

FOGSI-GESTOSIS-ICOG

Hypertensive Disorders in Pregnancy (HDP)

Good Clinical Practice Recommendations 2019

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Introduction:

- Hypertensive disorders in pregnancy (HDP) are the spectrum of disorders ranging from already existing chronic hypertension in the index pregnancy to complex multisystem disorder like preeclampsia leading to the complications like eclampsia, HELLP syndrome, acute renal failure, pulmonary edema, stroke and left ventricular failure.
- Severe preeclampsia and these complications are the major causes of maternal and perinatal morbidity and mortality. Among all maternal deaths 19 % deaths are due to hypertension in pregnancy (WHO 2014)¹ despite the phenomenal numbers of mothers seeking hospital-based delivery care, substantial gap is identified in the quality of care executed.
- The National Eclampsia Registry (NER) FOGSI -ICOG interim statistics reveals that the incidence of hypertensive diseases during pregnancy to be high with a substantial incidence of eclampsia. The incidence may be higher because many eclampsia cases which are managed by peripheral health workers remain unreported.
- Incidence of preeclampsia was found to be 10.3% (NER 2013). The incidence of eclampsia is 1.9% out of which more than 50% of the cases are antepartum, and approximately 13% of the cases occurred post-partum. Maternal Mortality attributed to eclampsia is 4-6 %.
- Due to myths and misconceptions in pregnancy, challenges in transport facilities, low socioeconomic status and lack of easy and expert antenatal care requiring multidisciplinary approach, lack of accurate prediction methods and scarcity of high dependency units (HDU) there is an unmet need in recognizing and managing HDP and its complications in low and middle-income group countries.

Need for Good Clinical Practice recommendations (GCPR):

- To categorize correct definitions based on disorder, for appropriate clinical implementation.
- To identify the risk factors for pre eclampsia and design strategy for effective predicting modalities and preventive measures.
- To outline the necessary investigations for diagnosis and management.
- To prevent and reduce maternal and neonatal mortality and morbidity because of HDP.
- To prevent eclampsia and other complications by early and effective management.
- To standardize the clinical management protocols.

Classification of HDP:²

Gestational hypertension: Blood pressure \geq 140/90 mmHg, detected beyond 20 weeks of gestation and returns to normal within 42nd postpartum day and is not associated with any other features of preeclampsia.³

Chronic hypertension: Known case of hypertension or a case of hypertension detected before 20 weeks of gestation in absence of neoplastic trophoblastic disease and multiple pregnancies.

Preeclampsia: It is a multisystem inflammatory disorder beyond 20 weeks of pregnancy with significant proteinuria characterized by de novo onset of hypertension (BP \geq 140/90 mmHg).

More recently, atypical variant of preeclampsia is recognized which is accompanied by neurological, hematological, hepatic, renal manifestations or fetal growth restriction, in absence of proteinuria.^{4,5}

Eclampsia: It is occurrence of seizures in association with preeclampsia.

It can also occur as atypical eclampsia.

Superimposed Preeclampsia: It is the occurrence of preeclampsia in women with chronic hypertension.

(Blood pressure reading should be reconfirmed after 4-6 hours before classifying a patient in particular group.)

Preeclampsia can be further classified as non severe and severe. It can also be classified as early onset and late onset as below.

Non severe preeclampsia: Blood pressure $\geq 140/90$ mm Hg and $\leq 160/110$ mm Hg
No premonitory symptoms and normal HDP laboratory parameters.

Severe preeclampsia: Blood pressure $> 160/110$ mm Hg with/without premonitory* symptoms with / without abnormal[#] HDP laboratory parameters[#].

Or

Blood pressure $\geq 140/90$ mm Hg with premonitory* symptoms and /or abnormal[#] HDP laboratory parameters.⁶

{*Premonitory symptoms: Headache, blurring of vision, vomiting, right upper quadrant pain, sudden excessive weight gain and severe edema.}

{#Abnormal HDP lab: Low platelets, elevated liver enzymes, elevated serum creatinine, and abnormal coagulation profile.}

Early onset preeclampsia: Onset of proteinuric hypertension is before 34 weeks of pregnancy.
The maternal complications are more severe.
Low birth weight, fetal growth restriction and iatrogenic prematurity are common.

