Review Article Available online through
www.ijrap.net
IJRAP

MANAGEMENT OF PREGNANCY INDUCED HYPERTENSION

Sharma Anjana*, Mahendra Poonam, Bisht Shradha
Pharmacology Division, School Of Pharmacy, Suresh Gyan Vihar University, Jaipur, India

Received: 01-11-2010; Revised: 15-11-2010; Accepted: 22-11-2010

ABSTRACT

Pregnancy induced hypertension (PIH) is a global problem and complicates approximately 10-17% of pregnancies and is therefore most common medical problem requiring special attention in the intrapartum period. Hypertension may, of course, precede pregnancy, but more commonly develops during it in which case blood pressure levels can change very quickly. The increase of BP rarely starts before 20 weeks, but may be a major problem by the third trimester (24-36 weeks). Pregnancy induced hypertension, although a common complication of pregnancy must not be taken lightly. It becomes very essential for a treating physician to know in detail about this particular complication of pregnancy. If PIH is detected early with prompt and effective treatment, the features disappear completely and the prognosis is not unfavourable, both for the mother and the baby. The primary objective of treatment in women with severe hypertension and preeclampsia is to prevent cerebral complications such as encephalopathy and haemorrhage. The threshold for treatment is usually a sustained diastolic blood pressure of 110 mm Hg or higher. Antihypertensive drugs can affect the foetus either indirectly, by lowering uteroplacental blood flow, or directly, by influencing the umbilical or foetal cardiovascular circulation. In patients with mild to moderate hypertension, both chronic and pregnancy induced, methyldopa treatment improves the maternal outcome. Among the different antihypertensive drugs that have been reported to be effective, safe and well tolerated during pregnancy, many clinical trials and studies conclusively state that methyldopa represents the more suitable option in pregnancy induced hypertension. In this article we have briefly gone through the various aspects of hypertension, stressing importance on its rising incidence globally and in India.

KEYWORDS: Pregnancy induced hypertension, Preeclampsia, Gestational diabetes,

***Corresponding Author**
Anjana Sharma
M.Pharm Student
Gyan Vihar School of Pharmacy,
Jaipur, Rajasthan, India
Email: aks.pharm@yahoo.com

INTRODUCTION

Historically speaking around four thousand years ago, people realised that there were certain conditions unique to pregnancy. In the beginning, there were two main mortal conditions associated with childbirth-related death. One was hemorrhage and the other was called toxaemia. Toxaemia, so called because it was supposed that toxins of some sort, caused this condition which was associated with seizures, swelling, and death anywhere from the beginning of the third trimester to a month or so beyond delivery. As science gloated over discoveries like blood types and blood pressure differences, late it was termed as "Pregnancy-Induced Hypertension" ("PIH"), to associated it with the uniqueness of pregnancy. Hypertension is one of the common complications met with in pregnancy and contributes significantly to maternal and perinatal morbidity and mortality. Hypertension is a sign of an underlying pathology, which may be pre-existing or appears for the first time during pregnancy. The identification of this clinical entity and effective management play a significant role in the outcome of pregnancy, both for the mother and her unborn baby [1-4].

According to ACOG (American College of Gynecology) Technical Bulletin (Number 219 January 1996) pregnancy induced hypertension is defined as sustained blood pressure to levels of 140 mmHg systolic or 90 mmHg diastolic[1,5].

Hypertensive disorders one the most common medical complications of pregnancy and are an important cause of maternal and perinatal morbidity and momortality worldwide. During normal pregnancy, systolic pressure changes little; however, diastolic pressure decreases by an average of 10 mm Hg early in gestation (13 to 12 weeks) and rises again to prepregnancy levels in the third trimester[5].

CLASSIFICATION OF PREGNANCY INDUCED HYPERTENSION (Fig.1)

Chronic Hypertension In Pregnancy

Chronic hyperetensive disease is defined as the presence of hypertension of any cause antedating or before the 20th week of pregnancy in the absence of hydatidiform mole or its presence long after delivery. The condition poses a difficult problem as regards the diagnosis and managements when seen for the first time, beyond the 20th week of pregnancy[1,4].

