Baha M. Sibai, MD
Professor and Chairman
Department of Obstetrics
and Gynecology
University of Cincinnati College
of Medicine

A practical plan to detect and manage HELLP syndrome

How to minimize the risk of serious morbidity, including tips on distinguishing HELLP from other conditions, stabilizing the patient, and managing labor, delivery, and the postpartum period.

Here's a disturbing fact: If it looks like HELLP syndrome, and impairs the patient like HELLP syndrome, it isn't necessarily HELLP syndrome. A plethora of diagnostic criteria from different investigators over the years has confused the issue of what constitutes this syndrome—not to mention how to manage it.

A management issue has also attracted recent attention: use of corticosteroids either antepartum to enhance maternal status so that epidural anesthesia can be administered, or postpartum to improve platelets. Such improvements are only transient, however, and we lack definitive data on the benefits.

One thing is certain, however. The combination of hemolysis, liver dysfunction or injury, and platelet consumption in women with preeclampsia makes adverse maternal and perinatal outcomes more likely and leaves no room for expectant management.

HELLP syndrome also has become a major issue in litigation against obstetricians and medical and surgical consultants. Lawsuits usually allege misdiagnosed preeclampsia, delayed delivery, or improper recognition and management of complications.

Pinning HELLP down

One of the best tools to identify HELLP syndrome is a healthy dose of suspicion, since it can affect any pregnant woman at any time: antepartum, intrapartum, or within 1 week postpartum. Approximately 72% of cases are diagnosed before delivery, and the rest are diagnosed during the first week postpartum.

Weinstein noted that the signs and symptoms of HELLP syndrome can occur without clinical evidence of severe preeclampsia (severe hypertension and/or severe proteinuria). Indeed, he reported that hypertension can be mild or absent in most patients with HELLP, and proteinuria can be mild.

Weinstein coined the term HELLP syndrome in 1982 to describe these abnormalities in women with preeclampsia:

H = hemolysis
EL = elevated liver enzymes
LP = low platelets

Another obstacle to early detection: Patients may have nonspecific signs and symptoms, none of which are diagnostic of classical preeclampsia.

However, HELLP syndrome is most common in women who have already been diagnosed with gestational hypertension and/or preeclampsia.

CONTINUED

TABLE 1

Hallmarks of HELLP: Hemolysis, elevated liver enzymes, and low platelets

Hemolysis

Diagnosis requires at least 2 of the following:

- Abnormal peripheral smear (schistocytes, burr cells)
- Elevated serum bilirubin (≥1.2 mg/dL)
- Low serum haptoglobin
- Significant drop in hemoglobin levels, unrelated to blood loss

Elevated liver enzymes

- Aspartate aminotransferase or alanine aminotransferase at least twice the upper level of normal
- Lactate dehydrogenase at least twice the upper level of normal. This value is also elevated in severe hemolysis

Low platelets

- <100,000/mm^3

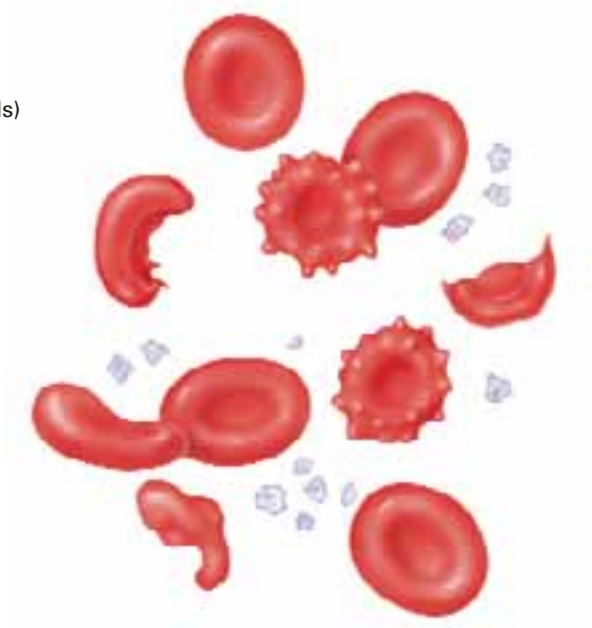


IMAGE: MAURA FLYNN

HELLP is more likely with severe hypertension

Overall, the incidence of HELLP syndrome in women with gestational hypertension/preeclampsia increases with the severity of the condition. HELLP syndrome also is more likely in women with early-onset hypertension/preeclampsia (before 34 weeks' gestation).