Late onset preeclampsia: Onset of proteinuric hypertension is after 34 weeks of pregnancy.
The maternal complications are less severe.
Low birth weight and fetal growth restriction is less common.

Prediction of Preeclampsia:

- ✓ Universal screening is recommended but there is no single effective screening test.
- ✓ None of the tests proposed till date to predict the at-risk population for preeclampsia qualify to be recommended for the general population screening
- ✓ Thus, assessment of clinical risk factors helps us to be more vigilant.
- ✓ A careful history taken early in first trimester can warrant attention for effective prediction and prevention towards mothers 'at risk' very early.
- ✓ This can be done by any health care worker by using **HDP-Gestosis Score**.

HDP-Gestosis score: Effective and feasible prediction policy

Primary clinical assessment for screening and prediction of preeclampsia can be objectively performed by 'easy to use' HDP-Gestosis score.

Process of risk scoring:

- ✓ This score involves all the existing and emerging risk factors in the pregnant woman.
- ✓ Score 1, 2 and 3 is allotted to each clinical risk factor as per its severity in development of preeclampsia.
- ✓ With careful history and assessment of woman a total score is obtained time to time.
- ✓ When total score is ≥ 3 ; pregnant woman should be marked as 'At risk for Preeclampsia'.

Prevention of Preeclampsia:

All 'at risk' women should be started with **Aspirin 75-150 mg** ⁷.

Dose-

The optimum dose of aspirin is unclear; studies have used 60-75-100-150 mg.

Low-dose aspirin has a good maternal and fetal safety profile.

Number of patients exposed to doses over 100 mg is low.

The safety of prevention based on 150 mg of aspirin per day has to be confirmed.⁸

Aspirin tablets of 75 mg are readily available and are easiest to prescribe.

When to start?

Aspirin for this indication should be started even earlier than 12 weeks.⁹

Defective placentation is considered as the causative factor of preeclampsia.

Early aspirin balances the levels of thromboxane A₂ and prostacyclin which will maintain adequate uteroplacental blood flow and improve placentation without increasing the risks of adverse maternal and perinatal outcomes. Therefore, it appears safe to use low-dose aspirin as a prophylaxis to prevent preeclampsia throughout pregnancy until 2 days prior to delivery or cesarean section.

Along with aspirin, **calcium 1-1.5 gm**¹⁰ daily (in low calcium intake group) is to be started.

RISK FACTOR	SCORE
Age older than 35 years	1
Age younger than 19 years	1
Maternal Anemia	1
Obesity (BMI >30)	1
Primigravida	1
Short duration of sperm exposure (cohabitation)	1
Woman born as small for gestational age	1
Family history of cardiovascular disease	1
Polycystic ovary syndrome	1
Inter pregnancy interval more than 7 years	1
Conceived with Assisted Reproductive (IVF/ ICSI) Treatment	1
MAP>85 mm of Hg	1
Chronic vascular disease (Dyslipidemia)	1
Excessive weight gain during pregnancy	1
Maternal hypothyroidism	2
Family history of preeclampsia	2
Gestational diabetes mellitus	2
Obesity (BMI > 35 kg/M ²)	2
Multifetal pregnancy	2
Hypertensive disease during previous pregnancy	2
Pregestational diabetes mellitus	3
Chronic hypertension	3
Mental disorders ^{\$}	3
Inherited / Acquired Thrombophilia	3
Maternal chronic kidney disease	3
Autoimmune disease (SLE / APLAS / RA)	3
Pregnancy with Assisted Reproductive (OD or Surrogacy) Treatment	3

Systemic Lupus Erythematosus ^ Anti-phospholipid Antibody Syndrome @ Rheumatoid Arthritis

Newer screening tests for prediction of preeclampsia^{11, 12, and 13}(Refer: Annexure-3)

Many biophysical and biochemical parameters are studied for predicting preeclampsia. They are still under evaluation and will require technical skills which may not be universally available and may not be feasible in many parts of India.

Maternal Alerts

Following signs, symptoms and investigations warrant urgent and prompt management.

