

Hypertensive Disorders Of Pregnancy (HDP)

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1.INTRODUCTION

Hypertensive disorders are common complications of pregnancy, affecting 5% to 10% of all gestations. Approximately 1/3 of hypertensive disorders in pregnancy (HDP) are due to chronic hypertension and 2/3 are due to gestational hypertension–preeclampsia. The spectrum of the disease ranges from mildly elevated blood pressures with minimal clinical significance to severe hypertension and multi organ dysfunction.

Eclampsia is associated with around 10% of maternal deaths and an estimated 50,000 women die each year having had an eclamptic convulsion (*Khan 2006*)

About one-third of women will have their first fit after delivery of the baby

Understanding the disease process, its impact on pregnancy and management protocols are important, as hypertensive disorders remain a major cause of maternal and perinatal morbidity and mortality.

FOGSI recognizes the problem of HDP and the need for recommendations as there is no uniformity in diagnosis and management protocols.

In addition members are encouraged to report to the FOGSI – ICOG National Eclampsia Registry to generate Indian data (www.ner-fogsi.in).

Context : The National Eclampsia Registry in its initial format(2008-10) has a report of 134775 delivery cases out of which 2554 had eclampsia . Thus the prevalence observed in the registry is 1.9% while the national sample surveys in the past have mentioned it to be 1-5 % .The prevalence of pregnancy with hypertension was reported to be 8.3% (n=11266) with the prevalence of preeclampsia being 11.71% with a total of 15784 cases . 3428 had severe preeclampsia and 1090 imminent eclampsia thus enhancing the importance of this guideline.

The NER in the new format since 2011 reveals prevalence of pregnancy hypertension continues to be 9 % and that of preeclampsia 5 %. EOPET (early onset preeclampsia) is of concern as 42% had onset of hypertension before 34 weeks while 55% were reported to have hypertension after 34 weeks.

2. Diagnosis of hypertensive disorders in pregnancy

- 2.1** Hypertension in pregnancy should be defined as a systolic BP of \geq 140 mm Hg and / or diastolic BP of \geq 90 mm Hg on two occasions at least 15 min apart, taken on same arm.
- 2.2** Preeclampsia is defined as BP \geq 140 / 90 mm Hg, with two readings taken at least 15 min apart with proteinuria* beyond 20 weeks of gestation.
- 2.3** Eclampsia is tonic clonic convulsions in women with preeclampsia.
- 2.4** Chronic hypertension in pregnancy is defined as BP \geq 140/90mm of Hg before 20 weeks of pregnancy.
- 2.5** Gestational hypertension is defined as BP \geq 140 / 90 mm Hg, without proteinuria beyond 20 weeks of gestation, which returns to normal within 42 days postpartum.
- 2.6** Superimposed preeclampsia is new occurrence of preeclampsia in pregnant patient with chronic hypertension.

- 2.7 Severe hypertension should be defined as systolic BP of ≥ 160 mmHg and /or diastolic BP of ≥ 110 mmHg.

{* Significant proteinuria is defined as greater than 300 mg protein in 24-hour urine collection. (Corresponds to DIPSTICK 3+)}

3. Measurement of blood pressure

- 3.1 BP should be measured with the woman in the sitting position with the arm at the level of the heart.
- 3.2 An appropriately sized cuff (i.e., length of 1.5 times the circumference of the arm) should be used.
- 3.3 While taking BP, device should be at heart level of patient.
- 3.4 Korotkoff phase V should be used to designate diastolic BP.
- 3.5 If diastolic BP is less than 40 mm Hg, Korotkoff phase IV is taken to designate diastolic BP.
- 3.6 BP can be measured using a mercury sphygmomanometer, calibrated aneroid device, or an automated BP device. (Automated BP machines should be validated as they may record lower BP readings.)

4 Assessment of proteinuria in HDP

- 4.1 Use of a urine protein dipstick (automated reagent-strip) reading device is recommended.
- 4.2 Significant proteinuria is defined as greater than 300 mg protein in 24-hour urine collection. (Corresponds to DIPSTICK 3+)
- 4.3 More definitive testing for proteinuria is encouraged by urinary protein: creatinine ratio or 24-hour urine collection when feasible.

5. Predicting preeclampsia

- 5.1 At the first antenatal visit, women having increased risk (any one high risk factor or any two/more moderate risk factors) for developing preeclampsia should be counseled and given special attention.

