A COMPLETE ANALYSIS OF HYPERTENSION IN PREGNANCY AND ITS CAUSES

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Abstract

Hypertension is the most common medical disorder encountered during pregnancy. Hypertensive disorders are most important clinical problem in pregnancy. Hypertension is one of the most frequently observed medical diseases, which considerably affects maternal and fetal morbidity and mortality. There is a progressive increase in the incidence of hypertensive disorders in pregnancy worldwide. However, provision of blood pressure at a level sufficient to preserve maternal end organs plays key role in pregnancies progressing with high blood pressure. Here, we discuss types, risk factors, diagnosis, and management strategies of hypertensive disorders in pregnancies in the light of current guidelines. Moreover, we review hypertension related preeclampsia and eclampsia. The existing diagnostic tools and the tests which have been proposed for screening preeclampsia are comprehensively described. We also highlight the short- and long term implications of preeclampsia. Finally, we review the current management guidelines, goals of treatment and describe the potential risks and benefits associated with various antihypertensive drug classes. Preeclampsia still remains an enigma, and the present management focuses on monitoring and treatment of its manifestations. We are hopeful that this in depth critique will stimulate the blossoming research in the field and assist practitioners to identify women at risk and more effectively treat affected individuals.

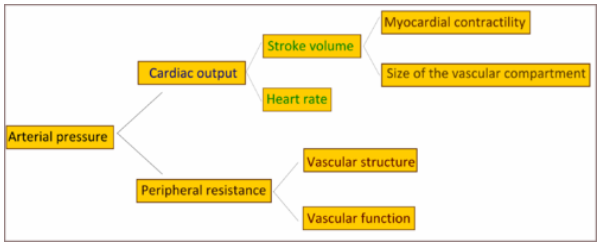
Keywords: *Hypertension, Pregnancy, Preeclampsia, Eclampsia, high blood pressure*

1. INTRODUCTION

Hypertension (HTN or HT), also known as high blood pressure (HBP), is a long-term medical condition in which the blood pressure in the arteries is persistently elevated. High blood pressure typically does not cause symptoms.[1] Long-term high blood pressure, however, is a major risk factor for coronary artery disease, stroke, heart failure, atrial fibrillation, peripheral vascular disease, vision loss, chronic kidney disease, and dementia.[2]

High blood pressure is classified as either primary (essential) high blood pressure or secondary high blood pressure.[3] About 90–95% of cases are primary, defined as high blood pressure due to nonspecific lifestyle and genetic factors.[4] Lifestyle factors that increase the risk include excess salt in the diet, excess body weight, smoking, and alcohol use.[5] The remaining 5–10% of cases are categorized as secondary high blood pressure, defined as high blood pressure due to an identifiable cause, such as chronic kidney disease, narrowing of the kidney arteries, an endocrine disorder, or the use of birth control pills.[5]

Figure 1. Hypertension



Blood pressure is expressed by two measurements, the systolic and diastolic pressures, which are the maximum and minimum pressures, respectively.[1] For most adults, normal blood pressure at rest is within the range of 100–130 millimeters mercury (mmHg) systolic and 60–80 mmHg diastolic.[7][12] For most adults, high blood pressure is present if the resting blood pressure is persistently at or above 130/80 or 140/90 mmHg [7] Different numbers apply to children.[13] Ambulatory blood pressure monitoring over a 24-hour period appears more accurate than office-based blood pressure measurement.[10] **Hypertensive disease of pregnancy**, also known as **maternal hypertensive disorder**, is a group of diseases that
includes preeclampsia, eclampsia, gestational hypertension, and chronic hypertension.

1.1 SIGNS AND SYMPTOMS

Hypertension is rarely accompanied by symptoms, and its identification is usually through screening, or when seeking healthcare for an unrelated problem. Some people with high blood pressure report headaches (particularly at the back of the head and in the morning), as well as lightheadedness, vertigo, tinnitus (buzzing or hissing in the ears), altered vision or fainting episodes.[20] These symptoms, however, might be related to associated anxiety rather than the high blood pressure itself.[21] On physical examination, hypertension may be associated with the presence of changes in the optic fundus seen by ophthalmoscope.[22] The severity of the changes typical of hypertensive retinopathy is graded from I to IV; grades I and II may be difficult to differentiate.[22] The severity of the retinopathy correlates roughly with the duration or the severity of the hypertension.[20]

