Diagnosis and management of hemolysis, elevated liver enzymes, and low platelets syndrome

John R. Barton, MD\textsuperscript{a,b,}\textsuperscript{*}, Baha M. Sibai, MD\textsuperscript{b}

\textsuperscript{a}Central Baptist Hospital, Perinatal Diagnostic Center, 1740 Nicholasville Road, Lexington, KY 40503-1499, USA
\textsuperscript{b}Department of Obstetrics and Gynecology, University of Cincinnati, 231 Albert Sabin Way, Cincinnati, OH 45267-0526, USA

Hemolysis, abnormal liver function tests, and thrombocytopenia have been recognized as complications of pre-eclampsia/eclampsia for many years [1–4]. According to Chesley [1], some of these components have been reported in the obstetric literature for almost a century. (Coagulation defects and microthrombi were first described by Schmorl in 1893). In 1982, Weinstein [5] described 29 cases of severe pre-eclampsia/eclampsia complicated by thrombocytopenia, abnormal peripheral smear, and abnormal liver function tests. He suggested that this collection of signs and symptoms constituted an entity separate from severe pre-eclampsia and coined the term \textit{HELLP syndrome}: \textit{H} for hemolysis, \textit{EL} for elevated liver enzymes, and \textit{LP} for low platelets. Since then, numerous articles and case reports describing this syndrome have appeared in the medical literature. In addition, the presence of this syndrome has become a major cause of litigation against obstetricians involving cases of allegedly misdiagnosed pre-eclampsia, particularly in patients who were complicated by severe liver involvement of their disease. This article reviews the diagnosis, presentation, pathologic findings, hepatic manifestations, and current management recommendations for pregnancies complicated by HELLP syndrome.
Terminology and diagnosis

A review of the literature by Sibai et al [6] revealed considerable variety in the terminology, reported incidence, reported cause, diagnosis, and management of HELLP syndrome. Goodlin considered it an early form of severe pre-eclampsia and labeled it a great imitator, equating it with impending edema, proteinuria, hypertension gestosis type B [2]. Weinstein [5] considered it a “unique variant” of pre-eclampsia, whereas MacKenna et al [7] considered it misdiagnosed pre-eclampsia. Conversely, several authors have theorized that HELLP syndrome is mild disseminated intravascular coagulation (DIC) that was missed because of inadequate laboratory investigation.

The diagnostic criteria used for HELLP syndrome are variable and inconsistent. Hemolysis, defined as the presence of microangiopathic hemolytic anemia, is the hallmark of the triad of HELLP syndrome [8]. The classical findings of microangiopathic hemolysis include abnormal peripheral smear (schistocytes, burr cells, echinocytes), elevated serum bilirubin (indirect form), low serum haptoglobin levels, elevated lactate dehydrogenase (LDH) levels, and significant drop in hemoglobin levels. A significant percentage of published reports included patients who had no documentation of hemolysis; hence, these patients may fit the criteria for “ELLP” syndrome [9–16]. Even in studies where hemolysis was mentioned, the diagnosis was based on the presence of abnormal peripheral smear (no description of type or degree of abnormalities) [7,17] or elevated LDH levels (threshold of 180 to 600 U/L) [18–23].

No consensus exists in the literature regarding the liver function test to be used or the degree of elevation used in these tests to diagnose elevated liver enzymes (EL) [8]. In his original report, Weinstein [5] mentioned abnormal serum levels of aspartate aminotransferase (AST) and abnormal alanine aminotransferase (ALT) and bilirubin values; however, the levels were not stated. In addition, he made no mention of LDH as a diagnostic test of liver involvement. In subsequent studies where elevated liver enzymes (either AST or ALT) were mentioned, the values considered abnormal ranged from 17 to 72 U/L [8]. In clinical practice, many of these values are considered normal or slightly elevated. In essence, some of these studies included women with low platelets syndrome. Some of these women may have had either severe pre-eclampsia with thrombocytopenia, gestational thrombocytopenia, or immune thrombocytopenic purpura.

Low platelet count is the third abnormality required to establish the diagnosis of HELLP syndrome. There is no consensus among various published reports regarding the diagnosis of thrombocytopenia. The reported cut-off values have ranged from 75,000/mm$^3$ to 279,000/mm$^3$ [7,9–18]. Therefore, some of the patients included in these studies fit the criteria for “EL” syndrome. In essence, these women had severe pre-eclampsia with mild elevation in liver enzymes [10,12].

Martin et al [24], in a retrospective review of 302 cases of HELLP syndrome at the University of Mississippi, Jackson, devised the following classification...
of subpopulations based on platelet count nadir. They defined class 1 HELLP syndrome as a platelet nadir below 50,000/mm$^3$, whereas patients with platelet nadirs between 51,000 and 100,000/mm$^3$ were classified as class 2. Finally, class 3 represents a platelet nadir between 101,000 and 150,000/mm$^3$. These classes have been used to predict the rapidity of postpartum disease recovery [24], the risk of recurrence of HELLP syndrome [25], perinatal outcome, and the need for plasmapheresis [26]. Miles et al [27], from the same institution, reported a strong association between the presence of HELLP syndrome and eclampsia. In this study, HELLP syndrome was present in 30% of patients with postpartum eclampsia and in 28% of patients having eclampsia before delivery. As a result, Miles et al suggested that the presence of HELLP syndrome may be a predisposing factor in the development of eclampsia. The criteria for the diagnosis of HELLP syndrome by several authors include the laboratory findings summarized in Table 1.

### Table 1
Classifications of HELLP syndrome

<table>
<thead>
<tr>
<th></th>
<th>Platelet count</th>
<th>AST</th>
<th>LDH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sibai et al [6]</td>
<td>&lt; 100,000/mm$^3$</td>
<td>≥ 70 U/L</td>
<td>≥ 600 U/L</td>
</tr>
<tr>
<td>Martin et al [21]</td>
<td>&lt; 150,000/mm$^3$</td>
<td>≥ 40 U/L</td>
<td>≥ 600 U/L</td>
</tr>
<tr>
<td>van Pampus [47]</td>
<td>&lt; 100,000/mm$^3$</td>
<td>&gt; 50 U/L</td>
<td>&gt; 600 U/L</td>
</tr>
<tr>
<td>Visser and Wallenburg [48]</td>
<td>&lt; 100,000/mm$^3$</td>
<td>&gt; 30 U/L</td>
<td>a</td>
</tr>
</tbody>
</table>

*a* Not included in their criteria.

