
بسم الله الرحمن الرحیم

Preeclampsia

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INTRODUCTION

- Preeclampsia is a multisystem progressive disorder characterized by the new onset of hypertension and proteinuria or the new onset of hypertension and significant end-organ dysfunction with or without proteinuria in the last half of pregnancy or postpartum

Criteria for the diagnosis of preeclampsia

Systolic blood pressure ≥140 mmHg or diastolic blood pressure ≥90 mmHg on at least 2 occasions at least 4 hours apart after 20 weeks of gestation in a previously normotensive patient AND the new onset of 1 or more of the following*:

- Proteinuria ≥0.3 g in a 24-hour urine specimen or protein/creatinine ratio ≥0.3 (mg/mg) (30 mg/mmol) in a random urine specimen or dipstick ≥2+ if a quantitative measurement is unavailable
- Platelet count <100,000/microL
- Serum creatinine >1.1 mg/dL (97.2 micromol/L) or doubling of the creatinine concentration in the absence of other renal disease
- Liver transaminases at least twice the upper limit of the normal concentrations for the local laboratory
- Pulmonary edema
- New-onset and persistent headache not accounted for by alternative diagnoses and not responding to usual doses of analgesics¶

FINDINGS

- Visual symptoms
- Stroke
- Generalized hyperreflexia
- Seizure
- Oliguria
- Peripheral edema
- Abruptio placentae

Epigastric, upper abdominal, or retrosternal pain

- Epigastric, upper abdominal, or retrosternal **pain** that often begins at night. **Nausea** and **vomiting** sometimes also occur. On examination, the **liver** may be **tender to palpation** due to stretching of Glisson's capsule from hepatic swelling or bleeding.
- **Liver rupture or hemorrhage** is rare but should be suspected when there is sudden onset of right upper quadrant pain associated with a decrease in blood pressure.
- Acute pancreatitis is a rare complication of preeclampsia and can mimic the epigastric pain of preeclampsia

pathophysiology

- The pathophysiology of preeclampsia likely involves both maternal and fetal/placental factors. In a normal pregnancy, the myometrial and decidual vasculature at the placental implantation site remodels such that the terminal part of the spiral arterioles is wide open, resulting in a high-capacity, low-resistance system to provide optimal maternal-fetal nutrient and oxygen exchange. In preeclampsia, however, shallow placentation and failure of the spiral arteries to remodel early in pregnancy, weeks to months before development of clinical manifestations of the disease, results in suboptimal uteroplacental blood flow and relatively hypoxic trophoblast tissue .

pathophysiology

- An exaggerated state of oxidative stress develops in the placenta, which in turn adversely affects villous angiogenesis . As pregnancy advances, the pathologic placenta increasingly secretes antiangiogenic factors into the maternal circulation that bind vascular endothelial growth factor (VEGF) and placental growth factor (PlGF), which results in widespread maternal vascular inflammation, endothelial dysfunction, and vascular injury, leading to hypertension, proteinuria, and the other clinical manifestations of preeclampsia

pathophysiology

- It has been proposed that there are several subtypes of preeclampsia, with a variety of pathophysiological pathways leading to maternal and fetal mortality and morbidity. The most commonly described subtypes of preeclampsia are characterized as early onset (<34 weeks of gestation) and late onset (≥34 weeks of gestation). The clinical features overlap, but the spectrum of disease and outcomes differ:

preeclampsia

- The American College of Cardiology and the American Heart Association have endorsed a lower cutoff point (systolic blood pressure 130 to 139 mmHg or diastolic blood pressure 80 to 89 mmHg) for diagnosing hypertension in nonpregnant patients. Some have suggested that this definition may also be appropriate for pregnant patients. However, it has not been widely studied, would increase the incidence of hypertension in pregnancy by about 10 percent, and would increase potentially unnecessary testing, hospitalization, and intervention in the absence of a proven benefit.

INCIDENCE

- In a systematic review, 4.6 % of pregnancies worldwide were complicated by preeclampsia
- 10% to 15% of direct maternal deaths
- one of the four leading causes of maternal death, along with hemorrhage, cardiovascular conditions, and thromboembolism

