**AN ADAPTED EVIDENCE-BASED CLINICAL PRACTICE GUIDELINE**

**ON**

**THE MANAGEMENT OF HYPERTENSIVE DISORDERS IN PREGNANCY**

**Overview**

This is an adapted evidence-based clinical practice guideline for the management of hypertensive disorders in pregnancy.

**Guideline adapter**

**This guideline has been adapted by the Egyptian Universities Obstetrics & Gynecology Guideline Working Group (EUOBGYN-GWG).**

**Release date**

July 2023

**GUIDELINE ADAPTATION METHODOLOGY**

This guideline was produced in accordance with the ADAPTE methodology and procedure for the adaptation of evidence-based clinical practice guidelines published by the ADAPTE Group (Fervers B, et al., Adaptation of clinical guidelines: literature review and proposition for a framework and procedure. Int J Qual Health Care 2006; 18(3): 167-176).

**sources of the guideline**

**This guideline was adapted from:**

1. National Institute for Health and Care Excellence (NICE, updated 2023). Hypertension in pregnancy: diagnosis and management, ng 133, June 2019, updated April 2023.
2. ACOG Practice Bulletin, Number 222. Gestational Hypertension and Preeclampsia. Obstet Gynecol. 2020 Jun;135(6):e237-e260.
3. US Preventive Services Task Force (USPSTF, 2017). Screening for Preeclampsia: US Preventive Services Task Force Recommendation Statement. JAMA. 2017;317(16):1661–1667.
4. Queensland Clinical Guidelines (2016). Hypertensive disorders of pregnancy, August 2015, amended August 2016.

# Introduction

Hypertensive disorders of pregnancy constitute one of the leading causes of maternal and perinatal mortality worldwide. It has been estimated that 2–8% of pregnancies globally are complicated by hypertensive disorders.

In Egypt, complications of hypertensive disorders with pregnancy are responsible for 15% of the causes of maternal mortality, second only to postpartum hemorrhage.

# Definitions And Spectrum of The Disease

**Hypertension:**

Systolic blood pressure (sBP) greater than or equal to 140 mmHg **and/or** Diastolic blood pressure (dBP) greater than or equal to 90 mmHg.

* **Moderate hypertension**
* sBP 141 mmHg to 159 mmHg **and/or** dBP 91 mmHg to 109 mmHg.
* **Severe hypertension**
* sBP greater than or equal to 160 mmHg **and/or** dBPgreater than or equal to 110 mmHg.
* sBP greater than or equal to 170 mmHg with or without dBP greater than or equal to 110 mmHg is a medical emergency, requires urgent treatment.

**White Coat Hypertension**: Hypertension in a clinical setting with normal BP in a non-clinical setting.

# Classification

* **Gestational hypertension:** hypertension; without proteinuria nor features of severity, developing after 20 weeks of gestation, with blood pressure levels returning to normal within 3 months postpartum.
* **Preeclampsia:** A multi-system disorder; characterized by hypertension and proteinuria or features of severity indicating involvement of one or more organ systems (see: parameters of severity).
* **Chronic hypertension occurring in pregnancy (Essential and Secondary):**
  + Hypertension confirmed preconception or prior to 20 weeks; with or without a known cause, or hypertension that is diagnosed for the first-time during pregnancy and that does not resolve within 3 months postpartum.
  + Pregnant women with confirmed hypertension; controlled by antihypertensive therapy, with normal blood pressure measurements.
* **Preeclampsia superimposed on chronic hypertension:** Where a woman with pre-existing hypertension develops systemic features of preeclampsia after 20 weeks gestation.
* **Eclampsia:** Is defined by new-onset tonic/clonic, focal, or multi-focal seizures; in the absence of other causative conditions such as epilepsy, cerebral arterial ischemia and/or infarction, intracranial hemorrhage, or drug use.

# Diagnosis of Preeclampsia

In a woman with a previously normal blood pressure, the development of systolic blood pressure of 140 mmHg or more or diastolic blood pressure of 90 mmHg or more, on two occasions at least 4 hours apart, after 20 weeks of gestation.

RECOMMENDATION: Blood pressure should be measured and documented during each ante natal visit.

# Parameters of severity

### **Systolic blood pressure of 160 mmHg or more or diastolic blood pressure of 110 mmHg or more.**

### **Presence of Proteinuria:**

* Protein/creatinine ratio of 0.3 mg/dL or more; or
* Dipstick reading of (2+) or more;(used only if other quantitative methods are not available)
  + Do not routinely use 24-hour urine collection to quantify proteinuria in pregnant women.
  + Do not use first morning urine void to quantify proteinuria in pregnant women.
  + If available: Use an automated reagent-strip reading device for dipstick screening for proteinuria in pregnant women.
  + If using *protein: creatinine ratio* to quantify proteinuria in pregnant women: use 30 mg/mmol as a threshold for significant proteinuria.
  + If using *albumin: creatinine ratio* to diagnose pre-eclampsia in pregnant women with hypertension, use 8 mg/mmol as a diagnostic threshold.

