Hypertensive Emergencies In Pregnancy

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ABSTRACT

The hypertensive disorders are always viewed seriously in pregnancy as they can complicate pregnancy as well outcome of pregnancy. Though most of the complications can be overcome successfully, some of them can be life threatening. Unless promptly intervened, such complications can be fatal. It is necessary to understand these complications in pregnancy with hypertension. Early recognition and prompt treatment therefore required in all such cases. The present article deals with the common emergencies in pregnancy.

INTRODUCTION

Hypertensive disorders complicate 5-10% of all pregnancies. Hypertensive disorders along with haemorrhage, infection form the deadliest triad and are one of the major causes of maternal mortality. In a review by WHO in 2006 in developed countries; hypertensive disorders attribute to 16 % maternal mortality[1] .The working group classification of hypertensive disorders complicating pregnancy describe four types of hypertensive diseases [1].

- Gestational hypertension -previously termed as pregnancy induced hypertension.
- Preeclampsia and eclampsia syndrome
- Preeclampsia superimposed on chronic hypertension
- Chronic hypertension
- pre eclampsia super imposed on chronic hypertension

The criteria for diagnosing the above five groups are as follows:

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1] Gestational hypertension:

Systolic blood pressure >/= 140mmHg or diastolic blood pressure >/ =90 mm Hg being detected first time in pregnancy.

Absence of proteinuria.

Return of BP to normal before 12 wks of postpartum.

Final diagnosis is made only during post partum period.

2] Preeclampsia:

Minimum criteria for diagnosis of Preeclampsia include

1. BP >/ = 140/90 after 20 wks of gestation.
2. Proteinuria > 300 mg/24 hrs or > 2+ on dipstick.

The certainty of preeclampsia is increased, if

- BP> 160/100 mm hg.
- Proteinuria 2 gm/24 hrs or > 2+ dipstick
- Serum creatinine >1.2 mg /dl
- Platelets < 1,00,000/ul
- Microangiopathic hemolysis - Raised LDH levels
- Raised AST or ALT
- Persistent headache or visual disturbances

· Persistent epigastric pain.

3] ECLAMPSIA:

The criteria for diagnosis are Seizures that cannot be attributed to other causes in woman during pregnancy along with clinical picture of pre eclampsia.

4] CHRONIC HYPERTENSION:

BP>/140/90 mm Hg before pregnancy or diagnosed before 20 wks gestation not attributable to gestational trophpblastic disease OR

Hypertension first diagnosed after 20 wks gestation and persistent after 12 wks postpartum.

5] pre eclampsia super imposed on chronic hypertension:

New onset Proteinuria > 300 mg/24 hrs in hypertensive women but no proteinuria before 20 wks gestation.

During pregnancy, many ladies present with complications of hypertension. These emergencies need to be diagnosed as early as possible and promptly treated to avoid fatal outcome.

Hypertensive emergencies in pregnancy are defined as increase in systolic and diastolic blood pressure associated with end organ damage.

The common hypertensive emergencies in pregnancy are[2].

1] Pre eclampsia &Eclampsia

2] Acute renal failure

3] Acute left ventricular failure presenting as pulmonary oedema

4] Hypertensive encephalopathy

5] Hypertensive intracerebral hemorrhage and/or cerebral oedema.

PRE ECLAMPSIA

The criteria for diagnosis of these two conditions are mentioned above. The pre eclampsia is associated with various risk factors. These are pregnancy associated risk factors, maternal risk factors and paternal risk factors. Most of these factors can be corrected or treated immediately so that the development of hypertension related complications can be avoided [3].

[A] Pregnancy associated risk factors:

· Chromosomal abnormalities

· Hydatiform mole

· Hydrops fetalis

· Multiple pregnancy

· Oocyte donation or donor insemination

· UTI

· Congenital/structural abnormalities

[B] Maternal specific risk factors:

1. Age greater than 35 yrs.
2. Age less than 20 yrs
3. Black race
4. Family history of pre eclampsia
5. Nulliparity
6. Pre eclampsia in previous pregnancy
7. Specific medical conditions like gestational diabetes, Obesity [BMI >35kg/m2 – incidence 13.3%], renal disease, thrombophilia.
8. Physical or mental stress
9. Poor antenatal care.