Persistent headache	Blurring of vision	Difficulty in breathing
Second trimester vomiting & epigastric pain		Feeling of ill being of patient
Uncontrolled hypertension	Oliguria	Brisk tendon reflexes
Altered consciousness	Sudden onset of massive edema	
sPO2 < 95 %	LDH >800 u/l	S. Creatinine >1.1mg/dl
AST / ALT- >2 times the normal	Platelets < 1, 00,000/mm ³	S. Uric Acid >8 mg/dl

Diagnosis

Signs and symptoms

1. Blood Pressure (Refer: Annexure-1)

- Blood pressure measurement is the most important clinical test to diagnostic HDP.
- BP assessment is to be done with utmost care and proper technique¹⁴ (Annexure-1). Mercury manometer periodically standardized is the ideal equipment to be used.
- The position of the pregnant mother especially after 20 weeks of gestation should be either in the sitting position or left lateral position with the zero level at the level of the heart.
- Any forearm left/right can be used to tie the cuff of the appropriate size snugly.
- In absence of mercury manometer, calibrated aneroid equipment may be used.

2. Proteinuria¹⁵

- Significant proteinuria is urinary excretion of > 300 mg protein in a 24-hour period.
- Once significant proteinuria is established, further quantification is not required as proteinuria does not have prognostic value from management point of view.
- However, if proteinuria is absent, pregnant woman with hypertension still requires frequent monitoring.
- The HDP Gestosis scientific group recommends the following methods till further research findings are out -
 - Urinary dipstick method (Visual / by automated device)
 - Spot urine protein: creatinine ratio¹⁶.
- Significant proteinuria: can be assessed by urinary dipstick: $\geq 2+$
Or urinary protein: creatinine ratio ≥ 30 mg/mmol.
- Urinary dipstick method is quick and allows women with negative result to return home quickly. It also helps quick assessment of severe proteinuria.
- The results of spot protein: creatinine also would be available within 2 - 4 hours.
- It is convenient for women at risk for pre-eclampsia and their health professionals.
- The gold standard of assessing proteinuria is 24-hour urine protein assessment.

3. Laboratory Investigations (Refer: Annexure-2)

When blood pressure reading of a pregnant woman is $\geq 140/90$ mmHg (or known case of chronic hypertension visits first time to the antenatal clinic), following investigations are advisable to assess severity of the disease.

- **Baseline HDP lab**
 - ✓ Urine albumin- by dipstick method **or** urine protein: creatinine ratio
 - ✓ Complete blood count: Platelet count and anemia assessment
 - ✓ Liver enzymes- Alanine aminotransferase (ALT), Aspartate transaminase (AST),
Lactate Dehydrogenase (LDH).
 - ✓ Serum bilirubin
 - ✓ Serum creatinine
 - ✓ Serum uric acid^{17,18}

- **Additional laboratory investigations**
 - ✓ Coagulation profile (when platelet count is $< 1,00000 /\text{mm}^3$)
 - ✓ Serum electrolytes (in severe disease)

4. Ultrasonography

- **Maternal ultrasonography** (USG abdomen and pelvis)
Following things are suggested to be assessed in addition to obstetric evaluation:
 - ✓ Liver: sub-capsular hematoma, hepatomegaly.
 - ✓ Kidney: signs of renal causes of hypertension, other changes in renal parenchyma.
 - ✓ Ascites and pleural effusion: as other worsening signs of preeclampsia.
- **Fetal surveillance and placental morphology** (Obstetric USG with doppler) ¹⁹
 - ✓ Fetal biometry, amniotic fluid volume (AFI), uterine artery doppler and umbilical artery doppler should be performed at the first diagnosis of preeclampsia.
 - ✓ In confirmed preeclampsia or in cases of fetal growth restriction, serial evaluation of fetal growth, AFI, uterine artery umbilical artery doppler is recommended.
 - ✓ More frequent ultrasound measurements and color doppler study are needed if there is a high resistance or absent or reversed end-diastolic flow in uterine artery with appropriate further management.
 - ✓ Placental location, morphology and any evidence of placental bed hemorrhage, abnormal adherence and presence of sinusoids should be documented.

5. Fundoscopy

- ✓ Fundoscopy may be required to differentiate chronic and new onset disease and to diagnose papilledema/ hemorrhages as these have ominous prognosis.