### **Presence of any of the following conditions (even in the absence of proteinuria):**

* Fetal growth restriction
* Serum creatinine concentrations greater than 1.1 mg/dL or a doubling of the serum creatinine concentration in the absence of other renal disease or oliguria.
* Thrombocytopenia: Platelet count less than100,000 /mm3.
* Hemolysis: schistocytes or red cell fragments on blood film, raised bilirubin, raised lactate dehydrogenase (LDH), decreased haptoglobin.
* Disseminated intravascular coagulation (DIC).
* Elevated liver transaminases (ALT, AST) to twice normal concentration.
* New-onset headache; unresponsive to medication, not accounted for by any alternative diagnoses.
* Visual symptoms (photopsia, scotomata, cortical blindness, retinal vasospasm).
* Hyperreflexia with sustained clonus.
* Convulsions (eclampsia).
* Stroke.
* Pulmonary edema.

**RECOMMENDATION: Parameters of severity should be identified and documented for every pregnant hypertensive woman.**

# Risk Factors

**Pregnant women with any of the following risk factors must be carefully screened for preeclampsia:**

* History of eclampsia or preeclampsia in previous pregnancy (particularly early-onset preeclampsia).
* History of delivering a low birth weight or small for gestational age neonate.
* History of previous adverse pregnancy outcomes (NND, IUFD, Mid-trimester miscarriages).
* Chronic hypertension.
* Antiphospholipid antibodies syndrome.
* Diabetes Mellitus. (IDDM, NIDDM, gestational diabetes).
* Multifetal gestation.
* Maternal age 35 years or older.
* Nulliparity.
* More than 10-year pregnancy interval.
* Pre-pregnancy body mass index greater than 30 kg/m2.
* Autoimmune diseases.
* Renal diseases.
* Hereditary Thrombophilia
* Low socioeconomic status
* Obstructive sleep apnea
* Conceiving through Assisted reproductive techniques

**RECOMMENDATION: Risk factors for the development of preeclampsia should be identified and documented for every pregnant woman.**

# Risk Reduction

* The only effective screening method for preeclampsia is blood pressure measurements throughout pregnancy.
* No treatment to date can reliably prevent preeclampsia in pregnant women.
* Women with risk factors must receive:
  + **Low dose Aspirin** (75-100mg daily) is to be used from 12 weeks till the birth of the baby.
  + **Calcium supplements** (1 gram of elemental calcium daily) from the beginning of pregnancy till delivery.
* Educate pregnant women to seek a healthcare professional immediately if they experience any of the symptoms of pre-eclampsia including:
* Severe headache
* Problems with vision, such as blurring or flashing before the eyes
* Severe pain just below the ribs
* Vomiting
* Sudden swelling of the face, hands or feet.
* Do not use the following to prevent hypertensive disorders during pregnancy:
  + Low molecular weight heparin
  + Diuretics
  + Progesterone
  + Nitric oxide donors
* There is insufficient evidence to support the use (for prevention or risk reduction of hypertensive disorders of pregnancy) of the following
* Magnesium or zinc supplementation
* Bed rest
* Dietary salt restriction
* Antioxidants
* Heparin Insufficient evidence to support routine use (other than in the specific case of APLS)

**RECOMMENDATION: Pregnant women at risk of developing preeclampsia should receive low dose aspirin (75-100 mg daily) beginning at 12 weeks gestation and till delivery, to reduce the risk of developing preeclampsia.**

**RECOMMENDATION: All pregnant women should receive Calcium supplementation (1 gram daily of elemental Calcium) from the first ante natal visit till delivery, to reduce the risk of developing preeclampsia.**

**RECOMMENDATION: Pregnant women with hypertension or with risk factors for developing preeclampsia should be educated about the symptoms and signs that require immediate attention and referral to health care facilities. A clear referral plan should be discussed with each woman.**

# Managing Different presentations

The goals of antenatal care in the presence of hypertension include control of BP, early detection of preeclampsia, prevention of eclampsia, and optimizing birth for both the woman and her baby.

## **1**- **HTN Presenting for the First time After 20 Weeks**

### **Initial tests**

#### Measurement of BP

* Correct measurement techniques are critical to the correct diagnosis of HDP.
* Confirm non-severe hypertension by measuring BP at least twice four hours apart.

#### Proteinuria

* Screen women for proteinuria with urinary dipstick test at each visit.
* Quantify by laboratory methods if:
  + Greater than or equal to (2+) proteinuria, or
  + There is repeated (1+) proteinuria, or
  + Preeclampsia is suspected.
* Spot urine *protein: creatinine ratio* greater than 30 mg/mmol is diagnostic of proteinuria in pregnancy.
* 24-hour urine collection is not necessary in routine clinical management.
* Once confirmed, Proteinuria testing does not need to be repeated.

#### Blood Tests

* Full blood count (FBC).
* Urea, creatinine, electrolytes and uric acid.
* Liver function tests (LFT)including LDH.

