similarly, in the present series, half of the patients with HELLP syndrome had the impaired conscious-ness due to uremia, cerebral hemorrhage and convulsions. In the most cases, there were hypertension, icter and hemorrhage. That is, clinical findings of the patients were severe.

The control of hypertension and immediate delivery is the best choice of treatment in severe cases (19). Therefore, pregnancy was finished immediately in many patients of the present series.

Dialysis had been performed 29-31% of cases with HELLP syndrome (7,16) and 55.5% of cases without HELLP (9). However, in present series, dialysis therapy was high frequency in the patients with and without HELLP syndrome (respectively, 86%, 56%). Severe clinical setting and complications, and early dialysis were the causes of high rate of dialysis.

Irreversible renal damage was seen in 11.1-11.6% of pregnancy-related ARF (9,17) and 3-17% of HELLP syndrome together with ARF (7,16,20). Therefore, it was seen that HELLP syndrome did not increase rate of irreversible renal damage. Similarly, in the present series, these rates were not found different in patients with and without HELLP syndrome.

In pregnancy-related ARF, maternal mortality rates were notified between 8.3% and 32% (8,9,12,21). Maternal mortality rates were between 12% and 34% in ARF with HELLP syndrome (7,16,20). Therefore, it was seen that HELLP syndrome did not increase mortality rate. As similar to this finding, in present series, mortality rates of patients with and without HELLP syndrome were not found different. In only HELLP syndrome, mortality rates were reported between 1.1% and 16.7%. (2,3,5,6). That is, outcome was better. In addition, it was declared that with proper supportive care, most patients with HELLP syndrome fully recovered kidney function (22). Therefore, it may be suggested that ARF was increased mortality rates.

Fetal outcome did not alter in patients with HELLP syndrome of the present series. This finding was similar to result of previous report (5).

As a result, in recent years, HELLP syndrome was the most frequent cause of pregnancy-related ARF, and its outcome were similar to patients with ARF in pregnancy without HELLP syndrome.

REFERENCES