1.2 SECONDARY HYPERTENSION

Hypertension with certain specific additional signs and symptoms may suggest secondary hypertension, i.e. hypertension due to an identifiable cause. For example, Cushing's syndrome frequently causes truncal obesity, glucose intolerance, moon face, a hump of fat behind the neck/shoulder (referred to as a buffalo hump), and purple abdominal stretch marks.[23] Hyperthyroidism frequently causes weight loss with increased appetite, fast heart rate, bulging eyes, and tremor. Renal artery stenosis (RAS) may be associated with a localized abdominal bruit to the left or right of the midline (unilateral RAS), or in both locations (bilateral RAS). Coarctation of the aorta frequently causes a decreased blood pressure in the lower extremities relative to the arms, or delayed or absent femoral arterial pulses. Pheochromocytoma may cause abrupt ("paroxysmal") episodes of hypertension accompanied by headache, palpitations, pale appearance, and excessive sweating.[23]

1.3 HYPERTENSIVE CRISIS

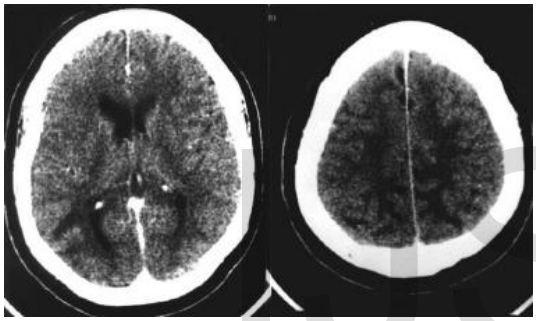
Severely elevated blood pressure (equal to or greater than a systolic 180 or diastolic of 110) is referred to as a hypertensive crisis. Hypertensive crisis is categorized as either hypertensive urgency or hypertensive emergency, according to the absence or presence of end organ damage, respectively.[24][25] In hypertensive urgency, there is no evidence of end organ damage resulting from the elevated blood pressure. In these cases, oral medications are used to lower the BP gradually over 24 to 48 hours.[26] In hypertensive emergency, there is evidence of direct damage to one or more organs.[27][28] The most affected organs include the brain, kidney, heart and lungs, producing symptoms which may include confusion, drowsiness, chest pain and breathlessness.[26] In hypertensive emergency, the blood pressure must be reduced more rapidly to stop ongoing organ damage,[26]

however, there is a lack of randomized controlled trial evidence for this approach.[28]

2. HYPERTENSION DURING PREGNANCY

Hypertension occurs in approximately 8–10% of pregnancies.[23] Two blood pressure measurements six hours apart of greater than 140/90 mm Hg are diagnostic of hypertension in pregnancy.[29] High blood pressure in pregnancy can be classified as pre-existing hypertension, gestational hypertension, or pre-eclampsia.[30]

Figure.2 Hypertension and Pregnancy



Pre-eclampsia is a serious condition of the second half of pregnancy and following delivery characterized by increased blood pressure and the presence of protein in the urine.[23] It occurs in about 5% of pregnancies and is responsible for approximately 16% of all maternal deaths globally.[23] Pre-eclampsia also doubles the risk of death of the baby around the time of birth.[23] Usually there are no symptoms in pre-eclampsia and it is detected by routine screening. When symptoms of pre-eclampsia occur the most common are headache, visual disturbance (often "flashing lights"), vomiting, pain over the stomach, and swelling. Pre-eclampsia can occasionally progress to a life-threatening condition called eclampsia, which is a hypertensive emergency and has several serious complications including vision loss, brain swelling, seizures, kidney failure, pulmonary edema, and disseminated intravascular coagulation (a blood clotting disorder).[23][31]

In contrast, gestational hypertension is defined as new-onset hypertension during pregnancy without protein in the urine.[30]

2.1 RISKS

Some women have a greater risk of developing hypertension during pregnancy. These are:

- Women with chronic hypertension (high blood pressure before becoming pregnant).
- Women who developed high blood pressure or preeclampsia during a previous pregnancy, especially if these conditions occurred early in the pregnancy.
- Women who are obese prior to pregnancy.
- Pregnant women under the age of 20 or over the age of 40.
- Women who are pregnant with more than one baby.
- Women with diabetes, kidney disease, rheumatoid arthritis, lupus, or scleroderma.

2.2 CHILDREN

Failure to thrive, seizures, irritability, lack of energy, and difficulty in breathing [32] can be associated with hypertension in newborns and young infants. In older infants and children, hypertension can cause headache, unexplained irritability, fatigue, failure to thrive, blurred vision, nosebleeds, and facial paralysis.[32][33]

3. TYPES

Preeclampsia

Preeclampsia is a condition that typically starts after the 20th week of pregnancy and is related to increased blood pressure and protein in the

mother's urine (as a result of kidney problems). Preeclampsia affects the placenta, and it can affect the mother's kidney, liver, and brain. When preeclampsia causes seizures, the condition is known as eclampsia--the second leading cause of maternal death in the U.S. Preeclampsia is also a leading cause of fetal complications, which include low birth weight, premature birth, and stillbirth.[34]

There is no proven way to prevent preeclampsia. Most women who develop signs of preeclampsia, however, are closely monitored to lessen or avoid related problems. The only way to "cure" preeclampsia is to deliver or abort the baby.