#### Additional Tests for Preeclampsia

* Urinalysis and microscopy on a carefully collected mid-stream urine sample for associated urinary tract infection.
* If there is thrombocytopenia or a falling hemoglobin, investigations for DIC and/or hemolysis including:
  + Coagulation studies
  + Blood film
  + LDH
  + Fibrinogen
  + Hemolytic studies
* In severe or early onset preeclampsia, consider investigation for associated conditions (e.g., systemic lupus erythematosus (SLE), APLS, chronic renal disease)

#### **Fetal Surveillance**

* Cardiotocograph (CTG) if greater than 28weeks gestation
* Ultrasound scan (USS) assessment of:
  + - Fetal growth
    - Amniotic fluid volume (AFV) or deepest vertical pocket (DVP)
    - Umbilical artery flow (Doppler)

**RECOMMENDATION: During every ante natal visit, blood pressure measurement and urine tests for proteinuria should be performed and documented for every pregnant woman.**

**RECOMMENDATION: Health care providers should be trained on accurate blood pressure measurement, and antenatal care units should be equipped with facilities that allow for testing for proteinuria.**

**RECOMMENDATION: A clear referral plan for patients with severe preeclampsia must be developed and implemented in every health care unit.**

**RECOMMENDATION: Women with severe preeclampsia should have additional tests to detect multisystem involvement, and should have fetal surveillance to assure fetal wellbeing.**

### **Treatment**

#### **Moderate Hypertension:**

* Consider drug therapy if:
* sBP is 140–160 mmHg and/or
* dBP is 90–100 mmHg and/or
* There are associated signs and symptoms of preeclampsia.
* Target BP values

Aim for BP of 135/85 mmHg

**RECOMMENDATION: Consider drug therapy for MODERATE hypertension if systolic blood pressure is 140-160 mmHg and\or diastolic blood pressure is 90-100 mmHg, and\or there are signs and/or symptoms of preeclampsia. The target of therapy is to maintain blood pressure at 135\85 mmHg.**

**RECOMMENDATION: Familiarity and experience with the selected agent is the most important consideration in choosing a drug for the management of moderate hypertension in pregnancy. There is no clear evidence to recommend one antihypertensive drug therapy over another.**

**The following drugs are recommended for treatment of moderate hypertension:**

* **Methyldopa 250-500 mg**: 500-3000 mg/day orally in 2-4 divided doses. Maximum: 3 g\day
* **Labetalo**l **100 mg**: Initially: 100 mg BD Up to: 600 mg QID. Maximum: 2.4 g\day
* **Hydralazine25–50 mg**. Initially:25 mg BD Up to: 100 mg BD. Maximum: 200 mg\day
* **Nifedipine (SR)20 mg:** Initially: 20-30 mg BD Up to: 120 mg daily. Maximum: 120 mg\day
* **Nifedipine (immediate release)10-20 mg**Initially:10-40 mg BD Maximum: 80 mg\day

**The following drugs are NOT recommended for treatment of hypertension in pregnancy**:

* Magnesium Sulfate (although may be indicated for prevention of eclampsia).
* Diazoxide.
* Nimodipine.
* Chlorpromazine.
* ACE inhibitors.
* Sodium Nitroprusside or Glyceryl Trinitrate are only recommended when other treatments have failed, and birth is imminent.

#### **Severe Hypertension**

* A multidisciplinary team approach is required.
* Provide care in a high dependency unit or birth suite.
* Strict control of BP is required.
* Monitor BP 15–30 minutes until stable and then at a minimum 4 hourly.
* Perform a thorough assessment of maternal and fetal condition.
* Continuous fetal heart rate (FHR) monitoring is recommended.

**RECOMMENDATION: Multidisciplinary teams should be assembled and trained on provision of care for cases with severe hypertension with pregnancy.**

**RECOMMENDATION: Care for cases with severe hypertension during pregnancy should be provided in units that have facilities for continuous monitoring and strict control of blood pressure, and capabilities to perform thorough assessment and management of maternal and fetal conditions.**

##### Commence pharmacological treatment if:

sBP is greater than or equal to 160 mmHg and/or

dBP is greater than or equal to 100 mmHg

sBP greater than or equal to 170 mmHg with or without dBP greater than or equal to 110 mmHg is a medical emergency and requires urgent treatment

##### Target Blood Pressure

* Target BP range of 135 / 85 mmHg
* Aim for gradual and sustained lowering of BP so blood flow to the fetus is not compromised

**RECOMMENDATION Consider drug therapy for SEVERE hypertension if systolic blood pressure is more than 160 mmHg and\or diastolic blood pressure is more than 100 mmHg. The target of therapy is to maintain blood pressure at 135\85 mmHg.**

##### Choice of Antihypertensive

* The antihypertensive agent of choice for acute control has not been established.
* Initial therapy can be with one of a variety of antihypertensive agents.
* Persistent or refractory severe hypertension may respond to repeated doses.
* Concurrent administration of long-acting oral agents achieves more sustained BP lowering effect

**Treat women with severe hypertension who are in critical care during pregnancy or after birth immediately with one of the following:**

* **Labetalol:**
  + 10-20 mg IV, then 20-80 mg every 10-30 minutes to a maximum cumulative dosage of 300 mg\day, Or
  + Constant infusion 1-2 mg/min. I.V. *(Tachycardia is less common, fewer adverse effects).*
    - Onset of action: 1–2 minutes.