Pregnancy Induced Hypertension (PIH)

PIH is so called as hypertension develops as a direct result of gravid state. This is further classified on the basis of its presentation into[1,4,6,7].

- With oedema and/or proteinuria; having two subtypes as preeclampsia and eclampsia.
- Without gross oedema or proteinuria, also termed as gestational hypertension.

Gestational Hypertension

A sustained rise of blood pressure to 140/90 mmHg or more on at least two occasions 4 or more hours apart beyond the 20th week of pregnancy or during the first 24 hours after delivery in a previously normotensive woman is called 'Gestational Hypertension'. It should fulfill three criteria:

- Absence of any evidences, for the underlying cause of hypertension.
- Unassociated with other eviidences of preeclampsia (oedema or proteinuria)
- The blood pressure should come down to normal within 10 days following delivery[1,4,8].

Preeclampsia

Preeclampsia is a multi system disorder of unknown aetiology characterised by development of hypertension to the extent of 140/90 mmHg or more with oedema or proteinuria or both, induced by pregnancy after the 20th week. The pre-eclamptic features may appear even before the 20th week as in cases of hydatidiform mole and acute polyhydramnios.

It may present itself either as a primary disorder or may complicate pre-existing pathology like chronic hypertension or chronic nephritis. In these conditions, it is difficult at times to differentiate the clinical entity, especially, if the case is first seen during pregnancy. Moreover, an indistinguishable pattern[1,4].

Others

Coincidental Hypertension

When the hypertensive state in pregnancy is unrelated to pregnancy, also termed as chronic hypertension in pregnancy. This could be because of malfunctioning of other organs/systems in the body and can present as:

- Essential hypertension
- Renovascular hypertension
- Pheochromocytoma
- Coarctation of aorta
- Thyrotoxicosis
- Connective tissue disease like SLE (Systemic lupus Erythematosus)[1]

HYPERTENSION WORSENED BY PREGNANCY

When there is a history or documentation that the woman had hypertension in the pre-pregnant state, it is so called. Further, when this state demonstrates not only elevated pressure on more than one occasion but is complicated with gross oedema and proteinuria, it is termed as:

- Superimposed preeclampsia
- Superimposed eclampsia[1]

Eclampsia

The term eclampsia is derived from a Greek work, meaning "like a flash of lightening". It may occur abruptly, without any warning manifestations. Preeclampisa when complicated with convulsions and coma is called eclampsia.

In majority, over 80%, features of severe preeclampsia precede the disease. Therefore it may occur in-patients with preeclampsia or in-patients who have preeclampsia superimposed on essential hypertension or chronic nephritis.

ESSENTIAL HYPERTENSION IN PREGNANCY

Apart from the specific hypertensive disorder in pregnancy (PIH), essential hypertension is the common hypertensive state in pregnancy. Its incidence varies from 1-3%.

The criteria for Essential Hypertension:

- Rise of blood pressure to the extent of 140/90 mmHg or more during pregnancy prior to the 20th week (molar pregnancy excluded).
- Prospective follow up shows persistent rise of blood pressure even after at least 3 months following delivery.

However, confusion in the diagnosis arises when the case is first seen in later months of pregnancy, especially when the pre-pregnant level of blood pressure remains unknown[1,4,9].

THEORIES ABOUT THE CAUSE OF PREGNANCY–INDUCED HYPERTENSION

Any satisfactory theory must account for the observation that pregnancy induced or aggravated hypertension is very much more likely to develop in the woman who

(1) Is exposed to chorionic villi for the first time
(2) Is exposed to a superabundance of chronic villi, as with twins or hydatidiform mole
(3) Has preexisting, vascular disease or
(4) Is genetically predisposed to hypertension developing during pregnancy.

Although chorionic villi are essential, they need not support a fetus or be located within the uterus.

The risk of pregnancy induced hypertension is appreciably enhanced in circumstances where formation of blocking antibodies to antigenic sites on the placenta might to protect a renal transplant; where effective immunization by a previous pregnancy is lacking, as in first pregnancies; or where the number of antigenic sites provided by the placenta is unusually great compared with the amount of antibody as with multiple fetuses. Strickland and associates however, provided data that do not support "immunization" by a previous pregnancy. They analyzed the outcomes of over 29,000 pregnancies at Parkland Hospital and

reported that pregnancy-induced hypertension was decreased only slightly in women who previously had aborted and were now having their first baby.