Risk factors

Nulliparity
Preeclampsia in a previous pregnancy
Age >40 years or <18 years
Family history of preeclampsia
Chronic hypertension
Chronic renal disease
Autoimmune disease (eg, antiphospholipid syndrome, systemic lupus erythematosus)
Vascular disease
Diabetes mellitus (pregestational and gestational)
Multifetal gestation
Obesity
Black population
Hydrops fetalis
Poorly controlled hyperthyroidism
Woman herself was small for gestational age
Fetal growth restriction, abruptio placentae, or fetal demise in a previous pregnancy
Prolonged interpregnancy interval if the previous pregnancy was normotensive; if the previous pregnancy was preeclamptic, a short interpregnancy interval increases the risk of recurrence
Partner-related factors (new partner, limited sperm exposure [eg, previous use of barrier contraception])
In vitro fertilization
Obstructive sleep apnea
Elevated blood lead level
Posttraumatic stress disorder

the United States Preventive Services Task Force (USPSTF) high-risk criteria, which are also endorsed by the American College of Obstetricians and Gynecologists (ACOG)

- Previous pregnancy with preeclampsia, especially early onset and with an adverse outcome.
- Multifetal gestation.
- Chronic hypertension.
- Type 1 or 2 diabetes mellitus.
- Chronic kidney disease.
- Autoimmune disease with potential vascular complications (antiphospholipid syndrome, systemic lupus erythematosus).

prevention

We generally follow the USPSTF criteria and offer low-dose aspirin for preeclampsia prevention with **two or more of the following moderate risk factors** [20]:

- Nulliparity.
- Obesity (body mass index >30 kg/m^2).
- Family history of preeclampsia in mother or sister.
- Age ≥35 years.
- Sociodemographic characteristics (African American race, low socioeconomic level).
- Personal risk factors (eg, previous pregnancy with LBW or SGA, previous adverse pregnancy outcome [eg, stillbirth], interval >10 years between pregnancies).

prevention

- ACOG and Society for Maternal-Fetal Medicine recommend low-dose aspirin (81 mg/day) in women at high risk of preeclampsia and state it should be initiated between 12 weeks and 28 weeks of gestation (optimally before 16 weeks) and continued daily until delivery. They state low-dose aspirin should be considered for women with more than one of several moderate risk factors for preeclampsia

prevention

- They recommend against its use solely for the indication of a prior unexplained stillbirth, fetal growth restriction, or spontaneous preterm birth in the absence of risk factors for preeclampsia.

- **Use of low-dose** aspirin **for treatment of established preeclampsia**

PATIENT EVALUATION

All pregnant women with new-onset hypertension or worsening hypertension after 20 weeks of gestation should be evaluated for preeclampsia. Women with severe hypertension and/or symptoms suggestive of severe disease require hospitalization for initial maternal and fetal evaluation and management. Asymptomatic women with nonsevere hypertension may be followed closely as outpatients provided they are seen frequently and the maternal and fetal status is stable.

Laboratory tests

- C BC/ platelets
- Cr
- AST, ALT
- U/P
- Coagulation studies (pt, ptt, fib) are not routinely obtained but are indicated in patients with additional complications, such as abruptio placentae, severe bleeding, thrombocytopenia, or severe liver dysfunction.

Potential laboratory findings

- Proteinuria
- Elevated creatinine
- Thrombocytopenia
- Hemolysis
- Hemoconcentration
- Coagulation studies
- Liver chemistries
- Hyperuricemia

Assessment of fetal status

- Fetal status is assessed concurrently with the maternal evaluation or post-diagnosis, depending on the degree of concern when the mother is evaluated. At a minimum, a **NST** or **BPS** is performed, if appropriate for gestational age. **Ultrasound** is indicated to evaluate AF volume and EFW given the increased risk for oligohydramnios and IUGR.

