Preeclampsia

INTRODUCTION

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

- Approximately **90** percent of cases present in the **late preterm (≥34 to <37 weeks), term (≥37 to <42 weeks), or postpartum (≥42 weeks) period** and have **good** maternal, fetal, and newborn outcomes.

- The remaining **10** percent of cases have an early presentation (<34 weeks) and carry the additional high risks associated with moderately preterm, very preterm, or extremely preterm birth.

- Long-term, patients with preeclampsia are at increased risk for developing cardiovascular and renal disease.

DEFINITIONS/DIAGNOSTIC CRITERIA

- **SBP ≥140 mmHg or DBP ≥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+**
▪ **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
▪ **Visual symptoms** (eg, blurred vision, flashing lights or sparks, scotomata暗點)

DEFINITIONS/DIAGNOSTIC CRITERIA

preeclampsia with severe features (formerly severe preeclampsia)

Severe blood pressure elevation
SBP ≥160 mmHg or DBP ≥110 mmHg on 2 occasions at least 4 hours apart while the patient is on bedrest
Symptoms of central nervous system dysfunction
New-onset cerebral or visual disturbance, such as: 1. Photopsia閃光, scotomata暗點, cortical blindness, retinal vasospasm 2. **Severe headache** or headache that persists and progresses
Hepatic abnormality
Serum transaminase concentration >2 times the upper limit of the normal range or severe persistent right upper quadrant or epigastric pain
Thrombocytopenia: <100,000 platelets/microL
Renal abnormality
Renal insufficiency (serum creatinine >1.1 mg/dL [97.2 micromol/L] or a doubling of the serum creatinine concentration in the absence of other renal disease)
Pulmonary edema

DEFINITIONS/DIAGNOSTIC CRITERIA

Eclampsia & HELLP syndrome & chronic hypertension

- **Eclampsia**: the occurrence of a **grand mal seizure** in a patient with preeclampsia
- **HELLP syndrome** (**h**emolysis, **e**levated **l**iver enzymes, **l**ow **p**latelets): a type of preeclampsia with severe features
- **Preeclampsia superimposed upon chronic hypertension**:
  - **Chronic hypertension**: hypertension that precedes pregnancy or is present on at least two occasions before the 20th week of gestation or persists longer than 12 weeks postpartum
  - worsening or resistant hypertension (especially acutely), the new onset of proteinuria or a sudden increase in proteinuria, and/or significant new end-organ dysfunction after 20 weeks of gestation or postpartum in a patient with chronic hypertension

DEFINITIONS/DIAGNOSTIC CRITERIA

Gestational hypertension

- Hypertension **without** proteinuria or other signs/symptoms of preeclampsia-related end-organ dysfunction that develops **after** 20 weeks of gestation.

- 10 to 25 percent of these patients may ultimately develop signs and symptoms of preeclampsia.

- True gestational hypertension should **resolve by 12 weeks postpartum**. If it persists beyond 12 weeks postpartum, the diagnosis is "revised" to chronic hypertension

INCIDENCE & RISK FACTORS

- **4.6 percent** (95% CI 2.7-8.2) of pregnancies worldwide were complicated by p

Nulliparity	**Multifetal gestation**	Hydrops fetalis	Prolonged interpregnancy interval	
Chronic hypertension	**Diabetes mellitus (or GDM)**	**Autoimmune disease (eg, APS, SLE)**	**Chronic renal disease**	Poorly controlled hyperthyroidism
Vascular disease	**Obesity**	Obstructive sleep apnea	Elevated blood lead level	Posttraumatic stress disorder
Family history of preeclampsia	Past history of Preeclampsia	Woman herself was SGA	**Past history of FGR, abruption placentae, or fetal demise**	
Partner-related factors	Black population	**Age >40 years or <18 years**	**Use of assisted reproductive technology** (eg, in vitro fertilization)	

- Patients who smoke cigarettes have a **lower** risk of preeclampsia than nonsmokers

PATHOPHYSIOLOGY

Involve both maternal and fetal factors

- **Shallow placentation** and **failure of the spiral arteries to remodel** early in pregnancy (weeks to months before clinical manifestations)
- Suboptimal uteroplacental blood flow and relatively hypoxic trophoblast tissue
- An exaggerated state of oxidative stress develops in the placenta, which in turn adversely affects villous angiogenesis.
- The pathologic placenta increasingly secretes **antiangiogenic factors** (soluble fms-like tyrosine kinase-1 **[sFlt-1]** and **endoglin**) into the maternal circulation that bind vascular endothelial growth factor (**VEGF**) and placental growth factor (**PlGF**)
- **Widespread maternal vascular inflammation, endothelial dysfunction, vascular injury—> vasospasm, capillary leaking, increased platelet turnover**
- —> hypertension, proteinuria, thrombocytopenia…end organ failure