5.1.1 High risk factors :

Hypertensive disorder during previous pregnancy
Chronic renal disease
Systemic Lupus Erythematosus (SLE), Anti Phospho Lipid Antibody Syndrome (APLA)
Type 1 or Type 2 diabetes
Chronic hypertension

5.1.2 Moderate Risk Factors

First pregnancy
Age 40 years or older
Pregnancy interval of more than 10 years
Body mass index (BMI) of 30 kg/m² or more at first visit
Family history of pre-eclampsia
Multifetal pregnancy

Context : The NER observed that the disease afflicts the young women rendering them morbid and 79% of women were in the age group of 21 -

30 years and what was appalling was that 16-17% were from the adolescent age groups of 16-19 years of age . This is the reflection of the social reality of still existing teenage marriages and their consequences. The disease essentially is the disease of the primigavidas as 81% of the mothers were pregnant for the first time. 16.51% were multiparas while 2.2% were grandmultiparas

5.2 There is insufficient data to support other tests/markers for prediction of HDP.

6. Preventing preeclampsia and complications in women at increased risk

6.1 Calcium supplementation (at least 1 g/day) is recommended for women with low calcium intake.

6.2 Low-dose aspirin (75 mg/day) should be administered daily starting pre-pregnancy or from diagnosis of pregnancy till delivery.

6.3 There is insufficient evidence to support use of following in prevention of HDP. LMW heparin, progesterone, diuretics, nutritional supplements multivitamins selenium ,zinc ,magnesium ,vitamin C,vitamin E, garlic, other antioxidants, lifestyle intervention bed rest,, exercise, Salt Restriction , Isosorbide mono nitrate S-nitroglutathione, Calorie restriction in overweight women during pregnancy, Weight maintenance in obese women during pregnancy

7. Antenatal maternal surveillance in preeclampsia / gestational hypertension

7.1 Frequent maternal surveillance is recommended, at least once a week or even more as per maternal conditions.

7.2 The baseline laboratory investigations recommended are: CBC with platelet count, assessment of proteinuria, Liver Function Tests, and Renal Function Tests and additional tests (Coagulation profile, LDH) as and when required.

Context : The NER reveals that 35 % of patients had hemoglobin between 7-9 /dl while 4 % had severe anemia of less than 7gm/dl. LDH levels and platelet counts have been identified as important laboratory investigations to estimate the gravity of the disease and to help guide us about the existence of HELLP. It was observed that nearly 40 % of the eclamptics did not undergo LDH and 13 % didnot undergo platelet estimations. This calls for standardization in evaluation protocols of these patients

7.3 Women with gestational hypertension or mild preeclampsia before 34 weeks should be followed keeping close watch on signs and symptoms of severity of HDP.

Context : The early onset preeclampsia (EOPET) is surely a grave disease and 35% of the mothers(NER) reported with onset of preeclampsia between

28-34 weeks of gestation while 42% had hypertension starting after 34 weeks

7.4 The signs and symptoms of severity, requirement of admission, transport facility, knowledge of complications and management options as well as neonatal issues must be discussed with patient and relatives.

Context : The patients of eclampsia as per the registry had predominantly sought care in the second and the third trimester (90% : 49% ,40% respectively) . Very few (10 %) had sought antenatal care in the first trimester . The details of the contents of the care were not analysed and this can be an important area to be evaluated probably through retrograde analysis.

8. Fetal surveillance in mild gestational hypertension / mild preeclampsia

8.1 In women before 34 weeks of gestation, carry out ultrasound for fetal growth and amniotic fluid volume assessment and umbilical artery doppler velocimetry. If results are normal, do not repeat after 34 weeks, unless otherwise clinically indicated.

8.2 In women after 34 weeks of gestation, do not carry out ultrasound fetal growth and amniotic fluid volume assessment and umbilical artery doppler velocimetry unless clinically indicated.

8.3 NST can be done if woman complains about reduced fetal movements.

9. Fetal surveillance in severe gestational hypertension / severe preeclampsia

9.1 If conservative management is planned, carry out

a. USG for fetal growth and amniotic fluid assessment

b. Umbilical artery Doppler velocimetry

c. Non Stress Test (NST) (*It may be inconclusive before 32 wks*)

9.2 USG and Doppler are to be repeated two weekly. NST is repeated weekly.

9.3 Repeat NST in addition if any of the following occur:

Woman reports reduction in fetal movement

Vaginal bleeding

Abdominal pain

Deterioration in maternal condition

9.4 Based on fetal surveillance decision of delivery is to be considered.

10. Antihypertensive therapy for preeclampsia / gestational hypertension

10.1 Antihypertensive therapy should be started with systolic BP \geq 150 and /or diastolic BP \geq 100 mm Hg.

10.2 Aim of therapy should be to lower BP to less than 140 mmHg systolic and less than 90 mmHg diastolic.

10.3 Oral antihypertensive agents to be used are: alpha methyl dopa, labetalol, and nifedipine. The medical provider must be familiar with the

dose to be used, the expected onset of action, and potential side effects of each of these medications.