Making the diagnosis

HELLP syndrome is diagnosed when all 3 of the following are present:

- **Hemolysis,** defined as the presence of microangiopathic hemolytic anemia. This is the hallmark of the triad.
- **Elevated liver enzymes** (either aspartate aminotransferase [AST] or alanine aminotransferase [ALT]). This component signifies liver cell ischemia and/or necrosis.
- **Low platelet count** (<100,000/mm^3). **TABLE 1** summarizes the laboratory criteria for the diagnosis.

When to begin testing

In women with new-onset hypertension, order a complete blood count with platelets and liver enzyme analysis at the time of diagnosis and serially thereafter. The frequency of these tests depends on the initial test results, severity of disease, and onset of symptoms.

In women without hypertension, I recommend obtaining the same blood tests at the onset of any of the signs and symptoms listed in **TABLE 2**.

Assessing test results

Clinicians should be familiar with the upper limit for liver-enzyme tests in their laboratory. I suggest a cutoff more than twice the upper limit for a particular test.

Also keep in mind that these parameters are dynamic; some women will meet only some of the criteria early in the disease process. Moreover, maternal complications are substantially higher when all 3 components are present than when only 1 or 2 are present.

Look for these clinical findings

Hypertension. Most women with HELLP

FAST TRACK

HELLP syndrome is more likely when hypertension or preeclampsia is diagnosed before 34 weeks

TABLE 2

Conditions that heighten the risk of HELLP

- Preeclampsia-eclampsia
  - Early onset
  - During expectant management
- Severe gestational hypertension
- Early-onset hypertension, or severe intrauterine growth restriction
- Thrombophilias
- Abruptio placentae
- Nonspecific viral-syndrome-like symptoms
- Right upper quadrant, epigastric, or retrosternal pain
- Persistent nausea or vomiting in third trimester
- Bleeding from mucosal surfaces
- Unexplained hematuria or proteinuria
- Petechial hemorrhages or ecchymosis

TABLE 3

Signs and symptoms

CONDITION	FREQUENCY (%)
Hypertension	85
Proteinuria	87
Right upper quadrant or epigastric pain	40–90
Nausea or vomiting	29–84
Headaches	33–60
Visual changes	10–20
Mucosal bleeding	10
Jaundice	5

FAST TRACK

HELLP syndrome sometimes appears for the first time postpartum in women who had no evidence of preeclampsia before or during labor

syndrome have hypertension. In 15% to 50% of cases, the hypertension is mild, but it may be absent in 15%.

Proteinuria. Most patients also have proteinuria by dipstick (≥1+). Proteinuria may be absent in approximately 13% of women with HELLP syndrome, although they will likely have many of the symptoms reported by women with severe preeclampsia.

TABLE 3 lists the signs and symptoms to be expected in these patients, along with their frequency.

The usual times of onset

Antepartum cases. As was previously noted, HELLP syndrome usually develops before delivery, with the most frequent onset being before 37 weeks' gestation **(TABLE 4).**

In the postpartum period, most cases develop within 48 hours after delivery. Of these, approximately 90% occur in women who had antepartum preeclampsia that progressed to HELLP syndrome in the postpartum period. However, approximately 20% of postpartum cases develop more than 48 hours after delivery.

Another important point: HELLP syndrome can develop for the first time postpartum in women who had no evidence of preeclampsia before or during labor. Thus, it is important to educate all postpartum women to report new symptoms (listed in **TABLE 3**) as soon as possible. When these symptoms develop, evaluate the patient for both preeclampsia and HELLP syndrome.

Risk for life-threatening maternal complications

When all components of HELLP syndrome are present in a woman with preeclampsia, the risk of maternal death and serious maternal morbidities increases substantially (**TABLE 5**). The rate of these complications depends on gestational age at onset, presence of associated obstetric complications (eclampsia, abruptio placentae, peripartum hemorrhage, or fetal demise) or preexisting conditions (lupus, renal disease, chronic hypertension, or type 1 diabetes).

Abruptio placentae increases the risk of disseminated intravascular coagulopathy (DIC), as well as the need for blood transfusions.

Marked ascites (>1 L) leads to higher rates of cardiopulmonary complications.