### Box 1. Medical and surgical disorders confused with the HELLP syndrome

- Acute fatty liver of pregnancy
- Hyperemesis gravidarum
- Appendicitis
- Idiopathic thrombocytopenia
- Diabetes insipidus
- Kidney stones
- Gall bladder disease
- Peptic ulcer
- Gastroenteritis
- Pyelonephritis
- Glomerulonephritis
- Systemic lupus erythematosus
- Hemolytic uremic syndrome
- Thrombotic thrombocytopenic purpura
- Hepatic encephalopathy
- Viral hepatitis
An essential step in management is to confirm or exclude the diagnosis of HELLP syndrome from other conditions listed in Box 1. Laboratory evaluation should include a complete blood count with platelet count, a peripheral smear, coagulation studies, and serum AST, creatinine, glucose, bilirubin, and LDH levels. The authors’ diagnosis of HELLP syndrome requires the presence of all the following: platelet count of less than 100,000/mm³, AST level greater than 70 IU/L (>2 × upper limit for the authors’ normal values), abnormal peripheral smear, and LDH level greater than 600 IU/L (>2 × upper limit of normal) or bilirubin level greater than 1.2 mg/dL, or both. Patients who do not fit all these parameters are considered to have partial HELLP syndrome [28].

Clinical presentation

In the series reported by Sibai et al [6], patients with HELLP syndrome were significantly older (mean age 25 years) than patients with severe pre-eclampsia/eclampsia without features of HELLP syndrome (mean age 19 years). The incidence of the syndrome was significantly higher in the white population and among multiparous patients. The incidence of HELLP syndrome is also higher in pre-eclamptic patients with conservative management of their disease. Coincidentally, medial complications (notably diabetes mellitus and lupus nephritis) were no more common among the patients with HELLP syndrome. Other authors have made similar observations [7,14,17].

Patients with HELLP syndrome may present with various signs and symptoms, none of which are diagnostic and all of which may be found in patients with severe pre-eclampsia/eclampsia without HELLP syndrome. Sibai [8] noted that the patient usually presents remote from term, complaining of epigastric or right upper quadrant pain; some have nausea or vomiting, and others have nonspecific viral syndrome–like symptoms. Most patients (90%) give a history of malaise for the past few days before presentation. In Weinstein’s reports [5,17], nausea or vomiting and epigastric pain were the most common symptoms. Right upper quadrant or epigastric pain is thought to result from obstruction of blood flow in the hepatic sinusoids, which are blocked by intravascular fibrin deposition.

Patients with HELLP syndrome usually demonstrate significant weight gain with generalized edema. It is important to appreciate that severe hypertension (systolic blood pressure ≥160 mm Hg, diastolic blood pressure ≥110 mm Hg) is not a constant or even a frequent finding in HELLP syndrome. Although 68.8% of the 112 patients studied by Sibai et al [6] had a diastolic blood pressure of 110 mm Hg or greater at the time of admission to the hospital, 14.5% had a diastolic blood pressure of 90 mm Hg or less. In Weinstein’s [5] initial report on 29 patients, less than half (13) had an admission blood pressure of 160/110 mm Hg or greater. Only 66% of the 18 primigravidas and 44% of the nine multigravidas studied by MacKenna et al [7] had severe hypertension on admission. Aarnoudse et al [29] described six women presenting with severe
epigastric pain in the third trimester who had significantly elevated liver enzymes, a low platelet count, and evidence of hemolysis. None of these patients had a blood pressure greater than 140/90 mm Hg or proteinuria. Thus, patients with HELLP syndrome may present with a variety of signs and symptoms (Table 2), none of which is diagnostic of severe pre-eclampsia [30]. As a result, they are often misdiagnosed as having various medical and surgical disorders (see Box 1). Sibai [8] recommends that all pregnant women displaying any of these symptoms have a complete blood count, platelet count, and liver enzyme determinations, irrespective of maternal blood pressure.

Acute fatty liver of pregnancy (AFLP) is a rare but potentially fatal complication of the third trimester of pregnancy [31]. In its early presentation, AFLP may be difficult to differentiate from HELLP syndrome. Patients with AFLP typically present with nausea, vomiting, abdominal pain, and jaundice; however, hypertension and proteinuria are usually absent [32]. HELLP syndrome and AFLP are both characterized by elevated liver function tests, but the abnormalities tend to be greater in HELLP syndrome. Much rarer than HELLP syndrome are thrombotic thrombocytopenic purpura (TTP) and hemolytic uremic syndrome (HUS); these diseases are remarkably similar and have even been thought to be one and the same. HUS characteristically is a disease of children, impairing renal function and causing platelet and erythrocyte destruction. When it occurs in association with pregnancy, the presentation is typically post partum. TTP is more commonly recognized among adults, with similar manifestations to HUS. The classic pentad of TTP includes thrombocytopenia, microangiopathic hemolysis, neurologic symptoms, renal impairment, and fever. The article on imitators of severe pre-eclampsia/eclampsia by Sibai elsewhere in this issue further describes the diagnosis and management of these and other imitators of HELLP syndrome.

**Pathology findings**

Hemolysis, defined as the presence of microangiopathic hemolytic anemia, is the hallmark of the HELLP syndrome. Microangiopathic hemolytic anemia
is thought to result from the passage of red blood cells through small blood vessels with damaged intima and fibrin deposition [5,33], leading to the appearance on peripheral smear of triangular cells, burr cells, echinocytes, and spherocytes. Microangiopathic hemolytic anemia is not specific to HELLP syndrome and is also found in association with TTP, renal disease, HUS, eclampsia, and carcinomatosis.

In a study published by the authors’ group [34], the microscopic findings from liver biopsies obtained under direct visualization after cesarean delivery from pregnancies complicated by HELLP syndrome were categorized and correlated with the severity of the concurrent clinical and laboratory abnormalities. In comparing the histologic findings with the laboratory findings, the group found that periportal hemorrhage correlated with the presence of fibrin deposition but with none of the laboratory parameters measured. Similarly, fibrin deposition was not statistically correlated with any measured laboratory parameter. Although steatosis occurred in only one third of the patients, it correlated significantly with abnormalities in platelet count, AST, and total bilirubin—but not with periportal hemorrhage or fibrin deposition.

To test further for a relationship between the severity of histologic, clinical, and biochemical parameters in patients with HELLP syndrome, the study group was divided into two subgroups on the basis of histologic criteria, with six patients defined as having mild HELLP syndrome and five as having severe HELLP syndrome [34]. Statistical analysis demonstrated a significant difference for periportal hemorrhage and fibrin deposition between these two histologic criteria groups, but it failed to show any statistically significant difference in gestational age, mean arterial blood pressure, or any laboratory parameter.