Chesley (1974) observed that everyone from allergist to zoologist has proposed a theory and suggested "rational therapy" based upon that theory. Such schemes have included mastectomy, oophorectomy, renal decapsulation, trephinatino, alignment of the woman with the earth's magnetic field, and a myriad of medical regimens.

Cooper and Liston examined the possibility that susceptibility to preeclampsia is dependent upon a single recessive gene. They calculated the expected first-pregnancy frequencies of daughters of women with eclampsia; daughters-in-law served as controls.

Endothelins are potent vasoconstrictors, and it is possible that they play a role in the etiology or response to pregnancy-induced hypertension. Three endothelins have been identified. Endothelin-I is the only endothe; lin produced by human endothelium. Endothelin-2 is of renal origin, and endothelin-3 is produced in neural tissue. Plasma endothelin-1 has been reported to be increased in normotensive laboring and nonlaboring women, and even higher levels have been reported in preeclamptic women. Inhibition of endothelium-derived relaxing factor has been shown to increase mean arterial pressure, decrease heart rate and reverse the pregnancy-induced refractoriness to vasopressors in pregnant rats.

Wang and colleagues reported that normotensive pregnancies are characterized by progressive increases in the ratios of prostacyclin/ thromboxane and vitamin E/lipid peroxides[10].

MANAGEMENT OF PREGNANCY INDUCED HYPERTENSION

Hospital of Home/first Aid Treatment

Ideally all patients of pre-eclampsia are to be admitted in the hospital for effective supervision and treatment. There is no place of damiciliary treatment in an established case of pre-eclampsia.

In case of a seizure the patient, either at home or in the peripheral health centers should be shifted urgently to the tertiary referral hospitals. The patient must be heavily sedated before moving her to the tertiary hospital. Any one of the available drugs in helpful in maintaining sedation – intramuscular injection of Largactil 50 mg and Phenergan 25 mg or intravenous Diazepam 10 mg[11-13].

Treatment Modalities

Rest

Admission in hospital and rest is helpful for continued evaluation and treatment of the patient. While in bed patient should be in left lateral position as much as possible/to lessen the effects of venacavla compression. This achieves the following goals.

- Increases the renal blood flow diuresis
- Increases the uterine blood flow improves the placental perfusion and
- Reduces the blood pressure

Diet

The diet should contain adequate amount of protein (about 100 gm), Usual salt intake is not restricted. Fluids need not be restricted. Total calorie approximate 1600 cal/day.

Sedative

To cut down emotional factor, mild sedative may be given orally.

Diuretics

The diuretics should not be used injudiciously as they cause harm to the baby by diminishing placental perfusion and by electrolyte imbalance.

The compelling reasons for its use are:

- Cardiac Failure
- Pulmonary oedema
- Along with selective antihypertensive drug therapy, where blood pressure reduction is associated with fluid retention
- Massive oedema, not relieved by rest and producing discomfort to the patient.

Antihypertensives (Table 1)

Antihypertensive drugs have limited value in controlling blood pressure due to pre-eclampsia. The compelling indications of its use are:

- Persistent rise of blood pressure especially where the diastolic pressure is over 110 mm Hg. The use is more urgent if associated with proteinuria.
- In severe pre-eclampsia to bring down the blood pressure during continued pregnancy and during the period of induction of labour[11].

Obstetric Management of Preeclampsia

Management of preeclampsia complicated by HELLP syndrome is still controversial. The only known definitive cure remains delivery. Until recently, all patients with a diagnosis of severe preeclampsia/ HELLP syndrome were thought to need immediate delivery. Within the last years, expectant management of such patient has been reported with good success. The goal for managing preeclampsia with HELLP syndrome is ultimately of protect the mother and foetus and to prevent disease progression to eclamsia. Some authors recommend that pregnancies older than 32-34 weeks should be delivered[11].