[C] Paternal specific factors:

· First time father

· Previously fathered a pre eclamptic pregnancy in another woman.

The pre eclampsia and eclampsia can be diagnosed on various tests. These include

PREDICTOR TESTS [1]

These tests predict the early development of pre eclampsia. No test is 100% specific and sensitive to predict the development.

The various tests are

1]PROVOCATIVE PRESSOR TEST:

[A] Roll over test: This test is done at 28-32 wks in which BP is measured in supine and lateral position. A positive test is an elevation of 20 mm hg or more of blood pressure when patient rolls from lateral decubitus to supine position. This test has poor sensitivity.

[b]Isometric (sustained) hand grip test:

This test evaluates increase in BP in response to stimulus. In this test hand ball is squeezed and BP is noted.

[C] Angiotension sensitivity tests:

Angiotensin 2 infusion is given incrementally by gradually increasing dose intravenously & hypertensive response is quantified.

Conde & Agudeo [2009] found that the sensitivity to all the 3 tests is 70% & specificity is 85%.

[2]PLACENTAL PERFUSION TESTS:

[A]Doppler ultrasound: [1,4]

This is usually done in first and third trimester; specifically at 18-20 wks. Doppler velocimetries of the uterine artery is done; Presence of diastolic notch indicates early prediction.

[b]Pulse wave analysis:

Finger arterial pulse stiffness is an indicator of risk.

[3] FETOPLACENTAL UNIT ENDOCRINE DYSFUNCTION:

[A] Fibronectin glycoprotein:

Initially it was seen that increase in plasma levels of fibronectin precedes the development of clinical signs and symptoms of pre eclampsia but Leeflang and associates [2007] concluded neither cellular nor total fibronectin levels are effective.

[b] serum uric acid:

Hyperuricaemia is used to define pre eclampsia. Serum uric acid levels should be </ 4mg/dl. The sensitivity of this test ranges from 0-55% and specificity 77-95%.

[c] Microalbuminuria: [5]

Estimation of urinary albumin/creatinine ratio is done. Microalbuminuria precedes the proteinuria of pre eclampsia and hence its estimation has predictive value. The cut off value in both pregnant and non pregnant patients is 3.4 mg of albumin/mmol creatinine. The sensitivity and specificity of this test is 7-90% and 29-97% respectively.

[d]Coagulation activation:

Thrombocytopenia and platelet dysfunction are integral factors but are of limited use.

[e] Oxidative stress:

Increased levels of lipid peroxidises coupled with decreased antioxidant activity raised the possibility that markers of oxidative stress may predict pre eclampsia. Malondialdehyde is a marker of lipid peroxidation. Other pro-oxidants include iron, transferrin, ferritin, ascorbic acid and vitamin E. Vitamin C and Vitamin E are used in the preventive treatment of pre eclampsia.

[f]serum homocysteine levels:

Hyperhomocysteinemia causes oxidative stress and endothelial dysfunction. Clinical estimation is of less use.

[g]Angiogenic factors:

Angiogenic factors like vascular endothelial growth factors and placental growth factors decrease before clinical signs of pre eclampsia. The sensitivity and specificity of this test is 59-100% & 43-100%.

[h] Free fetal DNA:

Free fetal DNA is detected in maternal plasma using PCR. Free DNA is released by accelerated apoptosis of cytotrophoblasts hence Conde-Agiudo and associates concluded that free DNA quantitation is not useful for predictive purposes.

Pre eclampsia may present with severe

hypertension but without end organ damage. In such conditions there are chances of affecting the kidneys, retina or sometimes serious complications like pulmonary oedema. Acute cerebral complications like intracranial haemorrhage and cerebral oedema can occur.