In the case report by Hannah et al [35], frozen sections of liver from a patient with elevated liver enzymes and thrombocytopenia that were stained with hematoxylin and eosin and oil red O showed many small orangeophilic globules considered to be fat in hepatocytes, a finding comparable with AFLP. Similarly, the authors noted steatosis in several of the liver biopsy specimens from their study population. Although AFLP and the HELLP syndrome overlap both clinically and pathologically, the authors believe that these syndromes can be distinguished histopathologically. On light microscopy, the vacuolization and necrosis are more prominent in the central zone in AFLP, whereas in HELLP syndrome the necrosis is predominantly periportal. Although fat droplets may be present on electron microscopy in hepatocytes from patients with the HELLP syndrome, fat droplets are much more numerous in AFLP.

From the authors’ study [34] and from previous case reports [3,29,35–37] describing the histopathologic findings of hepatic lesions associated with HELLP syndrome, it appears that the classic lesion is periportal or focal parenchymal necrosis in which hyaline deposits of fibrin-like material can be seen in the sinusoids. In addition, immunofluorescence studies show fibrin microthrombi and fibrinogen deposits in the sinusoids in areas of hepatocellular necrosis and in sinusoids of histologically normal parenchyma [29,36]. These histopathologic findings may be related to the elevated liver enzymes and the right upper
quadrant pain and tenderness seen in patients with this syndrome. In certain cases, the cellular necrosis and infarction are severe enough to be seen by CT of the liver (Fig. 1).

**Maternal and perinatal outcomes**

It has been unclear whether women considered to have “partial,” “incomplete,” or “impending” HELLP syndrome should be managed in the same way as other women with severe pre-eclampsia. Audibert et al [28] compared the incidence of maternal complications among women with HELLP syndrome, women with isolated laboratory abnormalities, including one or two but not all three features of HELLP syndrome (ie, partial HELLP syndrome), and women with severe pre-eclampsia and normal laboratory tests. Three hundred and sixteen women were studied: HELLP syndrome (n = 67), partial HELLP syndrome (n = 71), and severe pre-eclampsia (n = 178). Mean gestational ages at delivery in the HELLP, partial HELLP, and severe pre-eclampsia groups were 31.7, 32.7, and 34.5 weeks, respectively (P < 0.001 between HELLP and severe pre-eclampsia). One maternal death from intracerebral hemorrhage occurred in the HELLP group. Women with HELLP syndrome had a higher incidence of cesarean section (P < 0.001) than the other two groups. Maternal complications noted in this study are summarized in Table 3. The authors concluded that the higher incidences of maternal complications in women with HELLP syndrome indicate the importance of strict criteria for the definition of HELLP syndrome, and that women with partial HELLP syndrome should be studied and managed separately from those with complete HELLP syndrome.
Women with HELLP syndrome have been reported to have an increased risk of adverse maternal outcome in comparison with those with severe pre-eclampsia but not HELLP syndrome. The differences in outcomes observed in these studies may be differences seen in women with severe pre-eclampsia alone and could also reflect a greater severity of the disease process [28,38]. Haddad et al [39] attempted to clarify this finding by conducting a study to determine whether the onset of HELLP syndrome at 28 or fewer weeks’ gestation was associated with an increased risk of maternal and perinatal morbidity in comparison with the risk associated with severe pre-eclampsia without HELLP syndrome at a similar gestational age. They noted that the overall rate of adverse maternal outcomes observed in women with HELLP syndrome (44%) was similar to that observed in women with severe pre-eclampsia but not HELLP syndrome (38%) during the second trimester. Except for hematologic changes, the incidences of all other adverse maternal outcomes studied among women with HELLP syndrome and those with severe pre-eclampsia but no HELLP syndrome were not statistically different [39].

From the same institution, Abramovici et al [40] compared the neonatal outcome after preterm delivery of infants whose gestation was complicated by HELLP syndrome, partial HELLP syndrome, or severe pre-eclampsia. There were no significant differences in complications among the 269 neonates studied in the three groups at each gestational age. These findings are summarized in Table 4. As expected, a significant decrease in morbidity and mortality was seen with advanced gestational age. The authors concluded that, in severe pre-
eclampsia, neonatal morbidity and death are related to gestational age rather than to the presence or absence of HELLP syndrome [40].

**Initial management**

The clinical course of women with HELLP syndrome is characterized by usually progressive and sometimes sudden deterioration in maternal and fetal conditions. Therefore, patients with suspected diagnosis of HELLP syndrome should be hospitalized immediately and observed in a labor and delivery unit. The first priority is to assess and stabilize maternal condition, particularly coagulation abnormalities (Box 2). Patients with HELLP syndrome who are remote from term should be referred to a tertiary care center.

Such patients should be managed as patients with severe pre-eclampsia and should initially receive intravenous (IV) magnesium sulfate as prophylaxis against convulsions and antihypertensive medications to keep systolic blood pressure below 160 mm Hg or diastolic blood pressure below 105 mm Hg [41]. This effect can be achieved with a 5-mg bolus dose of hydralazine, to be repeated as needed every 15 to 20 minutes for a maximum dose of 20 mg/h. Blood pressure is recorded every 15 minutes during therapy and every hour once the desired values are achieved. If hydralazine does not lower blood pressure adequately or if maternal side effects such as tachycardia or headaches develop, another drug, such as labetalol or nifedipine, can be used. The recommended dose of labetalol is 20 to 40 mg IV every 10 to 15 minutes for a maximum of

---

**Table 4**

Pregnancy outcomes for 269 women with HELLP syndrome, partial HELLP syndrome, and severe pre-eclampsia with normal laboratory values

<table>
<thead>
<tr>
<th></th>
<th>HELLP syndrome (n = 67)</th>
<th>Partial HELLP syndrome (n = 71)</th>
<th>Severe pre-eclampsia (n = 178)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Latency (days, median)</strong></td>
<td>0***</td>
<td>1*</td>
<td>2</td>
</tr>
<tr>
<td><strong>Gestational age at delivery (wk)</strong></td>
<td>30.7 ± 3.2*</td>
<td>31.2 ± 3.3***</td>
<td>32.7 ± 2.8</td>
</tr>
<tr>
<td><strong>Cesarean delivery</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall (%)</td>
<td>79****</td>
<td>54</td>
<td>53</td>
</tr>
<tr>
<td>For fetal distress (%)</td>
<td>13</td>
<td>18</td>
<td>13</td>
</tr>
<tr>
<td>5-min Apgar score ≤ 6 (%)</td>
<td>29*</td>
<td>23*</td>
<td>13</td>
</tr>
<tr>
<td>Birth weight (g)**</td>
<td>1340 ± 562*</td>
<td>1552 ± 731***</td>
<td>1795 ± 706</td>
</tr>
<tr>
<td>Intrauterine growth restriction (%)</td>
<td>28</td>
<td>31</td>
<td>22</td>
</tr>
</tbody>
</table>

* P < .005, compared with severe preeclampsia; ** P < .05, compared with partial HELLP syndrome; values are expressed as mean ± standard deviation; *** P < .05, compared with severe preeclampsia.