Diagnosis

Unfortunately, there is no single test to predict or diagnose preeclampsia. Key signs are increased blood pressure and protein in the urine (proteinuria). Other symptoms that seem to occur with preeclampsia include persistent headaches, blurred vision or sensitivity to light, and abdominal pain.

All of these sensations can be caused by other disorders; they can also occur in healthy pregnancies. Regular visits are scheduled to track blood pressure and level of protein in urine, to order and analyze blood tests that detect signs of preeclampsia, and to monitor fetal development more closely.[34]

Classification

A classification of hypertensive disorders of pregnancy uses 4 categories:[35]

- chronic hypertension;
- preeclampsia-eclampsia;
- preeclampsia superimposed on chronic hypertension;
- gestational hypertension (transient hypertension of pregnancy or chronic hypertension identified in the latter half of pregnancy).

This terminology is preferred over the older but widely used term pregnancy-induced hypertension (PIH) because it is more precise. The newer terminology reflects simply relation of pregnancy with either the onset or first detection of hypertension and that the question of causation, while path genetically interesting, is not the important point for most health care purposes. This classification treats HELLP syndrome as a type of preeclampsia rather than a parallel entity.[35]

Prevention

Blood pressure control can be accomplished before pregnancy. Medications can control blood pressure. Certain medications may not be ideal for blood pressure control during pregnancy such as angiotensin-converting enzyme (ACE) inhibitors and angiotensin II (AII) receptor antagonists. Controlling weight gain during pregnancy can help reduce the risk of hypertension during pregnancy. [36]

Prognosis

The effects of high blood pressure during pregnancy vary depending on the disorder and other factors. Preeclampsia does not in general increase a woman's risk for developing chronic hypertension or other heart-related problems. Women with normal blood pressure who develop preeclampsia after the 20th week of their first pregnancy, short-term complications--including increased blood pressure--usually go away within about 6 weeks after delivery.Some women, however, may be more likely to develop high blood pressure or other heart disease later in life. More research is needed to determine the long-term health effects of hypertensive disorders in pregnancy and to develop better

methods for identifying, diagnosing, and treating women at risk for these conditions. Even though high blood pressure and related disorders during pregnancy can be serious, most women with high blood pressure and those who develop preeclampsia have successful pregnancies. Obtaining early and regular prenatal care is the most important thing you can do for you and your baby.[36]

4. CONSEQUENCES OF HYPERTENSION IN PREGNANCY

Hypertension in pregnancy is a major cause of maternal morbidity and mortality in the Pakistan. There is approximately one maternal death due to preeclampsia-eclampsia per 100,000 live births, with a case-fatality rate of 6.4 deaths per 10,000 cases . The outcome of hypertension in pregnancy is, not surprisingly, affected by multiple factors. These embrace (but are not limited to) gestational age at onset, severity of disease, and the presence of co morbid conditions including diabetes mellitus, renal disease, thrombophilia, or preexisting hypertension [37]. Adverse outcomes related to hypertension in pregnancy can be divided into short-term versus long-term complications. While short-term complications can be further sub grouped into maternal and fetal complications, long-term outcomes are mainly maternal.

4.1. Short-Term Complications

4.1.1. Maternal. Outcomes for pregnancy complicated by hypertension range from uneventful pregnancy in women with chronic, controlled hypertension to death in cases of preeclampsia-eclampsia. The major adverse outcomes include central nervous system (CNS) injuries such as seizures (eclampsia), hemorrhagic and ischemic strokes, hepatic damage ranging from transaminase elevation, the so-called “HELLP syndrome” (hemolysis, elevated liver enzymes, and low platelets)

4.1.2. Fetal. The effects of chronic, controlled hypertension in pregnancy on the fetus are minimal. However, preeclampsia-eclampsia can lead to higher frequency of induced labor, fetal growth restriction, neonatal respiratory difficulties, and increased frequency admission to neonatal intensive care unit. Hypertension in pregnancy, even in its more severe forms, causes only minimal increased risk for perinatal or fetal death [38].

4.2. Long-Term Complications.

Though hypertension in pregnancy/preeclampsia is usually thought of as a short-term problem that resolves itself with delivery, it still carries significant risk for remote complications.