Differential diagnosis

When diagnosing HELLP syndrome, confirm or exclude the conditions listed in **TABLE 6**, since the presenting symptoms and clinical and laboratory findings in women with HELLP syndrome overlap those of several microangiopathic disor-

TABLE 4

Usual times of onset*

RELATION TO DELIVERY	PERCENTAGE
Antepartum	72
Postpartum	28
≤48 hours	80
>48 hours	20
GESTATIONAL AGE (WEEKS)	**PERCENTAGE**
17–20	2
21–27	10
28–36	68
>37	20

* Based on 700 cases

TABLE 5

Maternal complications

COMPLICATION	FREQUENCY (%)
Death	1
Adult respiratory distress syndrome	1
Laryngeal edema	1–2
Liver failure or hemorrhage	1–2
Acute renal failure	5–8
Pulmonary edema	6–8
Pleural effusions	6–10
Abruptio placentae	10–15
Disseminated intravascular coagulopathy	10–15
Marked ascites	10–15

FAST TRACK

In women with true HELLP, delivery can only be delayed for up to 48 hours for corticosteroid administration—and then only if both mother and fetus are stable

ders that can develop during pregnancy and/or postpartum. In some women, preeclampsia may be superimposed on one of these disorders, further confounding an already difficult differential diagnosis.

Because of the remarkably similar clinical and laboratory findings of these diseases, make every effort to achieve an accurate diagnosis, since management and outcomes may differ among these conditions.

Initial management

Hospitalize the patient

Because HELLP syndrome usually is characterized by progressive and sometimes sudden deterioration in maternal and fetal conditions, patients should be hospitalized and observed in a labor and delivery unit.

Initially, assume the patient has severe preeclampsia and treat her with intravenous magnesium sulfate to prevent convulsions and antihypertensive medications as needed to keep systolic blood pressure below 160 mm Hg and diastolic blood pressure below 105 mm Hg.

Blood tests should include:

- complete blood count with platelet count,
- peripheral smear evaluation,
- serum AST,
- lactate dehydrogenase,
- creatinine,
- bilirubin, and
- coagulation studies.

These tests help confirm the diagnosis and check for the presence of DIC, massive hemolysis, severe anemia, or renal failure.

The first priority is to assess the patient for the presence of cardiovascular complications, signs of liver hematoma or hemorrhage, and abruptio placentae. If any is present—particularly hypotension, hypovolemia, DIC, or pulmonary edema—make every effort to stabilize the maternal condition.

Can delivery wait 48 hours for corticosteroids?

Evaluate fetal status by heart rate monitoring or biophysical profile, and confirm gestational age. Then decide whether delivery is indicated or can be delayed for 48 hours so that corticosteroids can be given.

No room for expectant management. Do not consider expectant management in women with true HELLP syndrome. Delivery can only be delayed for a maximum of 48 hours—and only when both mother and fetus are stable, at 24 to 34 weeks' gestation, and awaiting the benefit of corticosteroids.

Corticosteroid dosing. My practice is to give 2 doses of either betamethasone 12 mg intramuscularly every 12 hours or dexamethasone 12 mg intravenously every 12 hours. This is to improve maternal status, at least temporarily.

Initiate delivery within 24 hours after the last steroid dose, with continuous monitoring in the labor and delivery unit.

CONTINUED

Although some women may demonstrate transient improvement in their blood tests (eg, increased platelet count or decreased AST levels), delivery is still indicated. Conversely, in some cases, maternal and fetal conditions may deteriorate, mandating delivery before the 2 doses of steroids are completed.

Delivery considerations

HELLP syndrome does not justify immediate cesarean

Patients with HELLP syndrome in labor or with rupture of membranes can deliver vaginally in the absence of obstetric complications. In addition, induction or augmentation of labor is acceptable with either oxytocin infusion or prostaglandins if the fetal gestational age is 32 weeks or more and the cervical Bishop score exceeds 5.

TABLE 7 lists the indications for elective cesarean delivery and summarizes management during surgery. It is important to stabilize the maternal condition, correct coagulopathy, and have blood or blood products available before initiating surgery.

Watch for oozing from surgical sites

In a cesarean section, generalized oozing from the surgical site can occur during the operation or immediately postpartum because of the continued drop in platelet count in some of these patients. Thus, it is advisable to insert a subfascial drain and to leave the skin incision open for at least 48 hours to avoid hematoma formation in these areas **(FIGURE 1)**.

Small doses of systemic opioids are best

For maternal analgesia during labor, give small, intermittent doses of systemic opioids. For repair of episiotomy or vulvar or vaginal lacerations, use local infiltration anesthesia.