**Caution: Avoid labetalol in women with asthma, preexisting myocardial disease, decompensated cardiac function, and heart block and bradycardia.**

* **Nifedipine (immediate release):**
  + Nifedipine: 10-20 mg orally, repeat in 20 minutes if needed; then 10-20 mg every 2-6 hours; maximum daily dose is 180 mg.
    - Onset of action: 5-10 minutes.

**Caution: May lead to reflex tachycardia and headaches.**

* **Intravenous Hydralazine**.
  + 5 mg I.V. or I.M., then 5-10 mg I.V. every20-40 minutes to a maximum cumulative dosage of 20 mg/day; or
  + Constant infusion of 0.5–10 mg/hour.
    - Onset of action: 10–20 minutes.

**Caution: Higher or frequent doses are associated with maternal hypotension, headaches, and abnormal fetal heart rate tracings.**

* **Diazoxide**
  + 15-45 mg as I.V. rapid bolus and repeat after 5 minutes
  + Maximum 150 mg/dose.
    - Onset: 3–5 minutes.

**Caution: Monitor Blood Glucose Levels.**

* **Sodium Nitroprusside and Glyceryl Trinitrate (Tridil)**
  + Only recommended when other methods have failed and delivery is imminent.

### 

### **Antenatal Care**

**RECOMMENDATION: At each antenatal care visit, following the detection of hypertension in pregnancy, a systematic clinical evaluation of symptoms, signs, laboratory investigations and fetal wellbeing must be performed.**

#### Outpatient Surveillance

**RECOMMENDATION: Women with moderate hypertension, with no evidence of preeclampsia, and with easy access to a nearby healthcare facility, may be managed on outpatient basis.**

* Consider combined obstetric and physician outpatient management if there is:
  + Previous pregnancy complicated by preeclampsia.
  + Known essential hypertension on drug therapy.
  + Known renal disease or recurrent urinary tract infection.
  + Other disease associated with hypertension (e.g., S.L.E.)
* Frequency of appointments is based on the individual clinical requirements of each woman:
  + - * + Suggested follow up is initially every 2 weeks, with the performance of blood tests at each visit.
  + Among women with gestational hypertension or preeclampsia without severe features, expectant management up to **37(+0/7)** weeks of gestation is recommended, during which frequent fetal and maternal evaluations recommended.
* Fetal monitoring by ultrasonography to determine fetal growth every 3-4 weeks of gestation, and amniotic fluid volume assessment at least once weekly.

#### Day Stay

Patients with moderate hypertension, with no evidence of preeclampsia, demonstrating some change to maternal or fetal condition, may be offered to be kept under observation and monitored over the duration of a day, to allow for a decision for continuing outpatient surveillance.

#### Inpatient admission (Hospitalization)

**RECOMMENDATION: Patients should be admitted as inpatients if there is concern about the fetal wellbeing, and/or if the sBP is greater than 140 mmHg, and/or dBP is greater than 90 mmHg, or if signs or symptoms of preeclampsia are present.**

##### Inpatient monitoring

* + - BP measurements every 4 hours, if stable.
    - CTG daily (from 28 weeks gestation).
    - Daily urine analysis, if proteinuria not previously confirmed.
    - Maintain accurate fluid balance record.
    - Daily follow up by obstetrician.
    - Normal diet.
    - Consideration of thromboprophylaxis.

#### Transfer of Care

Care options will depend on the services available at each facility. Consultation with and/or transfer to a higher-level service may be indicated for:

* Preterm pregnant women with hypertension (24-32 weeks gestation) developing preeclampsia, or any pregnant hypertensive woman developing severe preeclampsia, eclampsia or HELLP syndrome, should be transferred to a facility with capabilities to provide adequate care to the mother and the baby.
* Consider *Magnesium Sulfate* therapy prior to transfer in women with severe preeclampsia, eclampsia or HELLP syndrome

**RECOMMENDATION: Transfer of women with hypertension of pregnancy should be considered in situations where the health care provider believes that the health care facility is unequipped to manage the complications of hypertension of pregnancy.**

##### *Signs of Fetal Compromise*

Currently, there is no single fetal monitoring test that accurately predicts fetal compromise in women with hypertension or preeclampsia. A combination of any of the following tests is generally recommended.

* Decreased fetal movement perception.
* Abnormal FHR tracing (e.g., decreased variability).
* Decreased amniotic fluid:
  + Amniotic fluid index (AFI); 5 cm. or less.
  + Deepest amniotic fluid pocket measurement (DVP); 2 cm. or less.
* Ultrasound assessment of fetal growth
  + Asymmetrical intrauterine fetal growth.
* Doppler Flowmetry:
  + Umbilical artery: Showing increased resistance, absent or reversed end diastolic flow.
  + Ductus venosus: Absent or reversed “a” wave.
  + Middle cerebral artery: Decreased resistance, (brain sparing effect).