6. Additional imaging

- ✓ 2D maternal ECHO: May be required in special situations where the mother is at a higher risk of developing cardiovascular complications.
- ✓ Chest X-ray with shield: X-ray may be necessary in situations where ARDS, pulmonary edema or pulmonary embolism is suspected.
- ✓ MRI for brain imaging maybe necessary for diagnostic dilemma of eclampsia, venous sinus thrombosis and cerebrovascular accident.
Neuro imaging is not recommended universally in all cases of eclampsia.

Medical management

World Organization Gestosis recommends that a systolic BP of ≥ 140 and/or a diastolic BP of ≥ 90 mm Hg warrants antihypertensive therapy.²⁰

Target range of Blood Pressure to be kept:

Systolic ≤ 140 mm of Hg

Diastolic ≤ 90 mm of Hg

Avoid hypotension.

Anti-hypertensives (Mild Preeclampsia)

1. Labetalol²¹: 200 - 1200 mg / day in 2 divided doses

It is accepted as the first line and effective medication during pregnancy.

Preferred medication when baseline pulse is >100 /min

It is contraindicated in asthma, CCF, DM and cases of bradycardia.

2. Nifedipine²¹: 20-120 mg / day of slow releasing preparations in 2-3 divided doses

Preferred medication when baseline pulse is < 100 /min

Maternal adverse effects include tachycardia, palpitations, headaches, and facial flushing.²²

Never administer nifedipine sublingually.

3. Methyldopa²³: 500-2000 mg per day orally in 2-3 divided doses.

Methyl dopa is the most time tested and safe anti-hypertensive.

Nowadays it is not routinely available.

Drug is to be discontinued in postpartum period to avoid postpartum depression.

Drugs contraindicated in pregnancy: ACE inhibitors, ARBs, β - blockers and diuretics.

Anti-hypertensives for rapid control (Severe Preeclampsia)

Drug	Dosage	Points to remember
Nifedipine ²¹	10-30 mg orally (Not sublingually) If BP is not controlled, can be repeated within 30-45 minutes. Max total dose of 120 mg is not to be exceeded. Once controlled, slow release preparations are to be started.	Contraindicated in CCF and AV or SA nodal abnormalities
Labetolol ²¹	<u>Slow IV injections:</u> 10 to 20 mg IV, then 20 to 80 mg every 20 to 30 minute Max total dose of 300 mg is not to be exceeded <u>Alternate IV infusion regimen:</u> After initial loading dose, an infusion can be started at 1–2 mg/min and is titrated until desired effect. Oral tablets can be used in a conscious patient in the dose of 200mg	Contraindicated in CCF, DM, Asthma and bradycardia.
Hydralazine ²¹	5 mg, IV or IM, then 5 to 10 mg every 20 to 40 minutes; once BP controlled repeat every 3 hours; for infusion: 0.5 to 10.0 mg/h; if no success with 20 mg IV or 30 mg IM, consider another drug	It has been associated with more maternal and perinatal adverse effects than intravenous labetalol or oral nifedipine such as maternal hypotension, cesarean sections, placental abruptions and oliguria. ²⁴
Nicardipine ^{25,26}	The average starting dose is 1.5 mg/h It can be increased up to 6 mg/h for desired effect according to 0.5 µg/kg/min equation.	It is 100 times more water soluble than nifedipine, so it can be administered i.v. making it an easily titratable i.v. calcium channel blocker.

Target – < 140 / 90 mm Hg

Lower the blood pressure promptly but slowly.

Seizure prevention

Loading dose of MgSO₄ is recommended to prevent eclampsia in all cases of severe preeclampsia.

Delivery decision[#]

Gestational Hypertension:	Pregnancy can be continued till the term
Mild Preeclampsia:	To be delivered at 37 completed weeks.
Severe Preeclampsia:	To be delivered after 34 completed weeks.
Eclampsia:	Should be delivered once mother is stabilized after MgSO ₄ .

Labor induction with appropriate method can be carried out safely.

Cesarean section is done for obstetric indications only.

