

## Review On a Hypertension Disorders in Pregnancy

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**ABSTRACT:** Hypertension is a long-term medical condition which is defined by increase in blood pressure (140/90 mm of Hg) in arteries. It is the most common medical problem seen in pregnant women. The Hypertension disorders are classified as Chronic hypertension, Gestational hypertension, Pre-eclampsia and Eclampsia, Chronic hypertension with superimposed Pre-eclampsia and others such as White coat hypertension and Masked hypertension. The Hypertension disorders are managed by using Anti-hypertensive drugs such as Methyldopa, labetalol, Nifedipine and Hydralazine and other life style modifications.

### INTRODUCTION:

HYPERTENSION is also known as High Blood Pressure, is a long term medical condition, which is defined by persistent elevation of blood pressure in arteries.<sup>(1)</sup>

Hypertension is the most common medical problem encountered during pregnancy and cause serious maternal and perinatal morbidity and mortality.<sup>(2)</sup>

Hypertension disorders of pregnancy also known as “ Maternal Hypertension Disorders“. Nearly 10-12% of pregnancies cause hypertension.<sup>(3)</sup>

### MEASUREMENT OF BLOOD PRESSURE:

According to the Australian society for the study of Hypertension in pregnancy, measurement of hypertension in pregnancy includes some recommendations, they as follow

Patient should be seated for 2-3 minutes before measurement of blood pressure. Both arms should be measured at first antenatal visit. Palpate systolic pressure should go 20mm higher and deflate slowly 2mm every second. Use korotkoff5 ( or use 4 if 5 is absent) for diastolic blood pressure. If required repeat the measuring. Ambulatory monitoring useful for white coat hypertension.<sup>(4)</sup>

Automated machines are not recommended for measuring blood pressure in patients.<sup>(4)</sup>

### Calculation of Blood pressure based on Arterial pressure (MAP) <sup>(5)</sup>

MAP = systolic pressure + ( diastolic pressure)×2/3

A rise of 20mm of Hg MAP over the previous reading or when the MAP is 105mm

Of Hg or more should be significantly considered

### STAGES OF HIGH BLOOD PRESURE:<sup>(6)</sup>

According to the National Heart, lung and blood Institute (NHLBI) of the National Institutes of Health (NIH), the stages of high blood pressure are

**STAGE 1** :[ Non severe Hypertension ]

When the systolic pressure is 140-159mm of Hg and Diastolic pressure is 90-99 mm of Hg or higher is called as Stage 1 or Non severe Hypertension.

**STAGE 2** :[ Severe Hypertension ]

When the systolic pressure is 160 mm of Hg or higher and diastolic pressure is 100 mm of hg or higher is called as Stage 2 or severe hypertension.

### Classification Of Hypertension Disorders Of Pregnancy

According to International Society for the study of Hypertension in Pregnancy (ISSHP), the disorders are classified as below <sup>(7)</sup>

- Chronic Hypertension
- Gestational Hypertension
- Pre-eclampsia and eclampsia

Others such as

- White coat hypertension
- Masked hypertension

According to report on National high blood pressure education program (NHBPEP) and American college of obstetricians and gynecologists, they are classified as <sup>(8)</sup>

- Chronic Hypertension
- Pre-eclampsia – Eclampsia
- Pre-eclampsia superimposed on chronic hypertension
- Gestational Hypertension

### **CHRONIC HYPERTENSION :**

Hypertension (140/90mm of Hg) present in pregnancy or before 20 weeks of gestational or persistence for 12 weeks after delivery is called Chronic Hypertension<sup>(9)</sup>

Nearly 3%-5% of pregnancies are with chronic hypertension<sup>(10)</sup>

Classification of Chronic hypertension<sup>(11)</sup>

Chronic hypertension is sub classified as mild or severe depending on the blood pressure readings. (Severe-180/110 mm of Hg)

Chronic hypertension is sub divided into 2 types. They are

- Primary hypertension
- Secondary hypertension

Primary hypertension is most common cause of chronic hypertension seen during 90% of pregnancies and secondary hypertension is caused by presence of one or more underlying disorders in patients, it is nearly seen in 10% of pregnancies.