Box 2. Management outline of antepartum HELLP syndrome

1. Assessing and stabilizing the maternal condition

(a) Correction of coagulopathy if DIC is present
(b) Antiseizure prophylaxis with magnesium sulfate
(c) Treatment of severe hypertension
(d) Transfer to tertiary care center, if appropriate
(e) CT or ultrasound of the abdomen if subcapsular hematoma of the liver is suspected

2. Evaluation of fetal well-being

(a) Nonstress testing
(b) Biophysical profile
(c) Ultrasonographic biometry to rule out intrauterine growth restriction

3. Evaluation of gestational age

(a) If > 34 weeks’ gestation, delivery
(b) If < 34 weeks’ gestation, glucocorticosteroids, then delivery in 48 hours

220 mg over 1 hour, and the dose of nifedipine is 10 to 20 mg orally every 30 minutes for a maximum dose of 40 mg over 1 hour. During the observation period, maternal and fetal conditions are assessed.

The recommended regimen of magnesium sulfate is a loading dose of 6 g given over 20 minutes, followed by a maintenance dose of 2 g/h as a continuous IV solution. Magnesium sulfate is initiated at the beginning of the observation period and continued during labor and for at least 24 hours post partum. The next step is to evaluate fetal well-being using the nonstress test or biophysical profile, as well as to obtain ultrasonographic biometry for assessment of possible intrauterine growth restriction. Finally, it must be decided whether immediate delivery is indicated.

A review of the literature highlights the confusion surrounding the management of HELLP syndrome [6]. Some authors consider its presence to be an indication for immediate delivery by cesarean section, whereas others recommend a more conservative approach to prolong pregnancy in cases of fetal immaturity. Consequently, the literature describes several therapeutic modalities to treat or reverse HELLP syndrome. Most of these therapeutic modalities are similar to those used in the management of severe pre-eclampsia remote from term.
Corticosteroid therapy

It is well established that antenatal glucocorticoid therapy reduces neonatal complications and neonatal mortality in women with severe pre-eclampsia at 34 weeks’ or less gestation [42]. The recommended regimen of corticosteroids for the enhancement of fetal maturity is betamethasone (12 mg intramuscularly every 24 hours, two doses) or dexamethasone (6 mg intramuscularly every 12 hours, four doses) [43]. These regimens have been identified as the most appropriate for this purpose, because they readily cross the placenta and have minimal mineralocorticoid activity. It is unclear, however, whether these regimens are safe and effective in women with HELLP syndrome.

Few case reports describe the potential maternal/neonatal benefit of antenatal corticosteroid therapy in women with (H)ELLP syndrome. Heyborne et al [11] described five cases of HELLP syndrome at 24 to 30 weeks’ gestation in which temporary reversal of the HELLP syndrome was achieved using low-dose aspirin and corticosteroids. However, only one of the five women had true HELLP syndrome when dexamethasone was used, and she was delivered within 48 hours of its administration. Two of the remaining four women had ELLP syndrome, and the other two had elevated liver enzymes only (platelet counts >100,000/mm³). One of these four women developed eclampsia with disseminated intravascular coagulopathy, and two of the five pregnancies resulted in neonatal deaths.

Heller and Elliott [12] described four women with high-order multiple pregnancies complicated by ELLP syndrome who were treated with long-term corticosteroids. None of these women had hemolysis, three had elevated liver enzymes only (platelet count >100,000/mm³), and one had thrombocytopenia only when steroids were allegedly used to treat HELLP syndrome. Two of the women developed pulmonary edema with this therapy. The authors reported that dexamethasone resulted in stabilization of laboratory values and prolongation of gestation by 6 to 41 days [12].

Two reports by Magann et al [19,20] suggested that the use of corticosteroids either ante partum or post partum results in transient improvement in laboratory values and urine output in some patients diagnosed with HELLP syndrome. It is important to note that in the antepartum group, delivery was delayed by an average of only 41 hours and that the study was not placebo-controlled [19]. Tompkins and Thiagarajah [13] also assessed the benefit of corticosteroids in HELLP syndrome. In their study, 93 patients between 24 and 34 weeks’ gestation diagnosed with HELLP syndrome were given intramuscular injections of either betamethasone or dexamethasone. Precorticosteroid and postcorticosteroid platelet counts and liver function test results were compared. The authors noted that hematologic abnormalities improved after the administration of corticosteroids. The platelet count increased by \(23.3 \times 10^3/\mu L\) \((P < .001)\). A statistically significant decrease was seen in liver enzyme levels, with the ALT decreased by 31.6 IU/L and the AST decreased by 52.1 IU/L. Two doses of betamethasone given 12 hours apart was the most effective corticosteroid regimen [15].
O’Brien et al [15] reviewed corticosteroid dosing and laboratory changes in patients with antepartum HELLP syndrome. Patients were classified on the basis of their exposure to steroid use and dosage. A control group did not receive glucocorticoids, whereas one treatment group received standard corticosteroid dosing for fetal lung maturity enhancement and a second treatment group received a higher-dosed steroid regimen (ie, dexamethasone 10 mg IV every 6 hours × 2 doses followed by 6 mg IV every 6 hours × 2 to 3 doses). Liver function tests and platelet counts were analyzed in response to corticosteroid therapy. A dose-dependent improvement in platelet count and liver-function abnormalities was found with corticosteroids. These findings suggest that a higher dose of corticosteroids than standard regimens for fetal lung maturity enhancement may be needed for maximum resolution of abnormalities in HELLP syndrome [34].

O’Brien et al [16] assessed the impact of glucocorticoid administration on the rate of regional anesthesia in women with HELLP syndrome. The presence of thrombocytopenia on admission and the interval from presentation to delivery were evaluated to assess the impact of glucocorticoid use. In the 37 women who had platelet counts of less than 90,000/mm³, 0% in the untreated group (0 of 11) versus 42% in the steroid group (11 of 26) received a regional anesthetic (P = 0.015). Furthermore, the rate of regional anesthesia increased from 0% in the untreated group delivered within 24 hours (n = 10) to 57% (8 of 14) in the glucocorticoid group in which women attained a 24-hour latency from presentation to delivery (P = 0.006). The need for general anesthesia also decreased significantly in treated women who attained a 24-hour latency compared with untreated women who did not: 100% (n = 7) versus 22% (n = 9) (P = 0.003). Administration of glucocorticoids was found to increase the use of regional anesthesia in women with antepartum HELLP syndrome who had thrombocytopenia, particularly in those who achieved a latency of 24 hours before delivery [16].