**RECOMMENDATION: Capabilities for the evaluation of fetal wellbeing and detection of fetal compromise should be available in healthcare facilities providing care for pregnant women with hypertensive disorders.**

### *Planning and conducting Birth:*

In addition to appropriate management of labor and delivery, the two main goals of management of women with preeclampsia during labor and delivery are prevention of seizures and control of hypertension.

A *Multidisciplinary Approach*; where early consultation between experienced obstetricians, feto-maternal medical specialists, the anesthesia team, the neonatology team, and physicians specializing in hepato-renal, hematologic and neurological diseases may be involved.

The Multidisciplinary team should be alerted and informed when a woman with preeclampsia is admitted to birth suite.

**RECOMMENDATION: Multidisciplinary teams should be assembled, with prompt and instant communication between team members to allow for proper evaluations and timely decisions to be taken in women with preeclampsia.**

#### Indications for birth; conditions precluding expectant management:

**Maternal**

* Uncontrolled severe-range blood pressures (persistent systolic blood pressure 160 mm Hg or more or diastolic blood pressure 110 mm Hg or more not responsive to antihypertensive medication.
* Persistent headaches, refractory to treatment.
* Epigastric pain or right upper pain unresponsive to repeat analgesics.
* Visual disturbances, motor deficit or altered sensorium.
* Stroke.
* Myocardial infarction.
* HELLP syndrome.
* New or worsening renal dysfunction (serum creatinine greater than 1.1 mg/dL or twice baseline).
* Pulmonary edema.
* Eclampsia.
* Suspected acute placental abruption or vaginal bleeding in the absence of placenta previa.

**Fetal**

* Abnormal fetal testing with signs of fetal compromise.
* Persistent reversed end-diastolic flow in the umbilical artery.
* Fetal death.
* Fetus without expectation for survival at the time of maternal diagnosis (e.g., lethal anomaly, extreme prematurity).

#### Timing of birth

Timing of birth is dependent on the severity of the disease and the gestational age at which it presents. Prolongation of pregnancy carries no benefit for the mother but may be desirable at early gestations to improve the fetal prognosis

##### Moderate Hypertension

For women at low risk of adverse outcomes, Induction of labor from 37 weeks has been associated with a reduction in the incidence of severe hypertension, without an increase in the CS rate.

##### Preeclampsia with severe features

**RECOMMENDATION: Women with preeclampsia with severe features should be delivered PROMPTLY to prevent maternal and fetal complications.**

Expectant management for severe preeclampsia

A decision of expectant management to delay delivery and prolong pregnancy, for the possibility of improving fetal prognosis, while exposing the mother to grave risk, must be very carefully weighed after counselling the patient and consulting the multidisciplinary team.

Individual clinical factors such as the estimated fetal weight, signs of fetal compromise, presence of oligohydramnios, antenatal corticosteroids and the availability and effectiveness of neonatal intensive care services.

Components of Expectant Management

* Antihypertensive therapy, magnesium sulfate, and supportive measures, under intensive clinical observation and maternal and fetal monitoring, for 48 hours, or until the condition is stable, with satisfactory BP values, and reassuring clinical features, and with normalization of laboratory studies.
* Inpatient management till delivery:
  + Blood pressure measurements every 4-8 hours. Prompt delivery should be planned if measurements deteriorate.
  + Frequent assessment of maternal symptoms. Prompt delivery should be planned if symptoms deteriorate.
  + A complete blood count, serum creatinine, and liver function tests should be performed at least twice weekly. Prompt delivery should be planned if results deteriorate.
  + Regular assessment of fetal well-being. Prompt delivery should be performed if fetal condition deteriorates.
  + Complete the course of antenatal corticosteroids, if not already completed.
  + Magnesium sulfate can be discontinued48 hours from its beginning.

**RECOMMENDATION: Expectant management for preeclampsia with severe features in the early third trimester might be considered by the most senior consultant obstetrician in charge, after counselling the patient, and consulting with a multidisciplinary team of obstetricians, neonatologists, anesthesiologists and other involved specialties. Facilities for prompt delivery should be available and ready for implementation at any time.**

##### Severe Preeclampsia with HELLP

**RECOMMENDATION: Women with severe preeclampsia with features of HELLP should be delivered PROMPTLY, after stabilization of their condition, to prevent maternal and fetal complications.**

#### Stabilization before Birth

Except where there is acute fetal compromise, stabilize the woman before birth includes:

* Control of eclampsia or prophylaxis against eclampsia if indicated.
* Control of severe hypertension.
* Correction of coagulopathy.
* Correction to fluid and electrolyte imbalance.

#### Mode of Birth

* Recommend vaginal birth unless a caesarean section is required for other obstetric indications.
* If vaginal birth is planned and the cervix is unfavorable, recommend cervical ripening to increase the chance of successful vaginal birth.
* In the absence of contraindications, spinal anesthesia is preferred to epidural (because of more rapid onset) and to GA (because it avoids hypertensive response to intubation).