### **Pathogenesis of Chronic Hypertension:**<sup>(12)</sup>

The Pathogenesis of chronic hypertension is poorly understood. The factors that may include the development of Chronic hypertension are derangements in sympathetic neural activity or angiotensin -2 activity

### **Diagnosis:**

Evaluation of patient with chronic hypertension is directed at end organs and systems and most likely to be affected to eyes, heart, kidneys, uteroplacental circulation of fetus

The laboratory tests include a complete blood count (CBC), glucose screening, electrolytes panel, serum creatinine, urine analysis and urine culture<sup>(13)</sup>

A 24 hours collection of total protein and creatinine clearance is performed in early pregnancy by dipstick method to detect proteinuria and repeat this test around 26-28 weeks of gestation to define a new baseline in patients with possible renal disease<sup>(14)</sup>

Antinuclear antibodies and Anti double stranded DNA should be checked in patients with possibility of systemic lupus erythematosus with proteinuria<sup>(14)</sup>

Electrocardiogram, Echocardiogram or Ophthalmic examinations are performed in patients with presence of hypertension for severe years. Doppler flow studies or Magnetic resonance angiography are required to evaluate renal artery stenosis<sup>(14)</sup>

### **Differential Diagnosis:**<sup>(14)</sup>

The chronic hypertension can also be evaluated or suspected by absence of proteinuria, presence of family history of hypertension, obesity, multiparity or other diseases known to affect the kidney.

### **Risk factors:**<sup>(15)</sup>

The risk factors of chronic hypertension are obesity, older age, duration of high blood pressure (>15 years), presence of any medical disorders, family history of hypertension and presence of Thrombophilias.

### **Complications:**<sup>(15)</sup>

The complications of chronic hypertension include superimposed pre eclampsia, fetal growth restriction, preterm birth, placental abruption and caesarian section

### **Management of Chronic Hypertension:**

The goals of treatment of chronic hypertension is to control maternal blood pressure, minimize the risk of maternal complications and early detection of obstetrical or fetal complications.<sup>(16)</sup>

Management of Chronic hypertension includes both pharmacological treatment and non pharmacological treatment

### **Anti hypertensive therapy in chronic hypertension:**

Anti hypertensive therapy is not to improve fetal condition or to prevent pre-eclampsia.<sup>(17)</sup>

A drug of choice in past was methyldopa, but the main side effects of methyldopa is elevation of liver enzymes in patients. Labetolol is an alternate medication which has a dual effect. It acts has both alpha adrenergic and central beta blocking effects. Now – a – days, Nifedipine have come into use because it have a salutary effect on the uterine blood flow similar to effect on renal blood flow.<sup>(17)</sup>

### **ANTI HYPERTENSION AGENTS:**<sup>(18)</sup>

Single Anti Hypertension agents are initiated in the therapy

#### **METHYLDOPA:**<sup>(18)</sup>

It is used as oral tablet formulation. It acts through alpha receptor blockage, reduces sympathetic tone and peripheral resistance .Dose: 500mg -3g in 2 divided doses.

Side effects are Dizziness, light headedness, drowsiness, headache, stuffy nose, weakness.

### **LABETOLOL:**<sup>(18)</sup>

It is Used as Tablet or Intravenous formulation. Acts through alpha and non-selective beta blockers, it causes vasodilation, reduce cardiac output. Dose: Per oral -100-1200mg /day in 2-3 divided dose. Intravenous – 10 -20 mg, repeat 20-80 mg in every 30 min or 1-2mg/min, maximum to 300mg/day. Caution – not prescribe to Asthma patients. Side effects are Neonatal bradycardia and Hypoglycemia.

### **NIFEDIPINE:**<sup>(18)</sup>

It is Available in 3 oral formulations such as capsules with sustained release, intermediate release (prolong action), extended release (long action). Dose: 30-120mg/ day. It is a dihydropyridine calcium channel blocker act on vascular smooth muscle cause vasodilation and lowers systemic vascular resistance. Side effects are headache, reflex tachycardia, peripheral edema

### **HYDRALAZINE:**<sup>(18)</sup>

It is Available in oral and parenteral formulations. It acts through direct vasodilation to reduce peripheral vascular resistance. Dose : 50-300mg/day in 2-4 divided doses. Side effects are maternal hypertension, tachycardia, headache, still birth.