Five randomized trials comparing the use of high-dose dexamethasone either to no treatment [19,20,44,45] or to betamethasone [46] in women with presumed HELLP syndrome were summarized by Sibai [30] and are presented in Table 5. These studies demonstrated improved laboratory values and urine output in patients receiving dexamethasone, but no differences in serious maternal morbidity. In addition, the number of patients studied was limited, and the studies were not placebo-controlled.

The available evidence suggests that standard-dose corticosteroids as recommended by the National Institute of Health Consensus Development Panel improve perinatal outcome when used in women with HELLP syndrome at fewer than 34 weeks’ gestation [15,19,40]. In addition, some of these women exhibit transient improvement in maternal platelet counts that makes them eligible to receive epidural anesthesia [13,16]. Some evidence suggests improved laboratory values with the use of higher doses of dexamethasone in women with postpartum HELLP syndrome [15,22,23,44,45]. The dosage of dexamethasone considered “high” in these reports was 10 mg IV every 6 to 12 hours times two doses, fol-
allowed by 5 to 6 mg IV given 6 to 12 hours later, for two additional doses [15,22, 23,44,45]. It must be emphasized, however, that most of the patients included in these studies had incompletely documented HELLP syndrome. In addition, none of these studies reported improvement in clinically important maternal morbidity, such as the need for platelet transfusion or pulmonary, renal, or hepatic complications. Therefore, there is a definite need for placebo randomized trials in women with postpartum HELLP syndrome. Until these data are available, the use of high-dose dexamethasone to improve maternal outcome in women with HELLP syndrome beyond 34 weeks’ gestation or in the postpartum period remains experimental.

### Conservative management

Van Pampus et al [47] described the clinical progress and maternal outcome of the HELLP and ELLP (findings of HELLP syndrome, but without evidence of hemolysis) syndromes in 127 patients managed in the Academic Medical Center in Amsterdam between 1984 and 1996 with a live fetus in utero. The patients were treated by temporizing management, including the use of antihypertensives and magnesium sulfate. The predominant indication for terminating pregnancy was fetal distress or fetal death, not maternal condition. All serious maternal complications occurred at the onset of the syndrome. Two mothers with HELLP syndrome died following a cerebral hemorrhage. Serious maternal morbidity was more common in cases of HELLP than in cases of ELLP syndrome (eclampsia 21% versus 8%; cerebral ischemic lesions 6% versus 21%; serious complications 24% versus 10%). Seventy-nine (62%) of women were not delivered after 3 days, and 65 (51%) after 7 days. Although the authors

<table>
<thead>
<tr>
<th>Authors</th>
<th>Dexamethasone n</th>
<th>Control n</th>
<th>Key finding</th>
</tr>
</thead>
<tbody>
<tr>
<td>Magann et al [19]</td>
<td>12(^a)</td>
<td>13</td>
<td>Improved platelet, ALT, LDH values in dexamethasone group</td>
</tr>
<tr>
<td>Magann et al [20]</td>
<td>20(^b)</td>
<td>20</td>
<td>Improved platelet, AST, LDH, urine output, MAP in dexamethasone group</td>
</tr>
<tr>
<td>Vigil-De Gracia [44]</td>
<td>17(^b)</td>
<td>17</td>
<td>Improved platelet counts only with dexamethasone</td>
</tr>
<tr>
<td>Yalcin et al [45]</td>
<td>15(^b)</td>
<td>15</td>
<td>Improved platelet, AST, MAP, and urine output with dexamethasone</td>
</tr>
<tr>
<td>Isler et al [46]</td>
<td>19(^a)</td>
<td>21(^c)</td>
<td>Improved AST, LDH, MAP, and urine output with dexamethasone</td>
</tr>
</tbody>
</table>

**Abbreviations:** ELLP, elevated liver enzymes and low platelets; MAP, mean arterial pressure.

\(^a\) Antepartum.

\(^b\) Postpartum.

\(^c\) Received IM betamethasone.

considered it unlikely that a more aggressive approach would have reduced maternal mortality or morbidity, their sample size was inadequate to evaluate rare serious maternal complications of HELLP or ELLP syndrome.

In a study by Visser and Wallenburg [48], 128 consecutive pre-eclamptic patients with HELLP syndrome and a gestational age of less than 34 weeks were matched for maternal and gestational age with 128 pre-eclamptic patients without HELLP syndrome. Both groups were treated with volume expansion and pharmacologic vasodilatation under invasive hemodynamic monitoring with the aim of prolonging gestation and enhancing fetal maturity. Except for variables pertaining to HELLP syndrome, clinical and laboratory data and median prolongation of pregnancy did not differ between the groups. Complete reversal of HELLP occurred in 43% of patients. Perinatal mortality was 14.1% in HELLP syndrome patients and 14.8% in patients without HELLP. Because the perinatal outcomes in this study are similar to those of studies performed in the United States where delivery was effected within 48 hours of the diagnosis of HELLP syndrome, the benefit of temporizing management of HELLP syndrome remains questionable. Ultimately, only a well-designed randomized trial will resolve this management issue.

The conservative management techniques described here were often associated with the use of invasive procedures and medical and surgical treatments. These confounding variables make it difficult to evaluate any treatment modality proposed for this syndrome. Occasionally, some patients without the true HELLP syndrome may demonstrate antepartum reversal of hematologic abnormalities following bed rest, use of steroids, or plasma volume expansion. However, in the authors’ experience most of these patients demonstrate deterioration in either maternal or fetal condition within 1 to 10 days after conservative management. The potential risks associated with conservative management of HELLP syndrome include abruptio placentae, pulmonary edema, acute renal failure, eclampsia, perinatal death, and maternal death. Therefore, the authors doubt that such a limited pregnancy prolongation results in improved perinatal outcome, especially when maternal and fetal risks are substantial. The authors caution specifically against expectant management of women with DIC.

**Delivery management**

When HELLP syndrome develops at or beyond 34 weeks’ gestation, or when there is evidence of fetal lung maturity or fetal or maternal jeopardy before that time, delivery is the definitive therapy. Without laboratory evidence of DIC and absent fetal lung maturity, the patient can be given steroids to accelerate fetal lung maturity and be delivered 48 hours later. Maternal and fetal conditions should be assessed continuously during this time (Fig. 2).