Avoid pudendal block because of the potential for bleeding and hematoma formation in this area. Epidural anesthesia may be used after consultation with the anesthesiologist if the platelet count exceeds 75,000/mm^3.

Some authors report rising platelet counts after intravenous dexamethasone and, with the improved platelets, greater use of epidural anesthesia, especially in women who achieved a 24-hour latency period before delivery. However, since the platelet

TABLE 6

Differential diagnosis

- Acute fatty liver of pregnancy
- Acute pancreatitis
- Antiphospholipid syndrome
- Cholecystitis
- Disseminated herpes simplex
- Fulminant viral hepatitis
- Hemolytic uremic syndrome
- Hemorrhagic or septic shock
- Immune thrombocytopenic purpura
- Stroke
- Systemic lupus erythematosus
- Thrombotic thrombocytopenic purpura

TABLE 7

Cesarean delivery: Indications and management

Indications for cesarean

- Nonreassuring fetal status
- Abnormal fetal presentation
- <30 weeks' gestation and Bishop score <5
- <32 weeks' gestation with intrauterine growth restriction or oligohydramnios and Bishop score <5
- Known subcapsular liver hematoma
- Suspected abruptio placentae

Management during cesarean

- General anesthesia for platelet count <75,000/mm^3
- Transfuse 6 units of platelets if count <40,000/mm^3
- Insert subfascial drain
- Secondary skin closure or leave subcutaneous drain
- Observe for bleeding from upper abdomen prior to closure

FAST TRACK

Avoid pudendal block because of the risk for bleeding and hematoma formation in this area

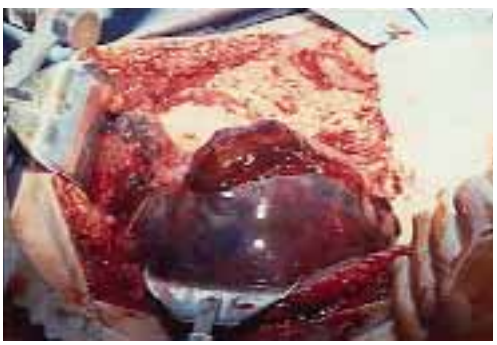
FIGURE 1

Insert subfascial drain at cesarean section

Because generalized oozing from the surgical site can occur intraoperatively or immediately postpartum, insert a subfascial drain and leave the skin incision open for at least 48 hours to avoid hematoma formation.

FIGURE 2

Rare but life-threatening: Subcapsular liver hematoma



Liver hematomas can develop antepartum, intrapartum, or postpartum. Presenting symptoms may include severe epigastric or retrosternal pain in association with respiratory difficulty (pain on inspiration), with or without shoulder or neck pain.

FAST TRACK

Profound hypovolemic shock in a previously hypertensive patient may be a sign of rupture of a liver hematoma

count may drop again, insert the epidural catheter once the desired platelet level (with anesthesiologist approval) is reached.

Suspected liver hematoma

A rare and potentially life-threatening complication of HELLP syndrome is subcapsular liver hematoma **(FIGURE 2)**. Unfortunately, the rarity of this complication sometimes causes it to be overlooked.

Early signs and symptoms

Liver hematomas can develop antepartum, during labor, or in the postpartum period. Presenting symptoms may include severe epigastric or retrosternal pain in association with breathing difficulty (pain on inspiration), with or without shoulder or neck pain.

When profound hypovolemic shock occurs in a previously hypertensive patient, suspect rupture of a liver hematoma. Diagnosis can be made by ultrasound or computed tomography (CT) imaging of the liver, both of which can also confirm intraperitoneal bleeding.

In most cases, rupture involves the right lobe of the liver and is preceded by a parenchymal liver hematoma.

Mortality can exceed 50%

Maternal and fetal mortality increase substantially when a subcapsular liver hematoma is present. In fact, mortality may exceed 50% when frank rupture of the capsule involves liver tissue.

Choose conservative management whenever possible

Management of subcapsular liver hematoma depends on maternal hemodynamic status, integrity of the capsule (ruptured or intact), and the fetal condition.

Conservative management is preferable in hemodynamically stable women with an unruptured hematoma. It consists of close monitoring of the patient's hemodynamic and coagulation status and serial assessment of the hematoma with ultrasound or CT scan.