ECLAMPSIA

This may develop before, during or after delivery. About 40% occur before & 16% occur more than 48 hrs after delivery. It is more common in third trimester of pregnancy.

Premonitory symptoms: [1,4]

1] Headache: frontal or occipital (50-75%); pulsatile or dull in character, more in early morning hours.

2] Visual disturbances: (20-30%)

- Scotoma first to appear followed by inability to focus and blurred vision.

- Blindness occurs in severe cases but recovery is quick & complete.

-Fundoscopy –Normal; if haemorrhage, exudates are present indicates chronic hypertension.

-Retinal ischemia or infarction causes blindness which is called as Purtscher Retinopathy.

§ Retinal detachment causes unilateral or bilateral blindness & vision returns to normal within a week after control of disease.

§ No surgical intervention required.

3] Epigastric pain or right upper quadrant pain:

- indicates severity.

- Increase in liver enzymes (AST/ALT) due to periportal hemorrhagic necrosis

- Haemorrhage from infracted area leads to haematoma formation.

- catastrophe if ruptures.

4] Neurological manifestations:

These include cerebral oedema which can lead to confusion or coma. There can be exaggerated deep tendon reflexes due to nerve irritability. The characteristic feature is generalised tonic clonic convulsions with uprolling of eyeballs & frothing at mouth. This is followed by post ictal phase which may range from confusion to coma. Some of these patients can develop Status eclampticus.

The eclampsia is important as an emergency because it can lead to complications due to seizures like aspiration pneumonia, tongue bite, head injury and hypoxic brain injury. It can also lead to intra cerebral haemorrhage and it can be fatal in some cases.

RENAL FAILURE [4,6]

Normal pregnancy is characterised by an increase in glomerular filtration rate & creatinine clearance. This is secondary to rise in renal glomerular filtration pressure and increased plasma flow. Presence or development of significant hypertension during pregnancy worsens hypertension. Endothelial injuries, development of glomerulonephritis or renal vein thrombosis are very common in pregnancy. This worsens both hypertension and renal functions and leads to acute renal failure in pregnancy.[8]

Definition: Abrupt decline in renal function characterised by urine output of less than 400ml/24 hr or less than 20ml/hr.

Renal hypoperfusion is the key event. This leads to decreased renal cortex blood flow, decreased glomerular filtration rate & decreased urinary volume. This is the prerenal azotaemia. If it persists for longer time it leads to persistent ischaemia resulting in acute tubular necrosis.

Incidence is 1 per 10,000 pregnant women. More commonly seen in preeclampsia with abruption. Mostly reversible damage occurs in cases of preeclampsia or eclampsia. The irreversible damage is common with acute

cortical necrosis in patients of abruption.

The development of acute renal failure is more common in third trimester of pregnancy and is characterised by sudden or rapid reduction in urinary output in pregnancy.

Such patients soon develop other clinical signs of acute renal failure in the form of retention of fluid in body as puffiness of face or oedema feet, drowsiness, nausea or vomiting, hematemesis and worsening of hypertension.

Diagnosis:

The diagnosis is established in a clinical setting of new onset or increase in pre existing hypertension &clinical signs of acute renal failure. The plasma creatinine is useful guide to detect early evidence of acute renal failure. Serum creatinine more than 1.6mg/dl alerts the onset of renal impairment. The urinary sodium > 40 mEq/L, FeNa >1 and renal failure index > 1 usually indicates acute ischaemic injury to kidneys. Other investigations include

1] Urinary osmolality: < 500 mosm/L indicates poor tubal function [9].

2] Urine to plasma osmolality ratio: If 1.5 or more indicates pre renal pathology

If 1.0 indicates acute tubular necrosis

3] Blood urea and serum creatinine levels: Rising trends are more important from management point of view.