- 10.4 Nifedipine should not be given sublingually.
- 10.5 Angiotensin converting enzyme inhibitors and angiotensin receptor blockers are contraindicated during pregnancy.
- 10.6 Chronic hypertensive women already on these medications should be switched to safer antihypertensive during pregnancy
- 10.7 Atenolol and Prazosin are not recommended

Context : There is a significant improvement in the care delivered noted as per the newer format of the registry with 96 % receiving antihypertensive treatment and 99% receiving magnesium sulphate .The Pritchard's regimen is more popular with 70.8% patient getting this while 7 % were offered Zuspan's regimen and 20 % cases were treated with low dose regimen . Nifedepine is a popular antihypertensive agent and methyl dopa next in the line of preference followed closely by labetalol . 1.3% patients also received atenolol in spite of it not being recommended antenatally

11. **Antihypertensive therapy for severe hypertension**

(BP of ≥ 160 mmHg systolic or ≥ 110 mmHg diastolic)

- 11.1 BP should be lowered to less than 150 mmHg systolic and between 80–100 mm of Hg diastolic.
- 11.2 Gradual reduction in blood pressure in first 60 minutes of therapy, i.e. systolic level of 155 to 160 mm Hg and a diastolic level of 100 to 110 mm Hg, is recommended.
- 11.3 IV Labetalol and/or Oral Nifedipine or IV Hydralazine can be used to treat severe hypertension in pregnancy as long as the medical provider is familiar with the dose to be used, the expected onset of action, and potential side effects of each of these medications.
- 11.4 Nifedipine and Hydralazine can cause tachycardia. They are not recommended to be used in patients with heart rate above 100/min. Labetalol is appropriate drug in such patients.
- 11.5 Labetalol should be avoided in patients with bradycardia (heart rate <60 bpm), asthma, and in those with congestive cardiac failure. Here, Nifedipine is the drug of choice.
- 11.6 MgSO₄ is recommended to prevent eclampsia and not as an antihypertensives.
- 11.7 Nifedipine and MgSO₄ can be used concurrently.
- 11.8 Sublingual Nifedipine is not recommended.
- 11.9 Diuretics are not recommended for routine use except some conditions like fluid challenge in oliguria and pulmonary edema.
- 11.10 In severe preeclampsia, Inj. MgSO₄, Pritchard regimen*/ZUSPAN# iv regimen is recommended till 24 hours post delivery
- 11.11 Antihypertensive treatment should be continued throughout labor and delivery to maintain systolic BP at <160 mmHg and diastolic BP at < 110 mmHg.
(Refer annexure I for details of antihypertensive medications).

Context : Out of the reported cases to the NER 50% had more than one convulsion before being admitted and 13 % even more than 4 .The duration between the onset of confusion and admission in the reporting facility was found to be more than 4 hours in 32% of the cases while 72% reported between 1-4 hours The facts revealed from this is that referral and transit therapy needs to be enhanced and also the access to the facility may not be easy in these situations. After admission 22.7% patients had convulsions while 78% received effective care and didnot have seizures.It was observed that only 44% patients had received magnesium sulphate before admission, 29% received nifedepine while 11% received diazepam. Looking at the magnanimity of the problem the need to train the healthcare personnel in delivering magnesium sulfate in the right dose and without fear is hugely felt.

12 Management of eclampsia

12.1 Following are the principles of management of Eclampsia :

Call for Help

Avoid tongue bite

Avoid injury

Maintain oxygenation O₂,

Minimize aspiration

Initiate

Control

Delivery

Insert airway / mouth gag

Padded bed rails, restraints.

pulse oximetry.

Lateral decubitus position, oral suction

Magnesium Sulfate.

Blood pressure.

(LSCS is preferred for obstetric/ fetal indications only.)