The presence of HELLP syndrome is not an indication for immediate delivery by cesarean section. Such an approach may prove detrimental to both mother and fetus. Patients presenting with well-established labor should be allowed to de-
liver vaginally in the absence of obstetric contraindications. Otherwise, labor may be initiated with oxytocin infusions as for routine induction in all patients with gestational age over 30 weeks, irrespective of the extent of cervical dilatation or effacement. A similar approach is used for patients at 30 weeks or less if the cervix is favorable for induction. In patients with an unripe cervix and gestational age under 30 weeks, prostaglandin induction or elective cesarean section are options for delivery management. A management protocol for the patient with HELLP syndrome requiring cesarean delivery is presented in Box 3.

Maternal analgesia during labor can be provided by intermittent use of small doses (25 to 50 mg) of intravenous meperidine. Local infiltration anesthesia can be used for all vaginal deliveries. The use of pudendal block is contraindicated in these patients because of the risk of bleeding into this area. Epidural anesthesia should be used with caution; however, many anesthesiologists are reluctant to place an epidural catheter with a platelet count of less than 75,000/mm³. General anesthesia is the method of choice for cesarean sections in the presence of severe thrombocytopenia.

Platelet transfusions are indicated either before or after delivery in all patients with HELLP syndrome in the presence of significant bleeding (eg, ecchymosis, bleeding from gums, oozing from puncture sites, wound, intraperitoneal bleeding) and in all those with a platelet count of less than 20,000/mm³. Correction of thrombocytopenia is particularly important before cesarean section. Repeated platelet transfusions are not necessary, however, because consumption occurs...
rapidly and the effect is transient. The authors’ policy is to administer 6 to 10 units of platelets in all patients with a platelet count of less than 40,000/mm³ before intubating the patient for cesarean section. Generalized oozing from the operative site is very common, and the risk of hematoma formation at these sites is approximately 20%. To minimize the risk of hematoma formation, the bladder flap should be left open and a subfascial drain should be used for 24 to 48 hours.

Briggs et al [49] evaluated wound complications in patients with antepartum HELLP syndrome with primary closure versus delayed closure and Pfannenstiel versus midline skin incisions. A total of 104 patients were identified; 75 had a primary skin closure and 29 had a delayed closure 48 to 72 hours postoperatively. Immediate wound complications (wound infection, hematoma) occurred in 18 patients (26%) who had primary closure and eight (24%) who had a delayed closure (odds ratio 1.13; 95% confidence interval 0.39 to 3.27). A late wound breakdown was seen in only one patient with primary closure and in none with delayed closure. There were no fascial wound dehiscences. No statistical difference in wound complication was found between midline (primary, delayed) and Pfannenstiel (primary, delayed) incisions (odds ratio 0.65; 95% confidence interval 0.23 to 1.88). The authors concluded that in women with antepartum HELLP syndrome delivered by cesarean section the frequency of wound complications is not influenced by the type of skin incision or the time of skin closure (primary or delayed) [49].

**Hepatic manifestations**

The authors reported hepatic imaging findings in selected patients with HELLP syndrome and correlated these findings with the severity of concurrent clinical and laboratory abnormalities [50]. Of the 34 patients evaluated in the
study, 16 patients (47%) had abnormal hepatic imaging results. The most common CT abnormalities were subcapsular hematoma of the liver (n = 13) and intraparenchymal hemorrhage (n = 6). An MRI of an unruptured subcapsular hematoma of the liver is depicted in Fig. 3. Comparison of the clinical characteristics and laboratory evaluations of patients with normal and abnormal hepatic imaging findings demonstrated a significant difference in platelet count nadir between the patients with normal and abnormal imaging findings but failed to show any statistically significant difference in gestational age, mean arterial pressure, or the other laboratory parameters studied. Of the 13 patients with severe thrombocytopenia (platelet count ≤ 20,000/mm³), 10 (77%) had abnormal hepatic imaging findings. A separate statistical analysis for patients with and without a subcapsular hematoma of the liver failed to demonstrate any statistical difference for gestational age, mean arterial pressure, or the other laboratory parameters. Emergency intervention was needed for six patients on the basis of these imaging findings. CT and MRI have excellent sensitivity for detecting acute liver hemorrhage, but because CT was more available, faster, and safer for potentially unstable patients, it was the imaging modality of choice.

The differential diagnosis of an unruptured subcapsular hematoma of the liver in pregnancy should include AFLP, abruptio placentae with disseminated intravascular coagulation, ruptured uterus, acute cholecystitis with sepsis, and TTP. Most patients with a subcapsular hematoma of the liver are seen in the late-second or third trimester of pregnancy, although cases have been reported in the immediate postpartum period. In addition to the signs and symptoms of pre-eclampsia, physical examination findings consistent with peritoneal irritation
and hepatomegaly may be present. Stimulation of the phrenic nerve at the diaphragm can produce referred pain along this nerve’s distribution to its origin in the C4-C5 cervical plexus, including the pericardium, peritoneum, pleura, and shoulder. Because the gall bladder and esophagus share innervation by the phrenic nerve with the diaphragm, irritation of the diaphragm may produce sensations of pain in these organs.

Surgical repair has been recommended for hepatic hemorrhage without liver rupture. More recent experience suggests, however, that this complication can be managed conservatively in patients who remain hemodynamically stable [51,52]. Management should include close monitoring of hemodynamics and coagulation status. Serial assessment of the subcapsular hematoma with ultrasound or CT is necessary, with immediate intervention for rupture or worsening of maternal status. In this conservative management, it is important to avoid exogenous sources of trauma to the liver such as abdominal palpation, convulsions, or emesis and to use care in transportation of the patient. Indeed, any sudden increase in intra-abdominal pressure could lead to rupture of the subcapsular hematoma [53].

Rupture of a subcapsular hematoma of the liver is a life-threatening complication of HELLP syndrome. In most instances, rupture involves the right lobe and is preceded by the development of a parenchymal hematoma. Patients frequently present with shoulder pain, shock, evidence of massive ascites, respiratory difficulty, or pleural effusions, or a dead fetus. An ultrasound or CT of the liver should be performed to rule out the presence of subcapsular hematoma of the liver and assess for the presence of intraperitoneal bleeding. Paracentesis confirms the presence of intraperitoneal hemorrhage suspected on the basis of examination or radiographic imaging.

Ruptured subcapsular liver hematoma resulting in shock is a surgical emergency requiring acute multidisciplinary treatment. Resuscitation should consist of massive transfusions of blood, correction of coagulopathy with fresh frozen plasma and platelets, and immediate laparotomy. Options at laparotomy include packing and drainage (preferred), surgical ligation of the hemorrhaging hepatic segments, embolization of the hepatic artery to the involved liver segment, and loosely suturing omentum or surgical mesh to the liver to improve integrity. Even with appropriate treatment, maternal and fetal mortality is over 50%. Mortality is most commonly associated with exsanguination and coagulopathy. Initial survivors are at increased risk for developing adult respiratory distress syndrome, pulmonary edema [54], and acute renal failure in the postoperative period [55,56].