Management During Labour

Blood pressure tends to rise during labour and convulsions may occur (intrapartum eclampsia). the patient should be in bed. Liberal sedatives should be given in the form of pethidine 75-100 mg intramuscularly and to be repeated at intervals. Antihypertensive drugs may be given if the blood pressure becomes high. One of the most early and the most often used drug is methyldopa-a drug from the group acting via central nervous system, causing the depression in the cardiovascular systems. Blood Pressure and urinary output are to be noted regularly so as to detect imminent eclampsia. Careful monitoring of the foetal well-being is mandatory[11,12].

GENERAL MANAGEMENT OF ECLAMPSIA

- The patient should be placed in a railed cot in an isolated room, protected from noxious stimuli that might provoke further fits. If the patient is unconscious, the position should be changed, at intervals to prevent hypostatic pneumonia and bedsore. The patient should have a doctor or at least, a trained midwife for constant supervision.
- Detailed history is to be taken from the relatives, relevant to the diagnosis of eclampsia, duration of pregnancy, number of fits and nature of medication administered outside.

Only when the patient is stabilized a thorough but quick general, abdominal and vaginal examination are made. If the patient is unconscious, a self-retaining catheter is introduced and the urine is tested for protein. The continuous drainaged facilitates measurement of the urinary output, periodic urine analysis and prevention of soiling of the bed due to incontience, likely to occur during fits.

- Half hourly pulse, respiration rates and blood pressure to be recorded. Hourly urinary output is to be noted. If undelivered, the uterus should be palpated at regular intervals to detect the progress of labour and the foetal heart rate is to be monitored. Immediately after a convulsion, foetal bradycardia is common probably due to maternal acidosis and hypoxia induced by the fit.
- **Fluid balance:** Crystalloid solution (Ringer's solution) is started as a first choice. Total fluids should not exceed the previous 24 hours urinary output plus 1000 ml insensible loss through lungs and skim. Normally, it should not exceed 2 liters in 24 hours. Infusion of balanced salt solution should be at the rate of 75-100 ml/hr. In pre-eclampsia-eclampsia although there is hypovolemia, the tissues are over loaded. An excess of dextrose or crystalline solutions should not be used, as it will aggravate the tissue overload leading to pulmanary oedeam and adult respiratory distress syndrome. Colloids (albumin or haemaccel) remain in the vascular tree and they withdraw fluids from the interstitial space. Unless used carefully, they can lead to circulatory overload. CVP monitaoring is needed for a patient with severe hypertension and reduced urine output. Invasive monitoring with Swan-Ganz catheter is rarely indicated.

  Antibiotic: To prevent infection, ampicillin 500 mg I.M. or I.V. six hourly is administered[11].

SPECIFIC MANAGEMENT OF ECLAMPSIA

Anticonvulsant and Sedative Regime

The aim is to control the fits and to prevent its recurrence. Magnesium sulphate is the drug of choice. Repeat injections are given only if the knee jerks are present , urine output exceeds 30 ml/hour and the respiration rate is more than 12 per minute. The therapeutic level of serum magnesim is 4-7 mEQ/L. Magnesium sulphate is continued for 24 hours after the last seizure. For recurrence of fits, further 2 gm I.V. bolus is given over 5 min. in the above regimens. Menon (1961) in India employed the lytic cocktail regime using chlorpromazine, phenergan and pethidine and has got satisfactory result with reduction of maternal mortality to 2.2%.

Antihypertensives in Eclampsia

Inspite of anticonvulsant and sedative regime, if the blood pressure remains more than 160/110 mm Hg, antihypertensive drugs should be administered.

Management During Fit

- In the premonitory stage, a mouth gag is placed in between the teeth to prevent tongue bite and should be removed after the clonic phase is over.
- The air passage is to be cleared off the mucus with a mucus sucker. The patient's head is to be furned to one side and the pillow is taken of. Raising the foot end of the bed, facilitates postural drainage of the upper respiratory tract.
- Oxygen is given until cyanosis disappears.

Status Eclampticus

Thiopentone sodium 0.5 gm dissolved in 20 ml of 5% dextrose is given intracenously very slowly. An expert anaesthetist should supervise the procedure. If the procedure fails, use of complete anaesthesia, muscle relaxant and assisted ventilation can be employed. In uresponisve cases, Caesarean section in ideal surroudings may be a life saving attempt.