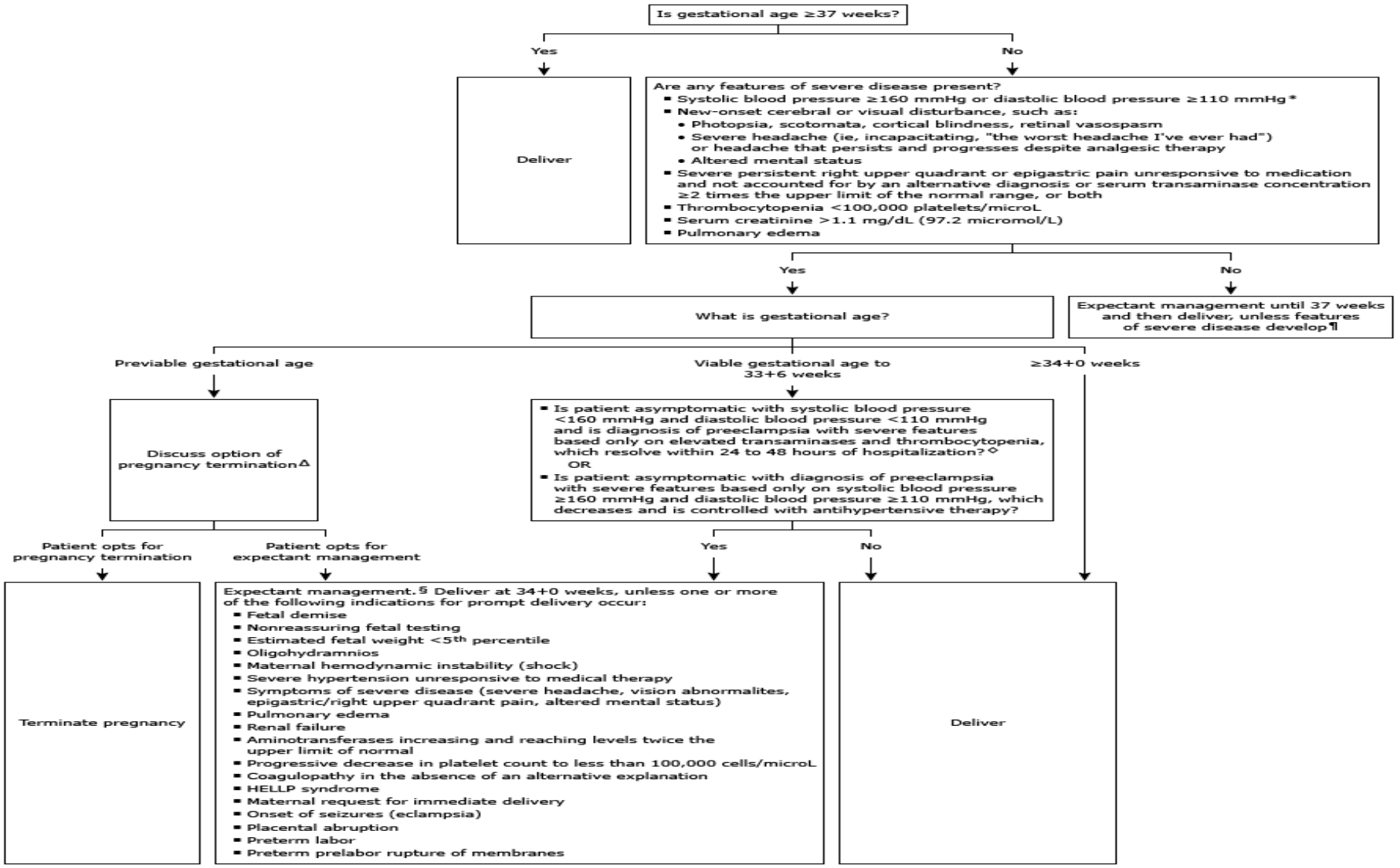
DIFFERENTIAL DIAGNOSIS

- chronic hypertension, chronic renal disease, other medical disorders (pheochromocytoma)
- use/withdrawal of some drugs.
- HELLP syndrome, acute fatty liver of pregnancy (AFLP), thrombotic microangiopathy eg, thrombotic thrombocytopenic purpura [TTP], (SLE), and antiphospholipid syndrome (APS).

Fetal complications

- growth restriction FGR and oligohydramnios
- medically or obstetrically indicated preterm birth
- perinatal morbidity and mortality

Timing of delivery



management

- In most patients, antihypertensive therapy is not indicated for systolic blood pressure <160 mmHg or diastolic blood pressure <110 mmHg.
- For women with a viable fetus and preeclampsia <34+0 weeks of gestation, we recommend a course of antenatal glucocorticoids (betamethasone) Use of steroids at 34 to 36 weeks is controversial.

management

- We recommend the use of magnesium sulfate as a first-line agent for seizure prophylaxis in preeclampsia
- We give a loading dose of 6 g magnesium sulfate intravenously over 15 to 20 minutes followed by 2 g/hour as a continuous infusion.

HELLP syndrome

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HELLP syndrome

- HELLP is an acronym that refers to a syndrome in pregnant and postpartum women characterized by hemolysis with a microangiopathic blood smear, elevated liver enzymes, and a low platelet count.

- probably represents a type of preeclampsia

PREVALENCE

HELLP develops in 0.1 % to 1.0 % of pregnant women overall. Among women with severe preeclampsia/eclampsia, 1 to 2 percent have microangiopathic hemolysis and thus can be considered to have HELLP.