**RECOMMENDATION: Women with severe preeclampsia with or without features of HELLP should be delivered vaginally, unless there is an obstetric indication for cesarean delivery.**

#### **Intrapartum Care**

##### Monitoring

* + - Monitor BP ½ hourly as a minimum.
    - Continuous CTG is recommended.
    - I.V. access is required.
    - An epidural (in the absence of contraindications) is a useful adjunct therapy for BP control (Different options to be discussed with anesthetist).

##### Drug Therapy

* + - Continue antihypertensive drug therapy throughout labor and birth.

##### Second Stage

* + - Assisted operative delivery is required if:
      * BP is poorly controlled
      * Progress is inadequate
      * There are premonitory signs of eclampsia

##### Third Stage

* Active management of third stage is recommended to decrease risk of postpartum hemorrhage.
* DO NOT GIVE Ergometrine or Syntometrine as it may produce an acute rise in BP.

### Postpartum

* Hypertension, proteinuria, eclampsia and other adverse conditions of preeclampsia may develop for the first time during the postpartum period.
  + De novo postpartum hypertension is most common on days 3–6
  + Peak postpartum BP occurs on days 3–6
  + 44% of eclampsia occurs in the postpartum period, usually in the first 48 hours after birth
* After birth, clinical and laboratory derangements of preeclampsia recover, often taking several days
  + Liver enzyme elevations and thrombocytopenia will often worsen in the first few days after birth before they improve
* Target Blood Pressure is 130/85
* Continue close monitoring (4 hourly or more frequently) including BP, pulse rate, respiratory rate and oxygen saturation until:
* BP is stable
* Urine output has normalized
* Blood investigations are stable or improving
* Frequency of monitoring is reduced after approval of the multidisciplinary team.
* Ask women about severe headache and epigastric pain each time BP is measured

#### Drug Therapy

##### Antihypertensive therapy

* Continue use of antenatal antihypertensive drug therapy.
* Cease or reduce when hypertensive changes are resolving.
* Avoid abrupt withdrawal to avoid rebound hypertension.
* If persistently hypertensive (sBP greater than or equal to 140 mmHg or dBP greater than or equal to 90 mmHg), start antihypertensive drug therapy (if not commenced prior to birth).
* If severe hypertension persists; refer to the section on severe hypertension.
* If Methyldopa was initiated during pregnancy, cease postpartum and commence alternative therapy as it is associated with psychologic depression.
* For women on beta blockers, consult with the neonatologist for possible neonatal hypoglycemia and arrange for neonatal blood glucose monitoring.

##### Venous Thromboprophylaxis

* + Actively consider VTE prophylaxis

##### NSAIDs

* + Non-steroidal anti-inflammatory drugs (NSAIDS) are not generally recommended because of the risk of worsening hypertension and renal impairment, especially in volume depleted women.

### Breast Feeding

* + Antihypertensive drugs without reported adverse reactions in breastfed infants include:

Nifedipine

Enalapril

Captopril

Metoprolol

Atenolol (other agents may be preferred if nursing a preterm infant)

Labetalol (other agents may be preferred if nursing a preterm infant)

### Psychological Support

* + Offer postnatal counselling regarding the pregnancy and birth experience including formal postnatal review to discuss the events of the pregnancy if required.

### Discharge and follow up

* + Following a pregnancy complicated by hypertensive disorders of pregnancy, the woman has an increased risk in future pregnancies for development of gestational hypertension and preeclampsia, as well as an increased risk of longer term cardiovascular and medical conditions.

Consider the risk of late seizures and the peak postpartum BP when timing discharge.

Recommend follow-up after 6 weeks to ensure resolution of pregnancy-related changes and ascertain the need for ongoing care.

Provide a detailed report or form about the events of the pregnancy and birth.

Provide advice regarding future pregnancy risk reduction (e.g., calcium supplementation, low dose aspirin).

* + - Counsel for contraception.
    - Arrange for screening for pre-existing hypertension and underlying renal disease to women with a history of early onset preeclampsia, or antiphospholipid antibodies.
    - Arrange for assessment of cardiovascular risk markers for women who became normotensive following a hypertensive disorder of pregnancy (e.g., Frequent BP check, serum lipids and blood glucose)

### Lifestyle Advices and Modifications

* + Advise women that they will benefit from avoiding smoking, maintaining a healthy weight, exercising regularly and eating a healthy diet.
  + Overweight and obese women should be helped to attain a healthy BMI for long term health and to decrease the risks of hypertensive disorders in future pregnancies.