### **NICARDIPINE:**<sup>(18)</sup>

Dose: Initial 5mg/hour, increased by 25mg/hour. Side effects such as headache, edema, tachycardia.

### **NITROPRUSIDE:**<sup>(18)</sup>

Direct vasodilator directly relaxes arterial, venous smooth muscles results in reduction of cardiac preload and afterload, Dose :0.3-0.5 to 2mcg /kg min., maximum duration to 24-28hours. Side effects such as fetal cyanide toxicity

### **AVOIDED ANTI HYPERTENSION DRUGS IN PREGNANCY:**<sup>(18)</sup>

**RAAS INHIBITORS:** These cause potential fetotoxicity, fetal renal toxicity and still birth. Atenolol, Cardio selective beta blocker : decrease placental perfusion which may lead to intra uterine deaths, Immature and premature deliveries. Thiazides and Thiazide like diuretics : reduce normal plasma volume cause expansion of pregnancy.

### **Non-Pharmacological management in Chronic hypertension:**<sup>(19)</sup>

Reduce salt intake, Limit alcohol consumption or avoid alcohol, Manage stress, Exercise

regularly, Weight reduction, Follow treatment plan regularly, Follow DASH diet.

### **GESTATIONAL HYPERTENSION:**

Elevation of Blood pressure to 140/90 mm of Hg after 20 weeks of gestation with absence of proteinuria and returns to normal, after 12 weeks of postpartum is called Gestation hypertension. It occurs in about 3 in 50 pregnancies<sup>(20)</sup>

It is also called as Pregnancy induced hypertension (PIH) or Transient hypertension.<sup>(21)</sup>

Classification of Gestational hypertension:<sup>(22)</sup>

Gestational hypertension is classified into mild or severe based on blood pressure readings. If blood pressure is 160/110 mm of Hg then it is severe gestational hypertension.

### **Pathogenesis:**<sup>(22)</sup>

The pathogenesis of gestational hypertension is unclear. Gestational hypertension is considered to be provisional diagnosis as many women with gestation hypertension will go on to be diagnosed with either pre-eclampsia or chronic hypertension.

### **Diagnosis:**

It is diagnosed when maternal blood pressure is elevated to 140/90mm of hg or higher in 2 occasions, 6 hours apart in a previously normotensive women > 20 weeks gestational and in absence of proteinuria<sup>(22)</sup>

The laboratory tests include urine analysis, liver function test, renal function test and blood clotting test, which evaluate the levels of hepatic transaminases, creatine, hematocrit, platelets, lactic acid dehydrogenase.<sup>(23)</sup>

### **Complications:**<sup>(23)</sup>

The complications of Gestational hypertension include preterm birth, Intrauterine growth restriction, placental abruption, Still birth and preterm birth.

### **RISK FACTORS:**<sup>(23)</sup>

They are Presence of Hypertension in pre or post pregnancy, Presence of renal disease, Presence of Diabetes, Multiple gestations, Younger than 20 years / elder than 40 years of age.

### **SYMPTOMS:**<sup>(23)</sup>

They are Headache, Edema, Sudden weight gain, Blurred or double vision, Nausea and

vomiting, small amounts of urine, Epigastric pain and Abdominal pain.

#### **Management of Gestational hypertension:**<sup>(24)</sup>

The treatment includes the patient education regarding symptoms of pre-eclampsia because gestational hypertension nearly causes 15-20% of risk of pre-eclampsia. Anti-hypertensive agents are given to control the blood pressure and to decrease the risks and complications of patients.

#### **PREECLAMPSIA:**

Preeclampsia is a multisystem disorder of unknown etiology characterized by development of hypertension to the extent of 140/90 mm of hg or more with proteinuria after 20 weeks of gestation.<sup>(25)</sup>

Presence of gestational hypertension and proteinuria is called Preeclampsia.<sup>(25)</sup>

It is the third leading cause of maternal mortality and a major cause of neonatal morbidity and mortality<sup>(26)</sup>

#### **Classification of Preeclampsia:**<sup>(27)</sup>

Pre eclampsia is classified into 2 types. They are mild and severe.

Mild pre-eclampsia – when the blood pressure is 140/90 - < 160/110 is called mild pre-eclampsia. It includes the presence of proteinuria (< 300mg/24 hour) with absence of symptoms

Severe pre-eclampsia - when the blood pressure is 160/110 or more on the 2 occasions 6 hours apart with presence of proteinuria (5g or more in 24 hours) and with presence of symptoms is called as severe pre-eclampsia.