ACUTE LEFT VENTRICULAR FAILURE

Acute left ventricular failure presenting as pulmonary oedema is seen in 2.9% patients of pre eclampsia[7]. It is more common in post partum period (70-80%) and mostly occurs in first 24-72 hrs after delivery. In multi parous women with chronic hypertension may develop pulmonary edema in the antenatal period. This is characterised by sudden onset of breathlessness, markedly raised blood pressure, central cyanosis, tachycardia, dyspnoea, bilateral crepitations in lung and third heart sound [9].

HYPERTENSIVE ENCEPHALOPATHY: [4]

It is seen in 1-2% patients of hypertension in pregnancy. It is common when systolic BP is >250mmHg & diastolic BP is >150mmHg. The onset is sub acute and usually appear over 24-72 hrs.

The clinical picture of hypertensive encephalopathy consists of symptom complex as severe hypertension, disordered consciousness, increased intracranial pressure, retinopathy and seizures. Focal neurological signs are unusual and its presence usually suggests intracerebral hemorrhage.

The diagnosis is made on onset of sudden severe hypertension with transient reversible neuro deficit. The clinical picture is same as of disease in non pregnant women.

HYPERTENSIVE INTRACEREBRAL HEMORRHAGE

This type of emergency in pregnancy is uncommon. It occurs only in those cases in which the levels of blood pressure are very high and not controlled by the drugs used for hypertension in pregnancy.

The clinical picture is same as that of intracerebral hemorrhage occurring in non pregnant women.

If present it is characterized by development within 30 -90 minutes with focal neurological deficit along with altered level of consciousness. The complication is due to rupture of deep penetrating arteries and can involve basal ganglion, cerebellum, brain stem and lobar areas.

The diagnosis is based on onset of sudden severe hypertension with altered consciousness. The CT/MRI is required for diagnosis.

MANAGEMENT

The mainstay in the management of hypertensive emergencies in pregnancy is the

control of hypertension as early as possible and control of seizures if present. The drugs for control of hypertension vary to some extent in pregnancy as compared to non pregnant women. The management of pre eclampsia and eclampsia is important to prevent further complications.

Goals of therapy in eclampsia and pre eclampsia are[4]

1) To reduce the BP to prevent the end organ damage. Normalising the BP affects the foetal circulation putting it at risk,
2) Birth of an infant who subsequently thrives,
3) Complete restoration of health of mother.

Management: This therefore include

1. Anti hypertensive treatment.
2. Delivery of the fetus if maturity is achieved.

A. Anti hypertensive treatment

1. LABETOLOL: - It is drug of choice in hypertensive emergency in pregnancy. The drug has alpha 1 and beta blocking action. It reduces peripheral vascular resistance & maintains peripheral, cerebral, renal and coronary blood flow. It does not affect utero-placental circulation[6,10].

Dose: 20 mg IV push q 5 minutes until target SBP reached Infusion 2-8 mg/min to a maximum of 300 mg/24 hours

2.HYDRALAZINE: This drug has direct action on arteriolar smooth muscle. It decreases peripheral vascular resistance & is used in repeated intravenous boluses. The drug has side effect like decrease in the utero-placental perfusion causing fetal heart rate decelerations and decrease in hyperdynamic circulation causing maternal tachycardia [1, 6, and 9].

Dose: as bolus injections of 5 to 10 mg every 15 to 20 minutes for a maximum dose of 20 mg.

3.Calcium channel blockers: This drug is used because it decreases the afterload by decreasing the peripheral vascular resistance and is equally effective as labetolol in decreasing the BP. It has side effects as Side effects like maternal tachycardia, headache & palpitation. It acts as tocolytic as well as antihypertensive[5,11].

Dose: Nifedepine is the drug of choice in this group. It is given as 10-20mg sublingually every 30 min & maximum upto 50 mg can be given.

4.Alphamethyl dopa: This drug is not the first line of therapy for rapid reduction of BP in emergencies because it has delayed onset of action. However the action is prolonged and hence used after initial control of BP. This drug therefore is useful for control of chronic hypertension[6].