## **Preeclampsia**

### Scope and Context

* Severe hypertension, headache, epigastric pain, oliguria, and nausea and vomiting, are ominous signs, requiring urgent hospital admission and management, as does any concern about fetal wellbeing.
* Severity, timing, progression and onset of clinical features are unpredictable.
* Increasing severity may be indicated by difficulty in controlling BP and deteriorating clinical condition.
* Birth is the definitive management and is followed by resolution, generally over a few days but sometimes much longer

### Antihypertensive therapy

Refer to the previous section on antihypertensives

### Venous Thromboembolism

* + Preeclampsia is an independent risk factor for venous thromboembolism (VTE) occurring in pregnancy or the puerperium.
  + There is a need to adopt prophylactic measures to guard against venous thromboembolism

### Fluid Management

* + Administration of large volumes of intravenous fluids before or after birth may cause pulmonary oedema or worsen peripheral oedema.
  + In the immediate postpartum period, oliguria is common, and does not require fluid therapy unless serum plasma creatinine is rising.
  + Strict fluid balance monitoring, with restriction of post-birth intravenous crystalloids to 1500 mL in the first 24 hours.
  + An indwelling urinary catheter for hourly measurements may be required.
  + Diuretics are usually inappropriate, unless there is fluid overload or pulmonary edema
  + Oliguria is considered if urine output is less than 80 mL/4 hour.

## **Eclampsia**

Defined as the occurrence of one or more seizures superimposed on preeclampsia.

### Goals of Treatment

* Terminate the seizure and prevent its recurrence.
* Control of hypertension and preventing further organ-system affection.
* Prevent maternal and fetal hypoxia.

### Scope

* There are no reliable clinical markers for prediction of eclampsia.
* Hypertension and proteinuria may be absent prior to the seizure.
* Seizures may occur antepartum, intrapartum or postpartum, usually within 24 hours of birth.
* Immediate measures include:
  + Calling for help,
  + Prevention of maternal injury,
  + Placement in lateral decubitus position,
  + Prevention of aspiration,
  + Administration of oxygen,
  + Monitoring vital signs, including oxygen saturation.

### Imminent eclampsia

Defined as at least two of the following symptoms:

* Frontal headache
* Visual disturbance
* Altered level of consciousness
* Hyperreflexia
* Epigastric tenderness

### Treatment

Magnesium Sulfate is the anticonvulsant drug of choice for the prevention and treatment of eclampsia.

* ***Magnesium sulfate regimens are considered in a separate section. Please refer to the section on Magnesium Sulfate.***
* If convulsions recur, a further 2–4 grams of magnesium sulfate should be administered I.V. over 5 minutes.
* If birth has not occurred, plan as soon as feasible and when the woman’s condition is stable
* Close clinical surveillance is required in an appropriately staffed area.
* In the rare cases of an extremely agitated patient, IV clonazepam mg, diazepam 10 mg, or midazolam may be used for sedation to facilitate the placement of the IV lines and Foley catheter, and the collection of blood specimens. These drugs should be used cautiously and only if absolutely necessary because they inhibit laryngeal reflexes increasing the risk of aspiration and also may depress the central respiratory centers leading to apnea.
* In cases refractory to magnesium sulfate (still seizing at 20 minutes after the bolus or more than two recurrences), a health care provider can use sodium amobarbital (250 mg IV in 3 minutes),
* Thiopental, or phenytoin (1,250 mg IV at a rate of 50 mg/minute).
* Endotracheal intubation and assisted ventilation in the intensive care unit are appropriate in these circumstances.
* Head imaging should also be considered because most of cases refractory to magnesium sulfate therapy may prove to have abnormal findings on brain imaging

## **HELLP Syndrome**

A variant of severe preeclampsia characterized by Hemolysis, Elevated Liver enzymes and Low Platelet count).

* In women with preeclampsia, the presence of any of the following is an indicator of development of HELLP:
  + Maternal platelet count of less than 100 x 109/L.
  + Elevated liver transaminases to more than double.
  + Microangiopathic hemolytic anemia with fragments/schistocytes on blood film.

### Management

* Assemble the multidisciplinary team including a physician hematologist.
* Contact other facilities/services if necessary.
* Consider immediate birth if gestation has progressed beyond 34 weeks gestation.
* Administration of Magnesium Sulfate [refer to the Section on Magnesium Sulfate]
* Consider platelet transfusion:
  + Prior to vaginal delivery or Cesarean section if PLT count below 20 to 25X109/L
  + There is significant bleeding postpartum attributable to preeclamptic thrombocytopenia

## **Magnesium Sulfate**

### Context

Magnesium sulfate should be used for the prevention and treatment of seizures in women with gestational hypertension, severe preeclampsia, or eclampsia.

### **Practical Considerations:**

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| **Please Check the concentration of the available preparation. In Egypt two preparations are available:**   * **A 10% solution of 25ml Ampoules (Otsuka, 10th of Ramadan-Egypt). *Each ampoule (25 ml of a 10% solution) contains 2.5 grams Magnesium sulfate.*** * **A 10% solution in 5 ml Ampoules (Memphis, Cairo-Egypt). Each *ampoule (5 ml of 10% solution) contains 0.5 gram Magnesium sulfate.*** |

### Resources required

* A dedicated, trained, healthcare provider, for the duration of therapy.
* Birth-suite or high dependency unit with resuscitation and ventilator support.
* Dedicated I.V. line for Magnesium Sulfate.
* Calcium Gluconate 1 gram Ampoule available in case of respiratory depression/overdose.