RISK FACTORS

- previous history of preeclampsia or HELLP is a risk factor for HELLP syndrome.
- In contrast to preeclampsia, nulliparity is **not** a risk factor for HELLP syndrome

PATHOPHYSIOLOGY

Microangiopathy and activation of intravascular coagulation can account for all of the laboratory findings in HELLP syndrome. Hepatic histology may show **microvascular fibrin deposition, neutrophilic infiltrate, fatty infiltration, lobular necrosis, and periportal hemorrhage.**

signs and symptoms of HELLP syndrome

Sign/symptom	Frequency, percent
Proteinuria	86 to 100
Hypertension	82 to 88
Right upper quadrant/epigastric pain	40 to 90
Nausea, vomiting	29 to 84
Headache	33 to 61
Visual changes	10 to 20
Jaundice	5

Complications

- Bleeding
- DIC – 21 percent
- Abruptio placentae – 16 percent
- Acute renal failure – 8 percent
- Pulmonary edema – 6 percent
- Subcapsular liver hematoma (or hepatic rupture) – 1 percent
- Retinal detachment – 1 percent
- Death – 1 percent

- Additional complications : ARDS, sepsis, stroke, cerebral hemorrhage and edema, hepatic infarction ,Wound complications
- HELLP syndrome with or without acute kidney injury *does not affect long-term renal function.*

DIAGNOSTIC EVALUATION

- CBC
- Peripheral smear
- AST, ALT, bilirubin
- Cr
- In patients with elevated liver chemistries, the author also obtains haptoglobin and LDH and coagulation studies (fib,PT, activated PTT).

Clinical presentation

Most cases of HELLP are diagnosed between 28 and 36 weeks of gestation, but symptoms may present up to 7 days postpartum.

Diagnosis

- The diagnosis of HELLP is based on the presence of all of the following criteria (Tennessee classification) :
- Hemolysis, established by at least two of the following:
  -**Peripheral smear** with schistocytes and burr cells
- Serum **bilirubin ≥1.2** mg/dL
  -Low serum **haptoglobin or (LDH) ≥2 times** the upper level of normal
  -Severe anemia, unrelated to blood loss
- Elevated liver enzymes:
  -Aspartate aminotransferase (AST) or alanine aminotransferase (ALT) ≥2 times the upper level of normal
- Low platelets: <100,000 cells/microL

Differential diagnosis

acute fatty liver of pregnancy(AFLP)

thrombotic thrombocytopenic purpura(TTP)

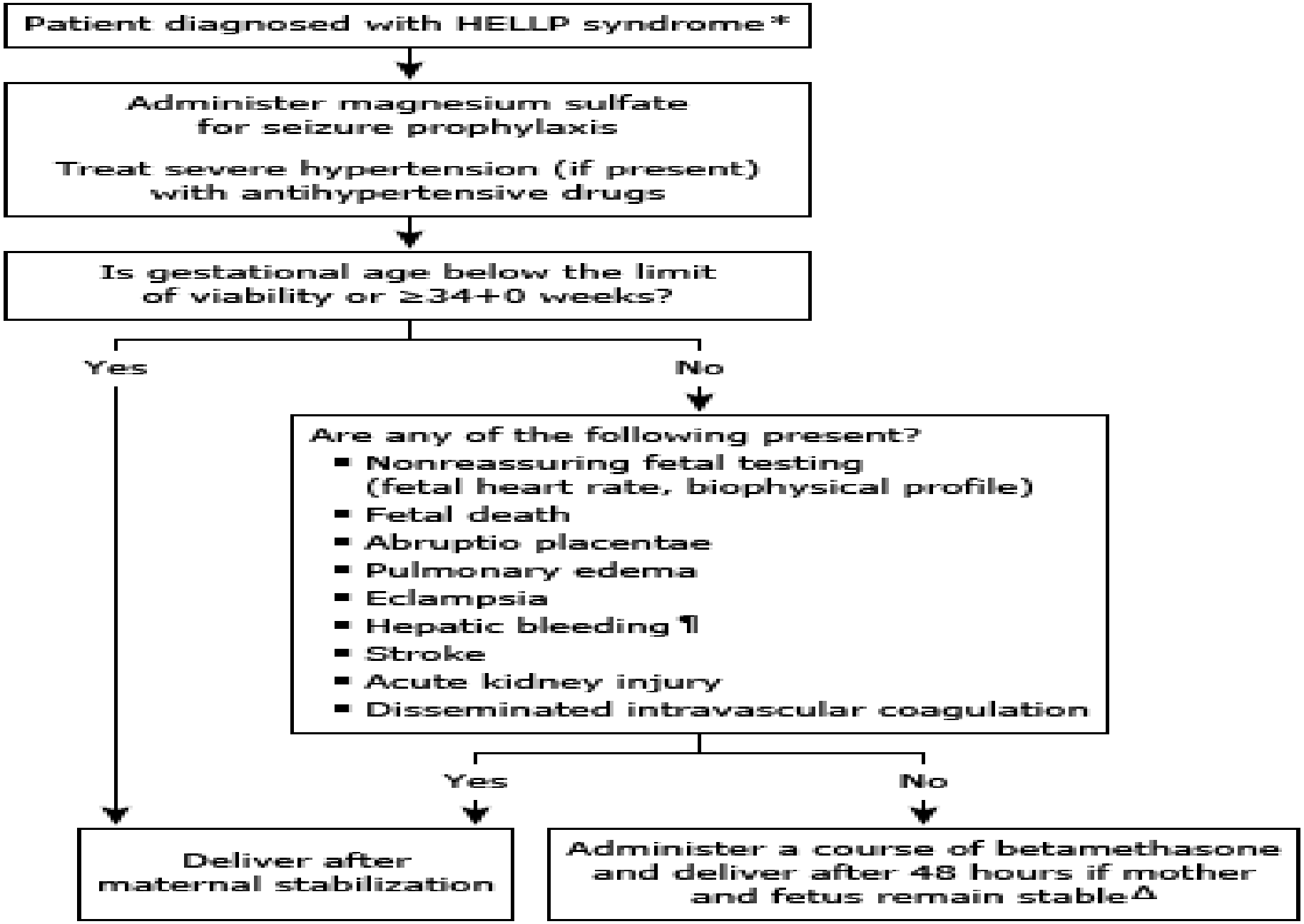
pregnancy-related hemolytic-uremic syndrome