Dose: 250 to 500 mg tds or qid depending on BP levels and maximum up to 3gms/day.

5.Verapramil: This drug is used mainly in the postpartum period if hypertension persists after delivery. It is not the primary line of therapy to manage hypertensive emergencies in pregnancy[6]. The dose of the drug is 40-80 mg orally 3 times a day

6.Atenolol + ACE inhibitors : THESE DRUGS ARE NOT USED IN PREGNANCY AS THEY HAVE FETAL EFFECTS LIKE GROWTH RETARDATION[6,11].

7.Diuretics: Frusemide is drug of choice. This drug is given only if associated complications like renal failure, pulmonary odema or congestive cardiac failure is present. This drug is not used in treatment of preeclampsia per se as it causes decreased utero placental perfusion and intra uterine fetal death.

(B) Delivery of the fetus

Depending on the maturity of fetus, parity of the patient, cervical status and associated complications; decision is taken.

Management of Eclampsia [4,6]

The goal of therapy in this emergency are

A] Control of seizures

B] Use of Anti hypertensives

C] Delivery of the fetus and

D] Management of associated complications.

A]Control of Seizures: [1,4,6]

Magnesium sulphate is the gold standard. It acts at the neuromuscular junction by blocking the acetyl choline release in response to nerve action potentials. Magnesiumsulfate can be given in intravenous infusion, bolus & in intramuscular form.

It is to be continued for 24 hrs post delivery or post seizure whichever is later.

Patients on magnesium sulphate therapy need to be monitored for urine output, respiratory rate & deep tendon reflexes and monitoring of serum magnesium.

Normal level of serum Mg++ is 1.6 to 2.1 meq/lt [6]

Level of Se. Mg++	Effect
4-7meq/lt	Convulsions
are	controlled
8-10meq/lt	Patellar reflex disappears
12meq/lt&more	Respiratory depression & paralysis

Various regimes of Magnesium sulphate therapy are [4,6]

1] Pritchard regime: This is commonly used regimen. In this IV loading dose of 4 gm given slowly over a period of 3-5 min (8ml of 50% Mgso4[4gm]+12ml distilled water). This is followed by IM loading dose of 5gm deep intramuscularly in outer quadrant of each buttock (10ml of 50%Mgso4[5gm]). This is then followed by maintainence dose of 5gm deep IM in alternate buttocks every 4 hourly till 24 hrs/delivery/occurance of side effects.

Disadvantages:

- High concentration of drug.
- Side effects like respiratory depression.
- Fetal respiratory depression.
- Atonicity more common

Other regimes used are

2]Sardesai's regime: The concentration of loading dose used is less and the dose is IV 2gm given slowly over a period of 3-4 min followed by 5 gm IM in each buttock alternately for 24 hrs. This regime has the same efficacy over seizure control with minimal maternal & fetal side effects.

Other drugs used as anticonvulsants are

1] Phenytoin: It is given as loading dose of 15-25mg/kg BW given IV slowly followed by 2nd dose 500mg IV after 12 hrs. This drug is also given as Prophylaxis in the dose of 100mg dose IM or IV every 4hrs to be continued later orally in postpartum period.

2]Diazepam (Lean regime): this drug is given as 40 mg IV slowly & further as 40 mg in 500ml of 5% dextrose is infused to be given at rate of 30 drops per minute or adjusted as per need. Main side effect is maternal respiratory depression and hence rarely used nowadays as newer molecules available.

(B) Use of Antihypertensives: The various antihypertensives to be used in eclampsia are same as that for pre eclampsia and include Labetolol and hydralzine. These drugs also help to prevent the damage to kidneys, eyes & other organs by controlling the blood pressure.

(C)Delivery of the fetus: Irrespective of the maturity of the fetus delivery is the definitive management.

Management of Acute renal Failure

The management is same as for any other case with acute renal failure and includes elimination of root cause of renal failure, volume & electrolyte balance, treatment of

hyperkalemia, treatment of acidosis and dialysis as Peritoneal or hemodialysis.