### Contraindications and Precautions

* Maternal cardiac conduction disorders as heart block.
* Hypermagnesemia.
* Myasthenia gravis.
* Reduced renal function monitor plasma magnesium level/urine output.

### Side effects

Related to hypermagnesemia

* Common (greater than 1%): nausea and vomiting, flushing
* Infrequent (0.1–1%): headache, dizziness

### Administration

#### **Loading dose**

4-6 grams, I.V. infusion, over 20-30 minutes, preferably via controlled syringe pump.

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| * 2 ampoules of the 25 ml 10% preparation (5 grams), or * 10 ampoules of the 5 ml 10% preparation (5 grams). * Added to 50 ml of normal saline. * By syringe pump over 20-30 minutes, or * 50 -75 drops per minute in case using an infusion set (converting each 1 ml into 15 drops), or * 5 ml each minute by slow IV injection. |

#### **Maintenance dose**

* + 1-2g /hour, for 24 hours after last seizure or birth (whichever is latest), then review for continuation/cessation.
* **Practical considerations:**

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| * **Remember that the maximum fluid intake is restricted to 1500 ml over 24 hours.** * **The following calculations are based upon a dose of approximately 1 gram of MgSO4 per hour.** * ***If you don’t have an infusion pump, please use a dropper who converts each ml into 15 drops.***   + - **Prepare 3 bottles of 500 ml saline + 10 grams of MgSO4:**     - **In case you are using the 10%, 25ml ampoule preparation: withdraw 100 ml from each of the bottles and add 4 ampoules to each of the bottles**     - **In case you are using the 10%, 5 ml ampoule preparation: withdraw 100 ml from each of the bottles and add 20 ampoules to each of the bottles**     - **Each of the 3 bottles will be given over 8 hours with the rate of 15 drops/minute.**     - **Continue the infusion for 24 hours after delivery of the last fit** |

#### Intra Muscular administration of Magnesium sulfate:

In case of difficulties with establishing venous access, magnesium sulfate can be administered by intramuscular (IM) injection,

* 10 g initially as a loading dose (5 g IM in each buttock), followed by 5 g every 4 hours.
* The medication can be mixed with 1 mL of xylocaine 2% solution because the intramuscular administration is painful.
* The rate of adverse effects is also higher with the IM administration.

#### Baseline observations

* BP, pulse, respiratory rate, level of consciousness.
* Oxygen saturation (SpO2).
* Patellar reflex (or Biceps reflex if epidural analgesia is being administered).
* If antepartum, abdominal palpation, FHR/CTG.

#### Monitoring during loading dose

BP, pulse, respiratory rate, SpO2 every 5 minutes, for a minimum 20 minutes,

If in labor; monitor contractions for 10 minutes every 30 minutes.

Continuous CTG if greater than 24 weeks gestation.

Auscultation of FHR every 30 minutes if less than 24 weeks gestation.

Observe for side effects.

Check deep tendon reflexes after completion of loading dose. Notify if absent and do not commence maintenance dose.

#### Monitoring during maintenance infusion

* Serum Magnesium level monitoring is not required if renal functions are normal.
* Consider serum Magnesium monitoring in patients with mild renal failure (serum creatinine 1.0–1.5 mg/dL) or oliguria (less than 30 mL urine output per hour for more than 4 hours), restrict maintenance dose to only 1 gm/hour.
* If Creatinine levels are more than 1.5 mg/dl, reduce maintenance dose to 0.5 g/hour

*Serum Magnesium Concentration*

* Therapeutic range: 5-9 mg/dL. (2-3.5 mmol/L. or 4-7 mEq/L.)
* Loss of patellar reflexes: above 9 mg/dL. (>3.5mmol/L. or >7 mEq/L.)
* Respiratory paralysis: above 12 mg/dL. (>5 mmol/L. or >10 mEq/L.)
* Cardiac arrest: above 30 mg/dL. (>12.5 mmol/L. or > 25 mEq/L.)

Discontinuation and urgent clinical evaluation

* If Respiratory rate is less than 12 breaths/minute.
* dBP decreases more than 15 mmHg below baseline.
* Absent deep tendon reflexes.
* Urine output less than 80 mL/4 hours.
* Magnesium serum levels greater than therapeutic level.

##### The following measures should be considered:

* + - Discontinuation of maintenance dose.
    - Endotracheal intubation.
    - Correction with calcium gluconate 10% solution, 10 mL I.V. over 3 minutes, along with furosemide intravenously to accelerate the rate of urinary excretion.
    - If serum level decreases to less than 8.4 mg/dL. (7 mEq/L) the infusion can be restarted at a slower rate than previously used.

#### Ceasing Therapy

* + Magnesium sulfate should not be discontinued until 24 hours after delivery or the occurrence of the last fit whichever comes last.
  + Magnesium Sulfate may be continued up to 48 hours if clinical assessment indicted persistent symptoms of severity (persistent headache, epigastric pain).