Delivery decision should be carefully decided after assessing maternal and fetal risks.²⁷

Corticosteroids

- ✓ Corticosteroids are recommended in all women delivering before 34 completed weeks²⁸ and in case of elective cesarean delivery before 38 completed weeks.
- ✓ Intramuscular dexamethasone: 6 mg 12 hourly 4 doses or
- ✓ Intramuscular betamethasone: 12 mg 24 hourly 2 doses can be used for reducing neonatal respiratory distress.
- ✓ Even a single dose of steroid at least an hour prior to delivery can reduce the neonatal respiratory distress syndrome remarkably.

Management of eclampsia

Eclampsia is a situation needs to follow the principles of ABCD of critical management.

Team work and personnel is needed for effective management.

Principles of management of eclampsia

“Call for help”: timely additional help is essential for effective management

- | | |
|----------------------------|--|
| (1) A: Airway: | Lateral decubitus position, mouth gag and neck extension
Avoid injury to the mother |
| (2) B: Breathing: | Nasal oxygen and suction
Pulse oximeter: oxygen saturation >96% |
| (3) C: Circulation: | IV access for maternal resuscitation
Laboratory investigations are sent.
Crystalloids: Ringer Lactate or Normal Saline 80 ml/hr.
Control of convulsions: Magnesium sulphate-Loading and maintenance dose.
Catheterization: Foley’s catheter is inserted.
Control of blood pressure: With anti-hypertensives
Corticosteroids: For gestational age <34 weeks |
| (4) D: Delivery: | Baby should be delivered once mother is stabilized. |

Magnesium Sulphate:

It is the safest drug recommended as first choice pharmacotherapy for eclampsia .²⁹

Pritchard regimen³⁰ is the preferred regimen worldwide.

Use 50% w/v ampoules preferably - as each ampoule contains 1 gram; easy for dose calculation.

MgSO₄ is to be continued 24 hours after delivery or last convulsions whichever is the last.

Serum magnesium monitoring is not required routinely.

Intramuscular regimen (Pritchard)

Loading dose (Total 14 gram = 4g slow IV as 20 ml (20% solution) + 5 g (50% solution) deep IM

Intravenous: 4gram (4 ampoules of 50% w/v MgSO₄ + 12 ml distilled water in 20 ml syringe) slow IV at the rate of 1 gram over 1 minute.

Intramuscular: 5gram (5 ampoules of 50% w/v MgSO₄ +0.5 ml 2% Lignocaine) deep i.m. (In 10 cc syringe& with 20-G long needle) in each buttock.

Maintenance dose (5 g deep IM in alternate buttock 4 hourly)

Intramuscular: 5gram (5 ampoules of 50% w/v MgSO₄ +0.5 ml 2% Lignocaine) deep IM in alternate buttock.

Maintenance dose will be given **only if** following parameters are present.

1. Respiratory rate > 16 / min
2. Patellar reflexes present
3. Urine output >100 ml in last 4 hours.

Absence of above parameters denote different approach

Intravenous regimen (Zuspan)

Loading dose (4 gram slow IV as 20 ml 20% solution)

Intravenous: 4gram (4 ampoules of 50% w/v MgSO₄ + 12 ml distilled water) slow i.v.

Maintenance dose 5 gm (5 ampoules of 50% w/v MgSO₄ to add in 500 ml RL)

Intravenous infusion rate 100 ml/ hour = 1 gm / hour preferably administered through infusion pump

Management of Magnesium over action:

Stop further doses of MgSO₄.

Oxygen (Nasal / by mask)

Intubation, if required.

10 ml 10% Calcium Gluconate is given slow i.v. over 10 minutes with ECG monitoring.

Management after stabilization

Deliver the patient after stabilization in the situations like eclampsia, HELLP, severe preeclampsia, chronic hypertension with superimposed preeclampsia and if gestational age is more than or equal to 34 weeks. Vaginal delivery may be considered if attainable in reasonable amount of time. In case of preterm pregnancy, expectant management can be considered with individual assessment and antenatal steroids and rationale use of antihypertensive medications with close supervision. When gestational age is ≤ 24 weeks, immediate delivery is a better option. Mothers with chronic hypertension can be offered expectant management under close surveillance. Approach should be individualized between the gestational age of 24-33 weeks as no evidence exists.