Management of acute left ventricular failure and pulmonary oedema

The basic principles of management of acute left ventricular failure and pulmonary oedema in pregnant ladies with severe hypertension is same as that of non pregnant ladies. The life of the mother is most important in this situation and hence attempt is made to control this complication as early as possible.

The basic principles of Treatment include:

- Propped up position
- Oxygen therapy
- IV diuretics
- After load reduction with IV hydralazine or labetolol
- Invasive monitoring
- Fluid infusion depending on CVP
- Delivery should be performed after hemodynamic stabilisation to avoid the deleterious effect of acute hemodynamic changes that occur during or after parturition.

Hypertensive Encephalopathy : [4, 12]

- This is a very serious emergency in pregnancy with hypertension. The life of mother as well as fetus is important and both should be saved.
- The principles of Treatment are :
- Intensive management during labour & delivery.
- Hospitalisation of patient
- Invasive monitoring of blood pressure, level of consciousness and seizures if present.
- The reduction of blood pressure is very important for immediate relief. The reduction of BP should be at least by 15 - 20%. Drugs used for this purpose are

1]Sodium nitroprusside:

- Dose: IV infusion 0.25 to 8.0 mg/kg/min maximum up to 10mg/kg/min over a period of 10 min effect lasts 3-5min after stopping the infusion. This drug causes 25% reduction in blood pressure in 2 -3 hours. This is the target reduction of BP in such cases. The side effect is Thiocynate toxicity.

2]Nitroglycerine: The alternate useful drug for control of BP is Nitroglycerine. The dose is IV infusion of 5mg/minute and the dose is increased every 3-5min to 10mg/minute till desired reduction of BP is achieved. The drug causes the side effect like Headache, tachycardia & meth hemoglobinemia.

Common Hypertensive Emergencies & Their Management (Table 1)

Conclusion : Eclampsia, pulmonary oedema and hypertensive encephalopathy are the common hypertensive emergencies in pregnancy. The control of blood pressure as early as possible an d control of additional symptoms like seizures is very important. The management of hypertension differ from the management of the same in non pregnant ladies. The life of mother as well as fetus is important and simultaneous attempt is made to save both.

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Type of Emergency	Drug of Choice	BP Target
Aortic dissection	β-Blocker + nitroprusside*	120 mm Hg systolic in 20 min (if possible)
Cardiac		
Ischemia/infarction	Nitroglycerin, nitroprusside, and/or nicardipine	Cessation of ischemia
Heart failure (or pulmonary edema)	Nitroprusside* and/or nitroglycerin	Improvement in failure (typically only a 10%-15% decrease is required)
Hemorrhagic		
Epistaxis, gross hematuria, or threatened suture lines	Any (perhaps with anxiolytic agent)	To decrease bleeding rate (typically only 10%-15% reduction over 1-2 h is required)
Obstetric		
Eclampsia or preeclampsia	$MgSO_4$, hydralazine, methyldopa	Typically <90 mm Hg diastolic, but often lower
Catecholamine excess states		
Pheochromocytoma	Phentolamine	To control paroxysms
Drug withdrawal	Drug withdrawn	Typically only one dose necessary
Cocaine (and similar drugs)	Phentolamine	Typically only 10%-15% reduction over 1-2 h
Renal		
Major hematuria or acute renal impairment	Fenoldopam	0%-25% reduction in mean arterial pressure over 1-12 h
Neurologic		
Hypertensive encephalopathy	Nitroprusside*	25% reduction over 2-3 h
Acute head injury/trauma	Nitroprusside*	0%-25% reduction over 2-3 h (controversial)
Subarachnoid hemorrhage	Nimodipine	Up to 25% reduction in previously hypertensive patients; 130-160 systolic for normotensive patients
Acute stroke in evolution	Nitroprusside* (controversial)†	0%-25% reduction over 6-12 h (controversial)†