
**HYPERTENSION: GLOBAL HEALTH IMPACT, PATHOGENESIS,
SYMPTOMS AND TREATMENT APPROACHES**

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ABSTRACT

High blood pressure is the principal factor responsible for heart diseases as well as early deaths globally. Due to the extensive usage of antihypertensive drugs, there have been no changes in average BP across the world within the last four decades or a slight reduction. However, the occurrence of hypertension has risen in the population, particularly in the low and middle-income countries (LMICs). It was estimated that 31.1% (1.39 billion people) of the adult population had hypertension in 2010. The occurrence of hypertension among adults was higher in LMICs (31.5%, 1.04 billion) compared to the high-income nations (28.5%, 349 million). Heart disease that results from high blood pressure, or HYPERTENSIVE heart disease, can be defined as the reaction of the heart to the load or stress that the heart has to deal with because of increased arterial pressure and total peripheral resistance brought about by hypertension in the blood vessels. Even though the reaction may appear exaggerated relative to the extent of the arterial pressure, it is mainly caused by the hemodynamic overload. Hypertension may lead to, or is associated with, several types of heart diseases, such as left ventricular hypertrophy, congestive heart failure, cardiac dysrhythmia, and ischemic heart disease. The risk of coronary artery heart disease is linked with the systolic and diastolic. However, stress leads to hypertension by elevating blood pressure repeatedly and also through nervous stimulation that results in production of many vasoconstriction hormones leading to high blood pressure. The factors that lead to changes in blood pressure due to stress include "white coat" hypertension, work related stress, race, environment, and emotional stress. Moreover, whenever a single factor that is capable of causing stress is combined with other such factors, the effects of that particular factor are greatly multiplied. In general, research has proved that stress alone cannot cause hypertension. Nevertheless,

there are some non-pharmacological ways of managing stress that help reduce the risk of developing hypertension; examples include meditation, acupuncture, biofeedback, and music therapy. Pulmonary hypertension describes any number of disorders that result either directly or indirectly in increased pressure within the pulmonary arteries. There are five primary categories of pulmonary hypertension that include a mean pulmonary artery pressure >20 mmHg: pulmonary arterial hypertension (rare), pulmonary hypertension secondary to left heart disease (very common), pulmonary hypertension secondary to lung disorders (common), pulmonary hypertension secondary to pulmonary artery obstructions due to thromboembolism (rare), and pulmonary hypertension due to unidentified and/or multiple factors (rare). Hypertension is an epidemic affecting a billion people and is the most common risk factor for mortality globally. The prevalence of hypertension was calculated to be 29.2 percent in males and 24.8 percent in females by the WHO statistics in 2012. About 90 percent for both genders who are non-hypertensive at the age of 55 to 65 years will acquire hypertension at the age of 80-85. Hypertension is not a problem faced only by affluent populations but is a problem of all economic categories of nations. In the total number of 58.8 million deaths in the year 2004, hypertension contributed 12.8% (7.5 million deaths). Globally, hypertension causes 51 percent of cerebrovascular diseases and 45 percent of ischemic heart diseases. Contrary to the popular opinion that hypertension is more significant for developed countries, the mortality rate due to hypertension is more than twice in less developed countries.

INTRODUCTION:

The current prevalence rate of hypertension in childhood is between 1-5%, while in minority adolescents, it may range from 10-15%¹⁻³. PH, which is sometimes called essential hypertension, was formerly seen as an adult disease, but its incidence has increased significantly among children owing to the rising prevalence of obesity in children^{4,5}. Children who are obese are thrice as likely to have hypertension compared to those who are not obese^{6,7}. Thus, this review will highlight obesity-related hypertension among adolescents. Non-obese adolescents with hypertension are also mentioned when there is available literature. Aging is an unavoidable phase of life that comes with two unwanted things; physiologic deterioration and disease process^[1]. Hypertension is considered to be one of the leading risk factors for cardiovascular diseases as well as death, especially among older people. This condition is regarded as being a serious yet symptomless disease process, which demands optimum treatment and compliance to prescribed medicines in order to minimize