Smith et al [57] reviewed their management of seven patients with spontaneous rupture of the liver occurring during pregnancy. Of the four survivors, the mean gestational age was 32.8 weeks and the mean duration of hospitalization was 16 days. All the survivors were managed with packing and drainage of the liver, whereas the three patients treated with hepatic lobectomy died. The authors also extracted 28 cases reported since 1976 from the literature. From a total of 35 cases analyzed, the overall survival rate for the 27 cases managed by packing and drainage was 82%, whereas only 25% of eight patients undergoing hepatic
lobectomy survived. The authors emphasized that hepatic hemorrhage with persistent hypotension unresponsive to transfusion of blood products may be managed surgically with laparotomy, evacuation of the hematoma, packing of the damaged liver, and draining of the operative site. In certain cases where the patient is stable enough to undergo angiography, transcatheter embolotherapy is a reasonable alternative to surgery [58].

In a review of 442 cases of HELLP syndrome managed at the University of Tennessee, Memphis, four patients were complicated by a ruptured subcapsular hematoma [59]. Three cases required transfusion of 22 to 40 units of packed

---

### Box 4. Management of patients with documented subcapsular hematoma of the liver

**General considerations:**

I. Have the blood bank aware of the potential need for large amounts of packed red blood cells, fresh frozen plasma, and platelet concentrate (ie, 30 units of blood, 20 units of fresh frozen plasma, 30–50 units of platelets).

II. Consult a general or vascular surgeon.

III. Avoid direct and indirect manipulation of the liver.

IV. Closely monitor hemodynamic status.

V. Administer intravenous magnesium sulfate to prevent seizures.

*If the hematoma is unruptured:*

I. Manage conservatively with serial CT scans or ultrasound.

*If the hematoma is ruptured:*

I. Massive transfusions

II. Immediate laparotomy

   A. If bleeding is minimal:
      1. Observe.
      2. Drain area with closed suction.

   B. If bleeding is severe:
      1. Apply laparotomy sponges as packs for pressure.
      2. Embolize the hepatic artery to the involved liver segment.
      3. Surgically ligate hemorrhaging hepatic segment.
      4. Loosely suture omentum or surgical mesh to the liver to improve integrity.
red blood cells and multiple units of platelets and fresh frozen plasma. Two of these three cases were complicated by pulmonary edema and acute renal failure, but all survived without any residual deficiency. The fourth case was a patient who presented in profound shock and with disseminated intravascular coagulopathy. This patient subsequently died secondary to a ruptured pulmonary emphysematous bleb during management of adult respiratory distress syndrome [59].

On the basis of their experience and review of the literature, the authors have developed an algorithm for the management of hepatic complications of HELLP syndrome (Box 4). This algorithm emphasizes the potential for transfusion of large amounts of blood and blood products and the need for aggressive intervention if rupture of the hematoma is suspected. The authors recommend that 30 units of packed red blood cells, 20 units of fresh frozen plasma, 30 to 50 units of platelets, and 20 to 30 units of cryoprecipitate be available when rupture of a subcapsular hematoma is suspected. Their experience is in agreement with the recent observations of Smith et al [57] to the effect that a stable patient with an unruptured subcapsular hematoma should be conservatively managed. Monitoring must be constant during this management, however, because patients can rapidly become unstable after rupture of the hematoma. Survival is associated with rapid diagnosis and immediate medical or surgical stabilization. Coagulopathy must be aggressively managed, because failure to do so is associated with an increased incidence of renal failure. In addition, these patients should be managed in an ICU facility with close monitoring of hemodynamic parameters and fluid status to avert potential pulmonary edema or respiratory compromise.

Postpartum follow-up for patients with subcapsular hematoma of the liver should include serial CT, MRI, or ultrasonography until the defect resolves. For patients receiving numerous transfusions, the hepatitis and HIV status and isoantibody development should be assessed. Although the data on subsequent pregnancy outcome after a subcapsular hematoma of the liver in pregnancy are limited, the authors have managed two such patients who have had subsequent normal maternal and fetal outcomes.

Postpartum management

The HELLP syndrome may develop ante partum or post partum. An analysis of 442 cases by Sibai et al [59] revealed that 309 (70%) had evidence of the syndrome ante partum, and 133 (30%) developed the manifestations post partum. Four maternal deaths occurred, and morbidity was frequent (Table 6). In the postpartum period, the time of onset of the manifestations ranged from a few hours to 7 days, with most developing within 48 hours post partum. Patients in this group are at increased risk for the development of pulmonary edema with acute renal failure [54,55]. Management is similar to that of the antepartum patient with HELLP syndrome, including the need for antiseizure prophylaxis (Fig. 4). Hypertension control may be more aggressive, however, because there is
no longer concern about compromising the uteroplacental circulation in the postpartum patient. Blood pressure goals of systolic blood pressure less than 155 mm Hg or diastolic blood pressure less than 105 mm Hg are suggested. The differential diagnosis in these cases should include TTP, HUS, and exacerbation of systemic lupus.

Table 6
Serious maternal complications in 442 patients with HELLP syndrome

<table>
<thead>
<tr>
<th>Complication</th>
<th>No.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disseminated intravascular coagulopathy</td>
<td>92</td>
<td>21</td>
</tr>
<tr>
<td>Abruptio placentae</td>
<td>69</td>
<td>16</td>
</tr>
<tr>
<td>Acute renal failure</td>
<td>33</td>
<td>8</td>
</tr>
<tr>
<td>Severe ascites</td>
<td>32</td>
<td>8</td>
</tr>
<tr>
<td>Pulmonary edema</td>
<td>26</td>
<td>6</td>
</tr>
<tr>
<td>Pleural effusions</td>
<td>26</td>
<td>6</td>
</tr>
<tr>
<td>Cerebral edema</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>Retinal detachment</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>Laryngeal edema</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>Subcapsular liver hematoma</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>Acute respiratory distress syndrome</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Death, maternal</td>
<td>4</td>
<td>1</td>
</tr>
</tbody>
</table>


Fig. 4. Algorithm for postpartum HELLP syndrome. APLS, antiphospholipid syndrome; DBP, diastolic blood pressure; SLE, systemic lupus erythematosus; SBP, systolic blood pressure.
Following delivery, the patient should be monitored closely in an intensive care facility for at least 48 hours. Most patients show evidence of resolution of the disease process within 48 hours after delivery. Some patients, especially those with DIC, may demonstrate delayed resolution or even deterioration. Such patients may require intensive monitoring for several days. They are at risk for development of pulmonary edema from transfusions of blood and blood products, fluid mobilization, and compromised renal function [55]. In a retrospective study, Martin et al [22] reported the puerperal courses of 43 women with postpartum HELLP syndrome who were treated with dexamethasone and compared them with 237 similar patients who did not receive corticosteroids. Dexamethasone 10 mg IV at 12-hour intervals was given until disease remission was noted in the treated patients, at which time up to two additional 5-mg IV doses were given at 12-hour intervals. Patients who received dexamethasone for post partum–onset HELLP syndrome experienced a shorter disease course, faster recovery, less morbidity, and less need for other interventionist therapy than patients with HELLP syndrome who did not receive dexamethasone [22].