Intrapartum management:

It is preferable to conduct delivery in a well-equipped birthing centre with facility of obstetrical expertise and accessible obstetric high dependency and/or critical care units with blood bank, anesthesiologist, neonatologist and a transfer facility.

Mode of delivery:

It depends upon the urgency to deliver, cervical Bishop's score, gestational age, severity of FGR and doppler study findings in the umbilical artery

Induction of labor:

Induction of labor should be offered to mothers eligible for vaginal delivery. Prostaglandins (PGs) (dinoprostone gel, suppositories or tablets) can be used for induction. Misoprostol may be used in patients remote from term. Mechanical dilatation of the cervix with-Foley's balloon or vaginal hygroscopic dilators may be considered. Augmentation of labor is to be done only with oxytocin.

Caesarean delivery:

Severe FGR or REDF in the umbilical artery on color Doppler or any obstetric contraindication for vaginal delivery or failure of induction may make cesarean delivery a preferred choice.

Fluid Management:

Inappropriate use of fluids can cause pulmonary edema and maternal death. Fluid restriction is advisable to reduce the risk of fluid overload in the intrapartum and postpartum periods. No fluid expansion should be used and total fluid restriction to

80ml/hr or 1ml/kg/hr is beneficial. Additional 700ml can be used for nonsensical loss. Crystalloids like Ringer's lactate or normal saline are used.

Intrapartum fetal monitoring:

Close monitoring of the fetus with continuous or intermittent Doppler device or EFM (electronic fetal heart monitoring) is preferred. Laboratory investigations may be repeated when required.

Preventing PPH:

Active management of third stage of labour and prophylactic administration of oxytocics in case of cesarean delivery should be followed in all cases. It is safe to use oxytocin 5 U bolus equally diluted over 2-3 minutes or prostaglandin (PG) injections. PG can be used also as misoprostol sublingual, transrectal or transvaginal.

Average blood loss of labour may not be well tolerated by these patients due to hemoconcentration.

Underlying endothelial dysfunction, hypertension and use of magnesium sulphate may make the mother more susceptible to PPH.

The use of fluids should be judicious. Recommendation is 80 ml/hr or 1ml/kg/hr as over-infusion can cause pulmonary edema in these women.

Post-delivery management

It involves close vigilance for eclampsia, PPH, HELLP, pulmonary edema, cardiovascular, cerebrovascular events and thrombo-embolic complications.

Continued postpartum surveillance has to be the norm to prevent additional morbidity as gestosis can develop post-delivery.

During the hospital stay, blood pressure should be closely monitored for first 48 hours post delivery. Postpartum use of NSAIDs should be avoided. Antihypertensive therapy is recommended for persistent BP of SBP > 150 and DBP > 100 mm Hg. Persistent BP of ≥ 160 SBP and or DBP of ≥ 110 mm Hg should be treated within one hour and magnesium sulphate considered for seizure prophylaxis.

Discharge planning:

After stabilization discharge can be considered with instructions for home surveillance and regular follow up. Patients should be made aware of warning signs and symptoms

(Annexure-4) and the importance of reporting to the hospital in case of they are encountered.

Post discharge management:

Home BP monitoring by self or a visiting HCP should be regularly practiced and OPD review must be within 3-5 days or earlier if symptoms persist or recur.

Postpartum Care

Every patient of preeclampsia should be monitored closely for 3 months with advice regarding antihypertensive medicines and regular visits. They should be guided and encouraged to use contraception at least for a period of 2-3 years. The preferred method would be an IUCD. They should be counseled regarding the importance of preconceptional counseling in subsequent pregnancy.

Long term surveillance:

Every mother should be advised long term surveillance as preeclampsia increases long-term risk of chronic hypertension, IHD, cerebrovascular disease, kidney disease, DM, thromboembolism, hypothyroidism and impaired memory.

Shifting to an equipped facility

When patient is shifted to better equipped facility following measures should be taken.

Magnesium sulphate- Loading dose of Pritchard regimen must be given and informed to the referral centre.

Antihypertensives in the form of Nifedipine 20 mg (slow release) or tablet labetalol 200 mg orally along with the regular antihypertensive if already being taken by the patient (No sublingual nifedipine)

Dexamethasone 8 mg or betamethasone 12 mg injection IM stat for fetal lung maturity if gestational age less than 37 weeks.