systemic lupus erythematosus(SLE)

Signs and symptoms	HELLP syndrome, percent	AFLP, percent	TTP, percent	HUS, percent	Exacerbation of SLE, percent
Hypertension	85	50	20 to 75	80 to 90	80 with APA, nephritis
Proteinuria	90 to 95	30 to 50	With hematuria	80 to 90	100 with nephritis
Fever	Absent	25 to 32	20 to 50	NR	Common during flare
Jaundice	5 to 10	40 to 90	Rare	Rare	Absent
Nausea and vomiting	40	50 to 80	Common	Common	Only with APA
Abdominal pain	60 to 80	35 to 50	Common	Common	Only with APA
Central nervous system	40 to 60	30 to 40	60 to 70	NR	50 with APA

Outcome/prognosis

- The outcome for **mothers** with HELLP syndrome is generally good, but serious complications such as **abruptio placentae, acute kidney injury, subcapsular liver hematoma or hepatic rupture, pulmonary edema, and retinal detachment** may occur.
- The short-term and long-term prognoses for the infant are primarily related to gestational age at delivery and birth weight: *Preterm delivery* and *low birth weight* are common*. Maternal HELLP does* ***not*** *affect* ***fetal/neonatal liver function***.
- Future pregnancies are at increased risk of developing HELLP, preeclampsia, and gestational hypertension.


Patient diagnosed with HELLP syndrome*
Administer magnesium sulfate for seizure prophylaxis
Treat severe hypertension (if present) with antihypertensive drugs
Is gestational age below the limit of viability or ≥34+0 weeks?
Yes
No
Are any of the following present?
Nonreassuring fetal testing (fetal heart rate, biophysical profile)
Fetal death
Abruptio placentae
Pulmonary edema
Eclampsia
Hepatic bleeding ¶
Stroke
Acute kidney injury
Disseminated intravascular coagulation
Yes
No
Deliver after maternal stabilization
Administer a course of betamethasone and deliver after 48 hours if mother and fetus remain stable Δ

Management

- The initial steps are to assess the mother, **stabilize** women who are unstable, and assess gestational age and **fetal status** (NST, ultrasound and BPS).
- Women with severe hypertension should receive **antihypertensive** therapy (eg, intravenous labetalol promptly to reduce the risk of stroke.
- Although uncommon, severe right upper quadrant/epigastric pain may be due to hepatic bleeding, which may remain contained or rupture the liver capsule. The management of a hematoma is to support the patient with **volume replacement** and transfusion of blood and blood products, as needed. Prompt **delivery** is indicated once she is hemodynamically stable and severe anemia and coagulopathy, if present, have been corrected. A team experienced in liver trauma surgery should be consulted during maternal stabilization and prior to delivery.
- Women with DIC, pulmonary edema, or renal failure should be stabilized and delivered.
- We recommend **not** administering dexamethasone for treatment of HELLP syndrome . Dexamethasone does not accelerate resolution of laboratory abnormalities or reduce the risk of maternal complications.
- **Magnesium sulfate** is given intravenously to patients on the labor and delivery unit to prevent **convulsion**s and for fetal/neonatal **neuroprotection** in pregnancies **between 24 and 32 weeks** of gestation with a live fetus