12.2 Drug of Choice is MgSO₄. It is safe drug. Pritchard regimen is preferred regimen.

12.2.1 Loading dose :4 gram {4 ampoules of 50% w/v MgSO₄ +12 ml normal saline or sterile water} slow I.V. at 4ml / 5min rate using 20 ml syringe is given.5 gram {5 ampoules of 50% w/v MgSO₄ +1 ml 2% Lignocaine} injection is given deep intramuscular in each buttocks using 10 ml syringe.

12.2.2 Maintenance dose : It is given every 4 hourly as 5 gram {5 ampoules of 50% w/v MgSO₄ +1 ml 2% Lignocaine} deep intramuscular injection in alternate buttocks monitoring following signs:

1. Respiratory rate - > 16 / min
2. Patellar reflexes are present
3. Urine output- > 100 ml in last 4 hours (25ml/hour)

(Serum monitoring of magnesium levels are not routinely recommended as not been shown to be superior to clinical monitoring). Maintenance dose is given till 24 hours past delivery or last convulsion whichever is late.

12.2.3 Administer the full magnesium sulfate loading dose before transfer to a higher level health-care if management of such patients is not possible at that facility.

12.2.4 Dose for recurrence of convulsion:After loading dose, if convulsions do not stop or / recur repeat 2 gram MgSO₄ slow IV or alternatively IV Diazepam or IV Thiopentone Sodium are given.

12.3 Alternate regimen is Zuspan IV regimen :

12.3.1 Loading dose :4 gram {4 ampoules of 50% w/v MgSO₄ +12 ml normal saline or sterile water} slow i.v. using 20 ml syringe is given at a rate not to exceed 1g/min.

- 12.3.2 Maintenance dose :It is given as an infusion of 1 g per hour till 24 hours past delivery or last convulsion whichever is late.
- 12.3.3 This regimen requires vigilant monitoring and is recommended in certain situations like thrombocytopenia (< 75000 platelets/ mm³) or DIC where intramuscular injections are avoided.
- 12.4 Vaginal delivery is preferred so induction of labor is recommended immediately after stabilization of patient. Cesarean section is done for obstetric indications.
- 12.5 Continue use of antenatal antihypertensive treatment during labor.

13 Place of care

- 13.1 Day care or home care may be considered for women with mild preeclampsia or non-severe gestational hypertension with more frequent antenatal visits.
- 13.2 For women with severe hypertension or severe preeclampsia and eclampsia in- patient care in well equipped hospital should be provided.

Context : Out of the 98 patients of eclampsia analyzed through the NER for complications 30 % were shifted to ICU care stressing the need of obstetric HDU .1 % died, 14 % had abruptio placentae ,10% postpartum hemorrhage , 7 % pulmonary edema, 6% status elcampticus and 1 % magnesium toxicity .20 % had HELLP syndrome while 3% adult respiratory distress syndrome and 4 % had ARF .

14 Antenatal corticosteroids

- 14.1 Antenatal corticosteroid therapy is recommended for all women who present with gestational hypertension /preeclampsia before 34 weeks' gestation.
- 14.2 Inj. Betamethsone 12 mg I.M. 24 hours apart two doses or Inj. Dexamethsone 6 mg I.M. 12 hours apart four doses.
- 14.3 In case of severe preeclampsia/eclampsia where delivery is imperative, total dose of 24 mg of either drug can be given within 24 hours.

15 Timing of delivery of women with preeclampsia/ eclampsia

- 15.1 In all women with mild preeclampsia/ mild gestational hypertension with 37weeks gestation, delivery should be considered.
- 15.2 Women with severe preeclampsia with =/<25 weeks gestation should be delivered.
- 15.3 For women at 25 - 34 weeks' gestation, expectant management of severe preeclampsia may be considered, but only in centers capable of caring for very preterm infants and provided there is no evidence of maternal complications as:
 - Organ involvement
 - Thrombocytopenia
 - HELLP Syndrome
 - Symptoms of cerebral irritation

- Labor
- Abruptio
- Immediate danger to the fetus if pregnancy is prolonged.
- 15.4 For women with severe preeclampsia, with > 34 weeks there is insufficient evidence to make a recommendation about the expectant management. Expectant management may be considered provided there is no evidence of maternal complications as:
 - Organ involvement
 - Thrombocytopenia
 - HELLP Syndrome
 - Symptoms of cerebral irritation
 - Labor
 - Abruptio
 - Immediate danger to the fetus if pregnancy is prolonged.
- 15.5 For women with eclampsia, after initial stabilization delivery should be planned irrespective of gestational age.