Transfer with attendance and monitoring and information to the receiving center along with the eclampsia kit

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Annexure 1: Precautions while taking blood pressure. (Technique and Device)

1. Patient must be seated, with feet supported, for 2–3 minutes before B.P. is measured.
2. Left lateral recumbence is preferred than supine position in the bed-bound mother.
3. Blood pressure should be taken on both arms at the first antenatal visit.
4. The right arm should be used thereafter if there is no significant difference between the arms.
5. First systolic blood pressure (SBP) should be taken at brachial artery by palpation method.
6. SBP is taken again with auscultatory method at Korotkoff phase I (K1).
7. Diastolic blood pressure (DBP) is recorded as Korotkoff phase V (K5) and if K5 is absent, it can be recorded as Korotkoff phase IV (K4).
8. A standard cuff should be used for arms with a circumference of ≤ 33 cm while the large cuff (15 × 33 cm bladder) when circumference is >33 cm with the lower end of the cuff 2.5 cm above the antecubital fossa.
9. The mercury sphygmomanometer is the ‘gold standard’ for blood pressure measurement.
10. In absence of mercury manometer, calibrated and properly standardized aneroid / digital equipments may be used.

Annexure 2: HDP laboratory parameters

Sr. No.	Test	Unit	Non pregnant	I trimester	II Trimester	III trimester
1	ALT	U/L	7-41	3-30	2-33	2-25
2	AST	U/L	12-38	3-23	3-33	4-32
3	Bilirubin	mg/dL	0.3-1.3	0.1-0.4	0.1-0.8	0.1-1.1
4	LDH	U/L	115 – 211	78 - 433	80 - 447	82 - 524
5	Uric Acid	mg/dL	2.5 - 5.6	2 - 4.2	2.4 - 4.9	3.1 - 6.3
6	Creatinine	mg/dL	0.5 - 0.9	0.4 - 0.7	0.4 - 0.8	0.4 - 0.9
7	Sodium	mEq/L	136 – 146	133 - 148	129 - 148	130 – 148
8	Potassium	mEq/L	3.5 – 5	3.6 - 5	3.3 - 5	3.3 - 5.1
9	Albumin	g/dL	4.1-5.3	3.1-5.1	2.6-4.5	2.3-4.2
10	Proteins (Total)	g/dL	6.7-8.6	6.2-7.6	5.7-6.9	5.6-6.7

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Annexure 2: HDP laboratory parameters

Uterine Artery doppler

Uterine artery doppler analysis is well studied in the second trimester of pregnancy as a predictive marker for preeclampsia.

The second trimester uterine artery doppler studies at 18-20 weeks have shown 70-80% detection rate for late onset preeclampsia and 30-40% early onset preeclampsia in high risk patients. It has a high negative predictive value of 92-94%.¹

In recent years, first-trimester Doppler of the uterine artery performs better in the prediction of early-onset than late-onset preeclampsia.

As an isolated marker of future disease, its sensitivity in predicting preeclampsia and fetal growth restriction in low risk pregnant women is moderate, at 40–70%.²

First trimester uterine artery PI combined with maternal characteristics could predict 45% of preterm preeclampsia at a false positive rate of 10%.³

Biochemical Parameters

Vascular endothelial growth factor (VEGF)

Soluble fms-like Tyrosine Kinase 1(sFlt-1)

Placental growth factor (PlGF)

Soluble endoglin

Glycosylated fibronectin

These above markers in combination increase the predictive value but are not cost effective at present.^{4,5}

There are many other markers used to improve predictivity but have not proven to be consistent while it is clear while it is clear that maternal characteristics combined with biochemical and biophysical markers are more sensitive in predicting preeclampsia than maternal characteristics alone⁶, there is currently insufficient evidence to support a recommendation on any particular approach.

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Annexure-4 Warning symptoms and signs for patients

Headache	Reduced fetal movements
Vomiting	Absence of fetal movements
Abdominal pain	Seizures
Giddiness	Bleeding from the genitalia
Syncope	Acute pain in the womb
Blurring vision	Hardening of the womb