#### **Etiopathogenesis:**<sup>(28)</sup>

The Etiopathogenesis of preeclampsia includes several steps as follows

- Imbalance in different components of prostaglandins
- Increased vascular sensitivity to the pressure agent angiotensin 2 which depressed the angiotensin activity
- Nitric acid – it relaxes the vascular smooth muscles, inhibits platelet aggregation and prevents intervillous thrombosis
- Endothelin-1, a potent vasoconstrictor cause hypertension
- Inflammatory mediators cause endothelial injury
- Abnormal lipid metabolism causes endothelial injury and dysfunction
- Imbalance of angiogenic and anti angiogenic proteins
- Others such as mutation of factor 5

#### **Risk factors:**<sup>(29)</sup>

The risk factors include nulliparity, multiple gestations, Hydatidiform mole, Diabetes mellitus, Thyroid disease, chronic hypertension, renal disease, collagen vascular disease, anti phospholipid syndrome, family history of pre-eclampsia, obesity, history of pre-eclampsia or eclampsia.

#### **Diagnosis:**<sup>(30)</sup>

Elevation of blood pressure to 140/90 mm of hg in 2 occasions in 6 hours apart, presence of proteinuria, ophthalmic examinations, increased levels of hematocrit, lactate dehydrogenase, serum transaminases and uric acid, thrombocytopenia.

#### **SYMPTOMS:**<sup>(31)</sup>

Presence of proteinuria, Severe headaches, Changes in vision such as loss of vision, blurred vision or light sensation, Nausea and vomiting, Pain in right side of abdomen, Decreased urine output, Thrombocytopenia, Swelling face and hands, Shortness of breath, Sudden weight gain, pulmonary edema

#### **Complications:**<sup>(32)</sup>

Maternal complications: eclampsia, oliguria and anuria, visual disturbances, preterm labor, HELLP syndrome, cerebral hemorrhage, acute respiratory distress syndrome (ARDS)  
Fetal complications: Intrauterine growth restriction, asphyxia, prematurity.

#### **Management of Preeclampsia:**

##### **Treatment for mild pre-eclampsia:**<sup>(33)</sup>

It is treated by delivery at 37 weeks or at time of diagnosis if after 37 weeks. Optimal treatment prior to 37 weeks is usually expectant management, close maternal and fetal monitoring is essential.

Regular fetal monitoring is needed such as growth ultrasound, amniotic fluid assessment for every 3-4 weeks, umbilical artery doppler velocimetry and once or twice weekly NST

Maternal monitoring includes weekly or semi-weekly blood pressure monitoring and undergoing periodic laboratory tests

>34 weeks gestational age with abnormal fetal testing and uncontrolled HTN should prompt to delivery.

### Management of Severe Preeclampsia:<sup>(33)</sup>

Treatment during 34 weeks: Careful monitoring and assessment of CBC metabolic panel should be strictly recorded and if indicated immediate caesarian delivery is needed and if there are no contractions to labor and patient with vertex fetus can deliver vaginally

Treatment between 24-34 weeks: expected management is required to control blood pressure. Fluid status, CBC, platelets and liver function tests should be monitored daily. Betamethasone 12g IM is administered 2 doses 24 hours apart for fetal lung development. Magnesium sulphate and IV anti hypertensives may be given initially. If complications are present delivery is indicated

### Seizure prophylaxis:<sup>(33)</sup>

Some patients with severe persistent pre-eclampsia may need seizure prophylaxis. The treatment is as follows

#### Magnesium sulfate:

It is the first agent of choice for seizure prophylaxis. The loading dose is 6g IV over 15-30 minutes and maintenance dose are 2g/hour. For IM loading dose is 5g (50% solution); maintenance dose is 5g every 4 hours

Magnesium toxicity: It is developed in patients with manifestations of loss of patella reflex (8-12mg/dl), feeling warmth, flushing (9-12mg/dl), somnolence (10-12 mg/dl), slurred speech (10-12mg/dl), muscular paralysis (15-17mg/dl), respiratory difficulty (15-17mg/dl), cardiac arrest (30-35mg/dl)

Management of Magnesium toxicity: discontinue magnesium sulfate, obtain Mg (serum) level, if magnesium level >15mg/dl, give 1g calcium gluconate IV incubate and assist ventilation.