Intensive Care Monitoring

Patient with multiple medical problems needs to be admitted in on intensive care unit where she is looked after by a team consisting of an obstetrician, a physician and on expert anaesthetist. Cardiac, renal or pulmonary complications are managed effectively[11].

OBSTETRIC MANAGEMENT OF ECLAMPSIA

During pregnancy

In majority of cases with antepartum eclampsia, labour start soon after convulsions. But when labour fails to start, the management depends on whether the fits are controlled or not and the maturity of the foetus.

During Labour

In the absence of any contraindication to vaginal delivery, as soon as the labour is well established, low rupture of the membranes is to be done to accelerate the labour. Second stage should be curtailed by forceps, ventouse or craniotomy, if the baby is dead[11].

UNUSUAL CAUSES OF HYPERTENSION IN PREGNANCY[15,16]

Pheochromocytoma

This is a rare but dangerous complication of pregnancy. All patients with proteinuric hypertension in pregnancy should be screened for phaeochromocytoma, although even then the diagnosis can be missed by false negative results. Provided the condition can be identified and treated before delivery the maternal mortality is reduced (to zero in cases where alpha adrenergic blockade has been used). Methods of diagnosis are the same as in non-pregnant individuals but radiological localization is precluded because of the risks to the fetus. Ultrasound or magnetic resonance imaging of the adrenal glands are good alternatives. Treatment with alpha-adrenergic blockade with or without addition of beta-adrenergic blockade is compatible with normal fetal survival.

Coarctation of the Aorta

Previously this condition was associated with a high enough mortality in pregnancy for termination to be recommended. Maternal death was primarily from dissection or rupture of the aorta. Contemporary experience is more favourable and decisions about the advisability may depend more on related factors

such as associated cardiac malformation. Surgical resection during pregnancy is not advisable. A previous successful resection is not a contraindication to undertaking pregnancy.

Cushing's Syndrome

Amenorrhoea and menstrual irregularities are common features of Cushing's syndrome so that the likelihood of conception is diminished. Many of the features of the syndrome – increased pigmentation, striae, weight gain, hyperglycaemia and hypertension – may occur during pregnancy in the absence of the disease. Adrenalectomy during pregnancy with a later successful outcome has been reported. Fetal loss is high in Cushing's syndrome and there may be neonatal adrenal insufficiently.

Conn's Syndrome

This is a rare cause of hypertension in pregnancy. It has usually been diagnosed either before or after pregnancy on the basis of hypokalaemia combined with hypertension. During pregnancy both plasma concentrations and urinary excretion of aldosterone are increased which makes diagnosis difficult. Remission of the disorder may occur during pregnancy possibly caused by progesterone which antagonizes the renal action of aldosterone. Successful pregnancies with and without medical treatment have been reported.

DISCUSSION

Although there is marked regional variation approximately three-quarters of the patients have pregnancy-induced hypertension (preeclampsia) and the remaining one-quarter have chronic hypertension of various types[5]. Perinatal mortality and morbidity reflect both the foetal syndrome of preeclampsia (intrauterine growth restriction-IUGR) and the consequences of iatrogenic prematurely resulting from deteriorating maternal disease or foetal condition[1].

While in developed countries, its prevalence is far and few but in the developing ones, particularly in the rural areas, it is still rampant and contributes significantly to the maternal deaths. In a developing country like India, with uncared pregnancy, this entity on many occasions remains undetected till major complications supervene. Imperfect documentation and lack of uniformity in the diagnostic criteria are the responsible factor in variation of its frequency. In the developing countries, the incidence is expected to be higher. Comparative low figures in the hospital statistics is due to inclusion of only severe degree of the syndrome, the minor ones being ignored[1,4]. The hospital incidence in eclampsia ranges from 1 in 500 to 1 to 30 pregnancies that are complicated with hypertension. It is more common in primigravidae (75%), five times more common in twins than in singleton pregnancies and occurs between the 36th week and term in more than 50% cases [1.4, 10].