Avoid exogenous trauma to the liver, such as frequent abdominal palpation, emesis, or convulsions. Any sudden increase in intraabdominal pressure can led to rupture of the hematoma.

When rupture occurs

This surgical emergency requires an acute multidisciplinary team, including an Ob/Gyn, anesthesiologist, highly qualified surgeon, and a representative of the hospital's blood bank.

CONTINUED

Maternal resuscitation should include:

- transfusion of packed red blood cells to maintain blood pressure and tissue perfusion,
- correction of coagulopathy with fresh frozen plasma and platelets, and
- laparotomy, preferably using a cell saver.

Options at laparotomy include:

- packing and drainage (preferred),
- ligation of the hepatic lacerations,
- embolization of the hepatic artery to the affected liver segment, and
- loosely suturing omentum or surgical mesh to the liver surface.

Postpartum care

In women who develop HELLP prior to delivery, closely monitor postpartum vital signs, intake and output, and symptoms in intensive care or a similar facility for at least 48 hours.

During this time, my practice is to give the patient intravenous magnesium sulfate and antihypertensive medications as needed to keep systolic blood pressure below 155 mm Hg (the standard is 160 mm Hg) and diastolic blood pressure below 105 mm Hg.

The rationale for this treatment is to prevent bleeding in the brain if the woman has thrombocytopenia.

When HELLP appears in the postpartum period

Several maternal complications from HELLP syndrome may not appear until immediately postpartum. Thus, all women with preeclampsia require close monitoring of vital signs, fluid intake and output, laboratory values, and pulse oximetry for at least 48 hours.

Also continue magnesium sulfate in the postpartum period and keep maternal blood pressure below 155 mm Hg systolic and 105 mm Hg diastolic.

Time to recovery

Most patients begin to improve or completely recover within 72 hours, while others deteriorate further or fail to recover for as long as 1 week after delivery. Thus, some women may require intensive monitoring for several days because of the risk of pulmonary edema, renal failure, or adult respiratory distress syndrome.

Keep in mind that, in some of these women, the cause of the postpartum deterioration may be something other than HELLP syndrome **(TABLE 6)**.

Watch for sudden hypotension

A sudden drop in blood pressure to hypotensive levels can be an early sign of severe hemolysis or unrecognized intraperitoneal blood loss (from surgical sites or ruptured liver hematoma), as well as sepsis.

In a woman with severe hemoconcentration (ie, severe vasoconstriction), sudden hypotension also may indicate excessive vasodilation from antihypertensive drugs such as hydralazine or nifedipine, resulting in relative hypovolemia.

Such a case requires volume resuscitation, blood transfusion (if indicated), and evaluation for unrecognized bleeding.

Use of steroids

Some authors recommend giving intravenous dexamethasone (5 to 10 mg every 12 hours) for approximately 48 hours after delivery in women who develop antepartum or postpartum HELLP. They claim this treatment improves maternal blood tests, shortens recovery, and reduces maternal morbidity.

However, at present, no data indicate this approach has clinical benefit—and the risks are unknown. For these reasons, treatment with intravenous dexamethasone after delivery remains empiric. ■

FAST TRACK

A sudden drop in blood pressure to hypotensive levels can signify severe hemolysis, unrecognized intraperitoneal blood loss, or sepsis

BIBLIOGRAPHY

Abramovici D, Friedman SA, Mercer BM, Audibert F, Kao L, Sibai BM. Neonatal outcome in severe preeclampsia at 24 to 36 weeks' gestation. Does HELLP (hemolysis, elevated liver enzymes, and low platelet count) syndrome matter? Am J Obstet Gynecol. 1999;180:221–225.

Audibert F, Friedman SA, Frangieh AY, Sibai BM. Clinical utility of strict diagnostic criteria for the HELLP (hemolysis,

elevated liver enzymes, and low platelets) syndrome. Am J Obstet Gynecol. 1996;175:460–464.

Egerman RS, Sibai BM. Recognizing and managing HELLP syndrome and its imitators. Contemporary Ob/Gyn. 1997; (October):129–149.

Magann EF, Perry KG Jr, Meydrech EF, Harris RL, Chauchan SP, Martin JN Jr. Postpartum corticosteroids: accelerated recovery from the syndrome of hemolysis, elevated liver enzymes, and low platelets (HELLP). Am J Obstet Gynecol. 1994;171:1154–1158.