#### Phenytoin:

It is the second choice of agent. Loading dose is given based on maternal weight

For <50kgs – 1000mg; 50-70 kgs – 1250mg; >70mg – 1500mg.

The first 750mg loading dose should be given at 25mg/min and the rest at 12.5mg/ml

Anti-hypertensive treatment:

It is indicated in patients with SBP > 160mm of Hg and DBP > 110mm of Hg. Anti hypertensive agents given for acute management while administering magnesium. The agents are Nifedipine, hydralazine, and Labetolol.

### HELLP Syndrome:<sup>(34)</sup>

It is a complication of severe pre-eclampsia. The term describes the periodic patients having hemolysis, elevated liver enzymes and a low platelet count

#### Diagnosis:<sup>(34)</sup>

It includes hemolysis, presence of peripheral smear, serum bilirubin, low serum haptoglobin, severe anemia, unrelated to blood loss, elevated liver enzymes and low platelet count

#### Management:<sup>(34)</sup>

Treatment is same as severe pre-eclampsia. Depending upon the severity of anemia and thrombocytopenia, transfusion of RBC, platelets are required after delivery.

### ECLAMPSIA:

The term Eclampsia is derived from a Greek word, which means “like a flash of lightning”<sup>(35)</sup>

It occurs without any warning manifestations. Pre eclampsia when complicated with grandmal seizures (general tonic-clonic convulsions) and / or coma is called eclampsia<sup>(35)</sup> It occurs 1 in 2000 or 1 in 3000 pregnancies.<sup>(35)</sup>

#### Pathogenesis:<sup>(36)</sup>

The Pathogenesis of eclampsia is unknown but it is related to arterial vasospasm which may lead to cerebral edema and increased intracranial pressure.

Onset of fits occurs as antepartum, peripartum or postpartum and fits mainly occurs in third trimester.

#### Complications:<sup>(37)</sup>

The complications include injuries such as tongue bite, bed sore, pulmonary complications, hyperpyrexia, cardiac failure, cardiomyopathy, renal failure, hepatic damage, cerebral complications, neurological deficits

#### RISK FACTORS:<sup>(38)</sup>

They are Obstetric history, Age, Family history, High blood pressure, Lupus, Renal diseases.

#### SYMPTOMS:<sup>(38)</sup>

They are Severe headaches, Weight gain, Nausea and vomiting, Stomach pain, Swelling of hands, feet and face, Muscle pain, Seizure.

**DIAGNOSIS:**<sup>(38)</sup>

Blood pressure, Renal function tests, Proteinuria, Platelet count, Cerebral and visual symptoms, Sr. Creatine level, Liver transaminase enzyme elevated twice to normal, Pulmonary edema.

**Management:**<sup>(39)</sup>

Management of airway, breathing and circulation (ABC), magnesium sulfate is the first choice of drug for seizures and phenytoin is the alternative drug. During acute eclamptic episodes, fetal bradycardia is normal, it usually resolves in 3-5 minutes. Emergency caesarian delivery should always be anticipated in case of rapid maternal or fetal deterioration.

**CHRONIC HYPERTENSION WITH SUPER IMPOSED PRE ELAMPSIA:**

This condition is developed with chronic high blood pressure before pregnancy, but then develop worsening high blood pressure and protein in urine and other complications during pregnancies<sup>(40)</sup>

**CAUSES:**

They are Essential hypertension, Chronic renal disease, Coarctation of arteries, Diabetes mellitus, Pheochromocytoma, Thyrotoxicosis<sup>(40)</sup>

**SYMPTOMS:**

Onset proteinuria,HELLP syndrome, Severe headache,Epigastric pain<sup>(40)</sup>

**WHITE COAT HYPERTENSION:**

Elevated blood pressure in office or clinic is called White Coat Hypertension.<sup>(41)</sup>

**MASKED HYPERTENSION:**

It is a condition in whose normal blood pressure is present in clinic / office visits but elevated at other times. It is mainly diagnosed by 24 hours Ambulatory blood pressure monitoring (ABPM)<sup>(41)</sup>

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