Pregnancy-induced hypertension more often affects nulliparous women., Older women, who accrue an increasing incidence of chronic hypertension with advancing age, are at greater risk of pregnancy-aggravated hypertension. Thus, women at either end of reproductive age have been considered in the past to be more susceptible[10].

Women with preeclompsia have an increased risk of convulsions. The degree of risk depends on the severity of the Preeclampsia and on the characteristics of the woman. Maternal and neonatal outcomes are usually good among pregnant women who have either mild chronic hypertension or gestational hypertension. In addition, antihypertensive drug therapy permits such women to continue their pregnancies to term. Close medical supervision and timely delivery are the keys to the treatment of Preeclampsia.

REFERENCES

1. Janga D. Pregnancy induced hypertension a uemplication of pregnancy. Obs and gynae Today 2005; X (7):395-398.
2. Tripathi KD. Essential of Medical Pharmacology. 2003; 5th Ed:5-20.
3. Sharma HL, Sharma KK**.** Principle of Pharmacology. 2007; Ist Ed:285-294.
4. Dutta DC, Konar H. Hypertension disorders in pregnancy. Text book of Obstetrics. 2000; 6th Ed:221-42.
5. Arora V. Pregnancy induced hypertension Aetio-pahcogenesis , features and complications. Obs and Gynal Today. 2005; X(8):446-451.

6. Brown MA, Mangas G, Davis G, Homer C. The natural history of white coat hypertension during pregnancy. BJOG 2005;112(5):601-6.
7. Bhasale L, Padia D, Malhotra H, Thakkar D, Palep HS, Algotar KM. Capsule "Surat" for comprehensive antenatal care and prevention of pregnancy induced hypertension. Lancet 1994; 343(8898):619-29.
8. Roberts J. Current Perspectives on Preeclampsia. Journal of Nurse Midwifery. 1994; 39(2);70-90.
9. Sibai BM. Pitfalls in diagnosis and management of preeclampsia. American Journal of Obstetrics and Gynecology. 1988; 159:1-5.
10. Cunninghom FG, et al. Williams Obstetrics. Norwalk, Connecticut: Appleton and Lange 1993; 19th ed:763-817.
11. Sharma JB. Management of pregnancy induced hypertension an overview of preeclampsia and eclampsia. O Obs and gynae Today 2005; X(10):576-81.
12. Dutta DC, Konar H. Hypertension disorders in pregnancy. Text book of Obstetrics. 2000; 6th ed:221-42.
13. Seremak-Marazikiewicz A, Drews K. Methyldopa in therapy of hypertension in pregnant women. Ginekol Pal 2004; 75(2):160-5.
14. Agrawal Umber. Role of antihypertensci in the treatment of pregnancy induced hypertension. Obs and Gynal Today 2005; X(11):632-637.
15. Michael de Sweit. Medical disorders in obsterics practice. 1989; 2nd edition:249-289.
16. Bing RF and Smith AJ. Plasma and interstitial volumes in essential hypertension : Relationship to blood pressure. Clinical Science 1981; 61:287-93.

Table 1: Drugs used for the management of hypertension during pregnancy

Molecule	Class	Comments and risks
Methyldopa	Central -agonist	Drug of choice by the NHBPEP* working Group
Diltiazem Verapamil	Calcium antagonists	Potential synergism with magnesium sulfate may lead to precipitous hypotension
Hydralazine	Direct vasodilators	Decreases systemic resistance through direct vasodilation of arterioles.
Nitroprusside		With prolonged (>4h) use, it can cause potential foetal cyanide toxicity
Metoprolol Atenolol	Beta-odrenergic receptor blockers	These may be associated with • Intrauterine growth restriction • Reduced symptoms of acute hypoglycaemia and masked signs of hyperthyroidism • Caution in impaired hepatic function • Discontinue therapy at signs of liver dysfunction
Labetalol	Combined alpha And bet-adrenergic blocker	
Frusemide Hydrochlorothiazide Triameterene Bumetanide	Diurectic	• Prevents normal physiologic volume expansion that occurs in pregnancy • May reduce uterine blood flow Recommended for chronic hypertension if prescribed before gestation or if patients are salt-sensitive. Not recommended in preeclampsia
Captopril Enalapril Lisinopril	ACE inhibitors	Foetal abnormalities including death, can be caused, and should not be used in pregnancy
Lasartan Valsartan	Angiotensin II receptor blockers	Highly unsafe in second and third trimesters of pregnancy