4.2.1. Risk of Recurrence. The risk of recurrent preeclampsia in subsequent pregnancies varies with the severity and time of onset of the acute episode. It is estimated that women with severe, early preeclampsia during their first pregnancy will have a high risk of recurrent preeclampsia in their subsequent pregnancies (25–65%) [38].

4.2.2. Cardiovascular Complications. The association between preeclampsia and cardiovascular diseases is both well described and well documented. Women with history of preeclampsia are at significantly increased risk to develop hypertension, ischemic heart disease, stroke, type II diabetes, and venous thromboembolism in comparison with women without history of the disease [39].

4.2.3. Renal Disease. More renal biopsies are undertaken in victims of preeclampsia than in unaffected women . There is also an increased risk for women with history of preeclampsia to

develop end-stage renal disease (ESRD), though the absolute risk appears to be low.

4.2.4. Cancer. Multiple observational studies evaluated the possible association between hypertension in pregnancy and cancer risk. Overall, women with preeclampsia were found to be at reduced risk or had no excess risk of cancer when followed by extended periods postpartum [40].

5. Treatment of Hypertension

The first principle of treatment of hypertension in pregnancy is to correctly diagnose the category (Table 1) and severity of the hypertension. Implicit to this guide is the aforementioned limited value of attempting to completely normalize the blood pressure in this setting. The second and perhaps even more important principle is to understand the potential vulnerability of the fetus to treatment.

Table 1: Classification of hypertension in pregnancy.

Chronic hypertension	(i) increased BP before week 20 (or known to exist prior to pregnancy) (ii) hypertension persistent for more than 12 weeks after pregnancy
Preeclampsia-eclampsia	(i) de novo appearance of hypertension after mid-pregnancy (ii) proteinuria at least 300 mg/24 hr
Preeclampsia superimposed upon existing hypertension	(i) new onset proteinuria
Gestational hypertension	(i) transient hypertension appearing after mid-pregnancy (ii) confirmed by return to normal BP postpartum (iii) no proteinuria

5.1. Chronic Hypertension. The estimated prevalence of chronic hypertension in pregnancy in Pakistan is 3% and has been increasing over time. This increase in prevalence has been attributed to the increased prevalence of obesity and delay in childbearing to ages, when chronic hypertension is more common [100].41

Women with the following conditions are at increased risk for maternal and fetal complications and should have a lower threshold for treatment [42].

- underlying renal disease;
- secondary hypertension;
- end-organ damage (e.g., ventricular dysfunction, retinopathy);
- maternal age over forty years old;
- micro vascular disease;
- history of stroke
- previous perinatal loss;
- diabetes.

5.2. Gestational Hypertension. Gestational hypertension is elevated blood pressure, which develops after 20 weeks of gestation in a previously normotensive woman, though without proteinuria. It complicates 6% of all pregnancies. These women are at high risk for developing preeclampsia that can occur at any time including the first postpartum week and need close monitoring. Approximately 15–45% will eventually develop preeclampsia [43] The goal of treatment is same as chronic hypertension.

5.3. Preeclampsia. The general principles as outlined to guide the treatment of women with chronic hypertension are applicable to the preeclamptic patients. Close monitoring to recognize fetal distress while receiving treatment is essential. Early onset preeclampsia (less than thirty-four weeks) requires careful use of antihypertensive medications, bed rest, and in-hospital monitoring of both mother and fetus. This approach may help delay delivery and thus improve fetal outcome. Often these patients are intravascularly depleted and are more susceptible to precipitous, drug-induced drops in blood pressure. If signs of other fetal or maternal distress are noted, delivery is the definitive treatment. Concerns about hypotension and decreased uteroplacental blood flow are central to the treatment of the preeclamptic patient, since placental ischemia is the focal point of preeclampsia pathophysiology. In most instances, delivery of preeclamptics is indicated

after 37 weeks of gestation or when fetal lung maturity has been confirmed.

5.4. Superimposed Preeclampsia. Superimposed preeclampsia complicates approximately 25% of pregnancies in women with chronic hypertension [44] Principles of management are the same as outlined earlier for preeclampsia, although these women have more likelihood of developing severe hypertension, requiring multiple antihypertensive medications.

6. CONCLUSION

Hypertension is most frequently encountered complication in pregnancy. It can be fatal for mother and it can cause severe morbidity and mortality in infant as well, if it is failed to provide appropriate therapy. Thus, early diagnosis, treatment and knowledge of conditions with hazardous potential will play an important role in reducing maternal and fetal morbidity and mortality.

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