Postpartum patients with delayed resolution of HELLP syndrome (including persistent severe thrombocytopenia) represent a management dilemma. Exchange plasmapheresis with fresh frozen plasma has been advocated as a treatment by some authors [26,60,61]. Because the majority of these patients will have spontaneous resolution of their disease, early initiation of plasmapheresis may result in unnecessary treatment. Schwartz [61] suggested that serial studies indicating a progressive elevation of bilirubin or creatinine associated with hemolysis and thrombocytopenia be considered an indication for plasmapheresis. Martin et al [26] reported the use of plasma exchange with fresh frozen plasma in seven women in the postpartum period with HELLP syndrome that persisted for more than 72 hours following delivery. All patients had persistent thrombocytopenia, rising LDH, and evidence of multiorgan dysfunction. Sustained increases in mean platelet count and reduction in LDH concentrations were associated with plasma exchange. The authors recommended that a trial of plasma exchange with fresh frozen plasma be considered in HELLP syndrome that persists for more than 72 hours after delivery and in which there is evidence of a life-threatening microangiopathy.

Since that publication, however, this group has reviewed 18 patients with HELLP syndrome who were treated at its institution post partum with single or multiple plasma exchange with fresh frozen plasma [60]. Patients were entered into the clinical trial either because of persistent evidence of atypical pre-eclampsia/eclampsia as HELLP syndrome more than 72 hours after delivery (group 1) or because of evidence of worsening HELLP syndrome at any time post partum in association with single or multiple organ injury (group 2). In the absence of other disease conditions, the nine patients in group 1 with persistent postpartum HELLP syndrome complicated only by severe clinical expressions of pre-eclampsia/eclampsia responded rapidly to one or two plasma exchange procedures with few complications and no maternal deaths. By contrast, the nine patients of group 2 with HELLP syndrome presentations complicated by other
organ disease had variable responses to plasma exchange, and there were two deaths in this group. This current series of patients details the successful postpartum application of plasma exchange therapy for unremitting HELLP syndrome, but it reveals that a uniformly positive response to this therapy will not be observed where there is additional single or multiple organ injury [60]. Potential adverse effects of this plasma exchange include plasma-transmitted infections, anaphylaxis, volume overload, sepsis, and maternal death.

Maternal counseling

Pregnancies complicated by HELLP syndrome may be associated with life-threatening complications for both the mother and her infant. Therefore, clinicians should be able to answer questions about subsequent pregnancy outcome and long-term prognosis. Women with a history of HELLP syndrome are at increased risk for all forms of pre-eclampsia in subsequent pregnancies (Table 7). In general, the rate of pre-eclampsia in subsequent pregnancies is approximately 20%, with significantly higher rates if the onset of HELLP syndrome was in the second trimester. The rate of recurrent HELLP syndrome ranges from 2% to 19%. The authors’ policy is to quote these women a recurrence risk of less than 5% [62–64]. Because of the above risks, these women are informed that they are at increased risk for adverse pregnancy outcome (preterm delivery, fetal growth restriction, abruptio placentae, and fetal death) in subsequent pregnancies. They require close monitoring during subsequent gestations.

Currently there is no preventive therapy for recurrent HELLP syndrome. Liver function tests were studied in 54 women at a median of 31 months (range: 3 to 101 months) after pregnancies complicated by HELLP syndrome [65]. Serum levels of AST, LDH, and conjugated bilirubin were found to be normal. However, total bilirubin levels were elevated in 11 (20%) of the studied women. The authors of this report suggested that a dysfunction of the bilirubin-conjugating mechanism represents a risk factor for the development of this syndrome [65].

Two reports describe long-term renal function after HELLP syndrome [55,66]. One of the reports included 23 patients whose pregnancies were complicated by HELLP syndrome and acute renal failure: eight of these women had 11 sub-

<table>
<thead>
<tr>
<th>Table 7</th>
<th>Pregnancy outcome after HELLP: normotensive women</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. of women</td>
</tr>
<tr>
<td>Sibai et al [62]</td>
<td>139</td>
</tr>
<tr>
<td>Sullivan et al [25]</td>
<td>122</td>
</tr>
<tr>
<td>van Pampus et al [63]</td>
<td>77</td>
</tr>
<tr>
<td>Chames et al [64]a</td>
<td>40</td>
</tr>
</tbody>
</table>

*a HELLP ≤28 wks in previous pregnancy.  
Adapted from Sibai BM. Diagnosis, controversies, and management of the syndrome of hemolysis, elevated liver enzymes, and low platelet count. Obstet Gynecol 2004;103:988; with permission.
sequent pregnancies, with nine resulting in term gestation [55]. All 23 women also had normal blood pressure and renal function at an average follow-up of 4.6 years (range: 0.5 to 11 years). The other study compared renal function at least 5 years after HELLP syndrome in 10 patients with the respective findings in 22 patients with previous normotensive gestation [66]. No differences in renal function tests were found between the two groups. These findings suggest that the development of HELLP syndrome with or without renal failure does not affect long-term renal function.

Summary

Pregnancies complicated by HELLP syndrome require a well-formulated management plan. The development of this syndrome after 34 weeks’ gestation or with documentation of maternal or fetal compromise is an indication for delivery. Vaginal delivery can be accomplished in most cases; however, if cesarean section is required, subfascial drains and preoperative platelet transfusion for platelet counts of less than 40,000/mm$^3$ can reduce the incidence of complications. AFLP, TTP, or HUS may present with signs, symptoms, and laboratory abnormalities that may be confused with HELLP syndrome. Thorough investigation is warranted because of the differences in proper management among these various complications of pregnancy. It is advisable that patients with complications of HELLP syndrome, such as pulmonary edema, acute renal failure, liver rupture, or extreme prematurity, be referred to a tertiary care center where maternal and neonatal facilities are available. Expectant management in patients with HELLP syndrome remote from term and the use of corticosteroids to improve postpartum maternal outcome remain experimental.

References