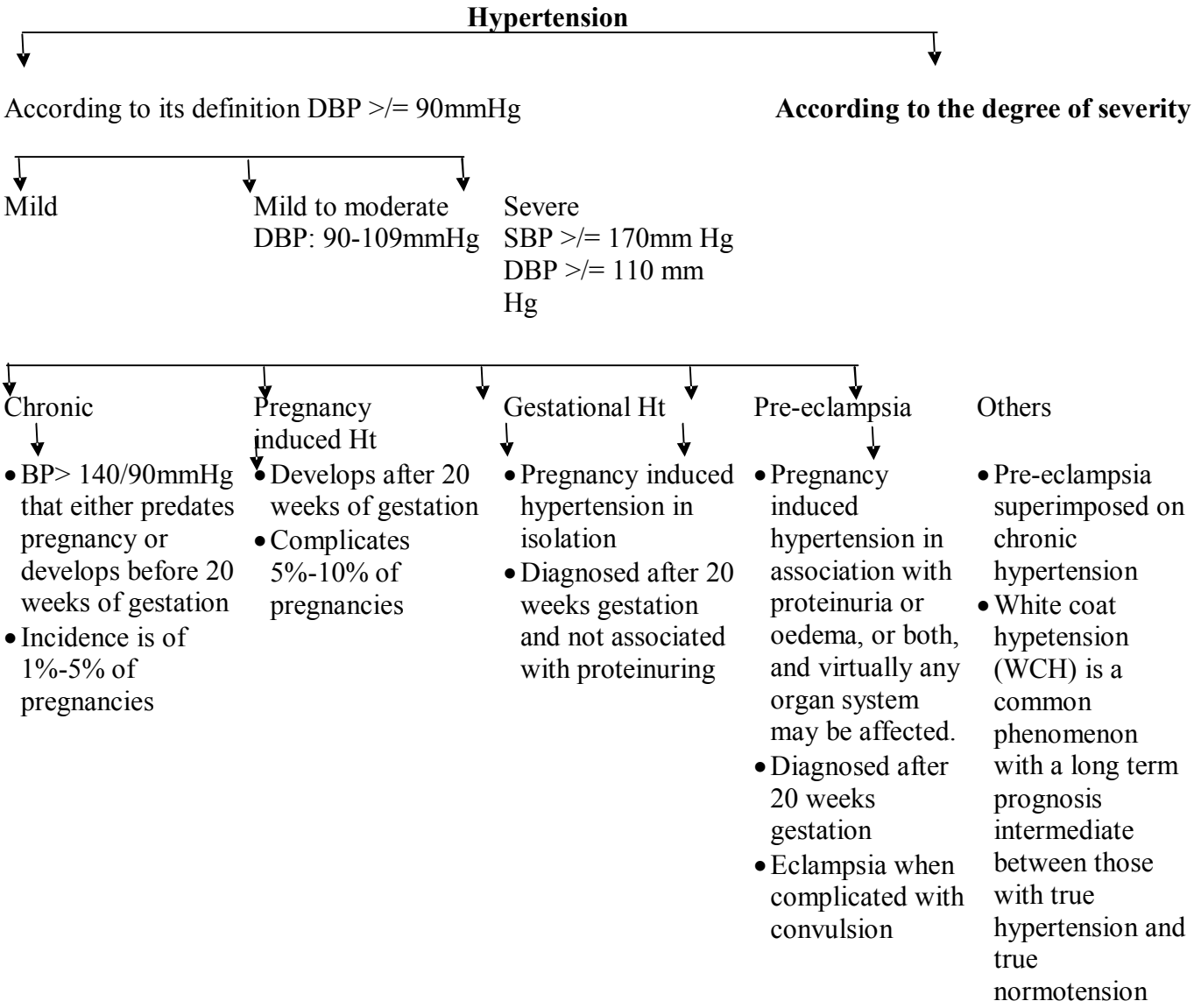

Figure 1: Pregnancy induced hypertension are classified