PATIENT EVALUATION

Potential clinical findings: Alarming findings

- Persistent and/or severe headache ("**worst headache of my life**")
- Altered mental status (confusion, altered behavior [agitation]): stroke, generalized hyperreflexia, seizure
- Visual abnormalities (scotomata, photophobia, blurred vision, or temporary blindness [rare])
- Epigastric, upper abdominal, or retrosternal pain
- New dyspnea, orthopnea: left heart failure, pulmonary edema
- Oliguria: preeclampsia: <100 mL over 4 hours/ severe :urine output <500 mL/24 hours
- Others: peripheral edema (rapid weight gain (eg, >2.3 kg/week) and facial edema), Abruptio placentae (<1% of preeclampsia)

PATIENT EVALUATION

- Accurate assessment of blood pressure
- Laboratory tests: CBC (**thrombocytopenia**, **hemoconcentration**), creatinine, AST, ALT, bilirubin, urinary protein determination (P/C ratio or 24-hour urine total protein)
- Peripheral blood smear: Schistocytes and helmet cells —> (**microangiopathic hemolysis**)
- Assessment of fetal status: nonstress test or biophysical profile +/- Ultrasound (AFV, fetal weight)—> (**oligohydramnios, FGR**)
- Neurology consultation: neurologic deficits/abnormal neurologic examination, ocular signs and symptoms, or a severe persistent headache that does not respond to repeat doses of acetaminophen and initial routine management of preeclampsia.
- Measurement of angiogenic factors (not all countries available): sFlt-1, PlGF

PREVENTION

LOW-DOSE ASPIRIN

- Candidates:

We generally follow the USPSTF criteria and recommend low-dose aspirin for preeclampsia prevention to patients with **two or more of the following moderate risk factors** [21]:

- Nulliparity.
- Obesity (body mass index >30 kg/m^2).
- Family history of preeclampsia in mother or sister.
- Age ≥35 years.
- Sociodemographic characteristics (Black persons, lower income level [recognizing that these are not biological factors]).
- Personal risk factors (eg, previous pregnancy with low birth weight or small for gestational age infant, previous adverse pregnancy outcome [eg, stillbirth], interval >10 years between pregnancies).
- In vitro conception

- Initiate prior to GA: **16 weeks,** dose: **81 to 150 mg**

MANAGEMENT

PREECLAMPSIA **WITHOUT** FEATURES OF SEVERE DISEASE

- Term pregnancies: **Delivery** (GA >= **37**+0 wks)
- Preterm pregnancies: **Expectant management**—blood pressure, laboratory follow-up, patient education, assessment of fetal growth/ fetal well-being, antenatal corticosteroids, timing of delivery

PREECLAMPSIA **WITH** FEATURES OF SEVERE DISEASE

- General approach: **Delivery** (1. GA >=**34**+0 wks, 2. GA **<24** wks, 3. GA <34+0 wks with **preterm labor or PROM**, maternal and/or fetal condition is **unstable**)
- Expectant management for stable maternal and fetal condition in GA 24-34 wks

MANAGEMENT

INTRAPARTUM MANAGEMENT

- Route of delivery: 儘速生產，不一定要剖腹產 even in the setting of preeclampsia with features of severe disease, does **not** mandate immediate cesarean birth unless prolonged induction or inductions with a low likelihood of success

- Management of **hypertension**: should be treated promptly (**within 30 to 60 minutes**) with intravenous **labetalol** (avoid in patients with asthma or heart rate <50 beats/minute) or **hydralazine** or, less commonly, intravenous **nicardipine** or oral **nifedipine** to prevent stroke.

- **Seizure** prophylaxis: **Magnesium sulfate** (適用於preeclampsia with severe features 的病人於產時和產後)

    - Side effects: loss of DTR, respiratory paralysis, altered cardiac conduction, cardiac arrest (**antidote: Calcium gluconate**)

    - Contradictions: **myasthenia gravis,** ~~pulmonary edema~~ (Alternative: levetiracetam, valproic acid)

MANAGEMENT

INTRAPARTUM MANAGEMENT

- Management of **thrombocytopenia**: platelet transfused in patients whose platelet count <20,000/microL/ excessively bleeding or oozing
- Fluids:
  - (Input - urine output) + estimated insensible losses [usually 30 to 50 mL/hour])
  - Severe feature (pulmonary edema or significant third-spacing): maintenance infusion of a balanced salt or isotonic **saline** solution at **80 mL/hour**
- Analgesia: neuraxial techniques

PROGNOSIS

- **Recurrence:**
  - **16 %** developed recurrent preeclampsia and **20 %** developed hypertension alone in a subsequent pregnancy.
    - 第一胎Early-onset, severe preeclampsia： 第二胎25 to 65 %
    - 第一胎preeclampsia without severe features：第二胎5 to 7 %
    - 第一胎normotensive：第二胎 < 1%

REFERENCE

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