Martin Jr JN, Thigsen BD, Rose CH, et al. Maternal benefit of high-dose intravenous corticosteroid therapy for HELLP. Am J Obstet Gynecol. 2003;189:830–834.

O'Brien JM, Milligan DA, Barton JR. Impact of high-dose corticosteroid therapy for patients with HELLP (hemolysis, elevated liver enzymes, and low platelet count) syndrome. Am J Obstet Gynecol. 2000;183:921–924.

O'Brien JM, Shumate SA, Satchwell SL, Milligan DA, Barton JR. Maternal benefit to corticosteroid therapy in patients with HELLP (hemolysis, elevated liver enzymes, and low platelets) syndrome: impact on the rate of regional anesthesia. Am J Obstet Gynecol. 2002;186:475–479.

Rinehart BK, Terrone DA, Magann EF, Martin RW, May WL, Martin JN Jr. Preeclampsia-associated hepatic hemorrhage and rupture: mode of management related to maternal and perinatal outcome. Obstet Gynecol Surv. 1999;196–202.

Sibai BM, Ramadan MK, Usta I, Salama M, Mercer BM, Friedman SA. Maternal morbidity and mortality in 442 pregnancies with hemolysis, elevated liver enzymes, and low platelets (HELLP syndrome). Am J Obstet Gynecol. 1993;169:1000–1006.

Sibai BM. The HELLP syndrome (hemolysis, elevated liver enzymes, and low platelets): much ado about nothing? Am J Obstet Gynecol. 1990;162:311–316.

Sibai BM. Diagnosis, controversies, and management of HELLP syndrome. Obstet Gynecol. 2004;103:981–991.

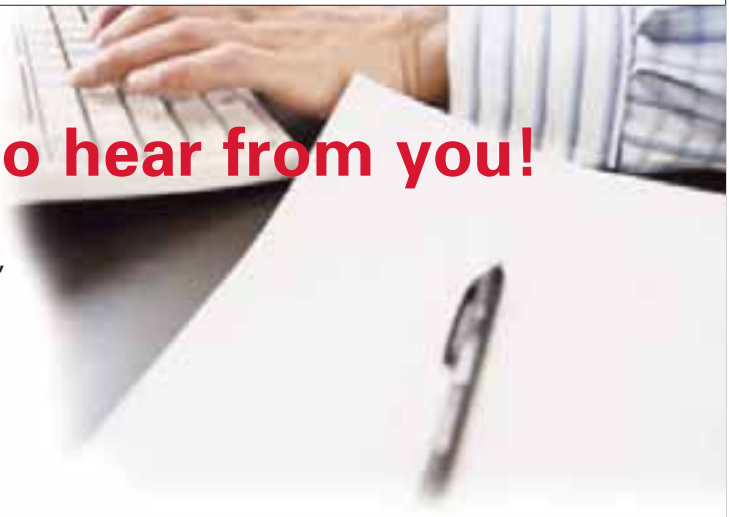
Tompkins MJ, Thiagarajah S. HELLP (hemolysis, elevated liver enzymes, and low platelet count) syndrome: the benefit of corticosteroids. Am J Obstet Gynecol. 1999; 181:304–309.

VanPampus MG, Wolf H, et al. Maternal and perinatal outcome after expectant management of the HELLP syndrome compared with preeclampsia without HELLP syndrome. Eur J Obstet Gynecol Reprod Biol. 1998;76:31.

Weinstein L. Syndrome of hemolysis, elevated liver enzymes, and low platelet count: A severe consequence of hypertension in pregnancy. Am J Obstet Gynecol. 1982;142:159–167.

Weinstein L. Preeclampsia/eclampsia with hemolysis, elevated liver enzymes and thrombocytopenia. Obstet Gynecol. 1985;66:657–660.

The author reports no financial relationships relevant to this article.



We want to hear from you!

Have a comment on an article, editorial, illustration, or department? Drop us a line and let us know what you think. **You can send letters 1 of 3 ways:**

E-mail:
obg@dowdenhealth.com

Fax: 201-391-2778

Mail: OBG MANAGEMENT
110 Summit Ave
Montvale, NJ 07645

Letters should be addressed to the Editor, OBG MANAGEMENT, and be 200 words or less. They may be edited prior to publication.

Please take a moment to share your opinion!

OBG MANAGEMENT

FAST TRACK

All women with preeclampsia require close monitoring of vital signs, fluid intake and output, lab values, and pulse oximetry for at least 48 hours after delivery