16 Mode of delivery in HDP

- 16.1 Vaginal delivery is preferred for women with any type of HDP.
- 16.2 Caesarean section is required for obstetric indications.
- 16.3 Choice of anesthesia for women undergoing caesarean section: Regional anesthesia provided there are no contraindications such as thrombocytopenia ($<75,000/ \text{mm}^3$) or altered coagulation profile.

17 Intrapartum care

- 17.1 During labor, monitor blood pressure hourly in women with mild hypertension and more frequently (20-30 min) in women with severe hypertension. Watch for signs and symptoms of imminent eclampsia.
- 17.2 Continue use of antenatal antihypertensive treatment during labor.
- 17.3 Repeat hematological and biochemical tests during labor.
- 17.4 Vigilant fetal monitoring is recommended.
- 17.5 Cut short the second stage of labor in women with severe hypertension not responding to initial treatment.
- 17.6 Do not use volume expansion in women with pre-eclampsia. Limit maintenance fluids to 80 ml/hour unless there are other ongoing fluid losses (for example, hemorrhage). Preferred IV fluids are Ringer Lactate and Normal Saline.
- 17.7 Active management of third stage of labor (AMTSL) should be done.
- 17.8 Inj. Ergometrine should be avoided.
- 17.9 Tab. Misoprostol 600 mg orally or rectally may be used to prevent PPH.
- 17.10 In case of eclampsia, MgSO₄ regimen should be continued during labor and till 24 hours past delivery or last convulsion whichever is late.

18 Postpartum care

- 18.1 Monitor BP for first 24-48 hours 4 -6 hrly postpartum. BP monitoring should be continued for 6 weeks ...periodic BP checkups at 48 hours, 6 days, 15 days and 42 days.

18.2 Continue MgSO₄ therapy if already on, for 24 hrs post delivery or last convulsion whichever is late.

Context : The patients reported in the registry significantly had postpartum convulsions (78%) with 9 % antepartum and 13% presenting with intrapartum convulsions . This calls for a very close vigilance during the postpartum period and continued eclampsia prevention measures even after delivery like monitoring, antihypertensive medication and magnesium sulphate

18.3 Following antihypertensive drugs have no known adverse effects on babies receiving breast milk so they are acceptable- Labetalol , Nifedipine , Atenolol , Metoprolol,Enalapril and Captopril.

18.4 Alpha methyl dopa should be avoided as it may increase incidence of postpartum depression.

18.5 In women who still need antihypertensive treatment in the postnatal period, avoid diuretic treatment for hypertension as the woman is breastfeeding.

18.6 There is insufficient evidence on the safety in babies receiving breast milk of the following antihypertensive drugs: ARBs, Amlodipine ACE inhibitors other than enalapril and captopril.

18.7 Every woman must be advised use of contraceptive.

18.8 Use of Progesterone only methods, intrauterine devices, and barrier methods are acceptable methods. Combined OC pills are not recommended during breastfeeding.

18.9 Sterilization can be offered to women who have completed their family and BP has reached normal level.

18.10 Couple must be given option of vasectomy.

ANNEXURE – I ANTI HYPERTENSIVES

Medication	Onset of action (min)	Dose	Adverse Effects
Alpha methyl dopa	6-8 hours	1-2 G/day in 3-4 divided doses	Postural hypotension , bradycardia ,xerostomia,headache ,dizziness ,reduced baseline variability on NST
Labetalol	10-15	20 mg IV, then 40-80 mg every 10 min up to maximum dose of 300 mg or continuous infusion at 1-2 mg/min	Dizziness, depression , bronchospasm , nausea, vomiting, diarrhea / constipation, heart failure, fatigue, Raynaud's phenomenon hallucinations,

			hypertriglyceridemia Hypercholesterolemia, psoriasis
Nifedipine	5-10	10 mg orally, repeated in 30 min, (20 mg) × 2 doses, then 10-20 mg every 4-6 h up to maximum dose 240 mg/24 h	Tachycardia, flushing Gastrointestinal disturbance hyperkalemia , edema headache
Hydralazine	10-20	5-10 mg IV every 20 min up to maximum dose of 30 mg	Headache, Tachycardia Anginal pectoris, Anorexia Nausea/vomiting, Diarrhea Lupus like syndrome, Rash Fluid retention

REFERENCES

1. NICE clinical guideline 107, 2011.
2. WHO recommendations for Prevention and treatment of pre-eclampsia and eclampsia, 2011.
3. SOGC clinical practice guidelines, 2008.