the risks of developing cardiovascular, cerebrovascular and renal diseases[2]. Elderly patients with hypertension present a dilemma to the CV specialists and other doctors. In addition, as a result of employing various combination therapies in hypertensive patients with certain risk factors aimed at achieving BP reduction beyond the traditional objectives, many questions arise regarding the aggressiveness of treatment in such patients. While the existence of some instances of hypertension can be attributed to specific factors, for example renal arterial narrowing, pheochromocytoma, increased aldosterone secretion from the adrenals, or genetic factors, about 95% of patients cannot be found to have any underlying cause, and as a consequence, their condition is regarded as essential. Essential hypertension usually occurs alongside obesity, lipid metabolism disturbances, age, and insulin resistance, and as a consequence, it may be viewed as a component of metabolic syndrome. Although hypertension is known as a significant contributor to morbidity and mortality, its mechanism of action is not yet fully understood. Recently, however, genetic techniques have been applied to study this particular disease to understand the molecular pathways behind the variability in blood pressure, thus understanding the mechanism of the disease and potential therapeutic targets. This review will specifically examine molecular pathways involved in blood pressure variability in humans. Control of Blood Pressure is essential for continuous perfusion of all important organs. For instance, when there is any block in the blood flow to the brain, it leads to loss of consciousness, whereas extended block leads to death of non-perfused organs. In contrast, elevated pressure in the body that gives rise to excess perfusion than the requirement does not contribute much to metabolism but rather causes vascular damage. The life expectancy trend keeps rising in all the developed nations of the world (Roberts, 2011). This means that the elderly, who can be described as people aged above 65 years, keep making more significant contributions to the population. Life expectancy has risen by 20 years since 1950 in all parts of the world. The total figure of older people in the U.S. will rise to about 80 million in the coming 30 years. Elevated blood pressure is one of the most common risks for CVD mortality that is treatable using antihypertensive medications, as the risk from elevated BP levels can be significantly reduced with proper medication and lowering of BP and target organ damage. A total number of 69 drugs belonging to 15 different classes, which may also include single-pill combinations, are currently approved for the treatment of hypertension in the USA.¹ However, despite all those treatment opportunities, up to 10%-15% of the total hypertensive population suffers from resistant hypertension, meaning that their BP is not under control even when they receive optimal treatment with 3 or more antihypertensive medications, including nonpotassium-

sparing diuretics.^{2,3} Moreover, approximately 0.5% of the total hypertensive patients suffer from refractory hypertension, or hypertension that cannot be

Types:

Primary hypertension: Also known as Essential Hypertension, primary hypertension is a chronic disorder that is characterized by constantly high blood pressure without any identifiable causes. Primary hypertension constitutes up to 90 to 95 percent of all hypertension instances. The disorder develops slowly as a result of interactions among genetic and non-genetic causes, including a diet rich in sodium, overweight, emotional stress, and physical inactivity. Although the disorder may not present any symptoms, it is capable of leading to life-threatening conditions such as heart disease, strokes, and damage to the kidneys. In cases of primary hypertension, high peripheral resistance and changes in vascular structure become important factors in sustaining high blood pressure. In the course of time, the constant high pressure causes damage to blood vessels and important organs such as the heart, the kidneys, the brain, and the eyes. In the absence of proper treatment, it increases the risks of developing diseases such as coronary heart disease, stroke, congestive heart failure, and chronic renal failure. Diagnosis is done by taking blood pressure measurements, which must remain above normal for some period of time. Treatment is aimed at the prevention of complications, and not cure. Changes in lifestyle like having a proper diet, low salt intake, regular physical activity, ideal body weight, and smoking cessation become mandatory. Pharmacological management includes antihypertensive drugs like diuretics, ACE inhibitors, or calcium channel blockers.

Secondary hypertension: Secondary hypertension is the kind of hypertension caused by an underlying factor that causes increased blood pressure levels. In contrast to primary (or essential) hypertension, secondary hypertension is due to particular factors and can be potentially curable or reversible. Secondary hypertension accounts for only 5-10% of all hypertension cases; however, it is prevalent among young people and resistant hypertension patients. Primary reasons of developing secondary hypertension include chronic kidney disease and renal artery stenosis because of the inability of the body to control blood pressure properly. Endocrine abnormalities like Cushing's syndrome, hyperthyroidism, hypothyroidism, and primary aldosteronism can cause hormonal imbalance, and hence affect blood pressure as well as volume of the liquid inside the body. Other possible factors include sleep apnea, coarctation of the aorta, and some forms of tumors like pheochromocytoma.

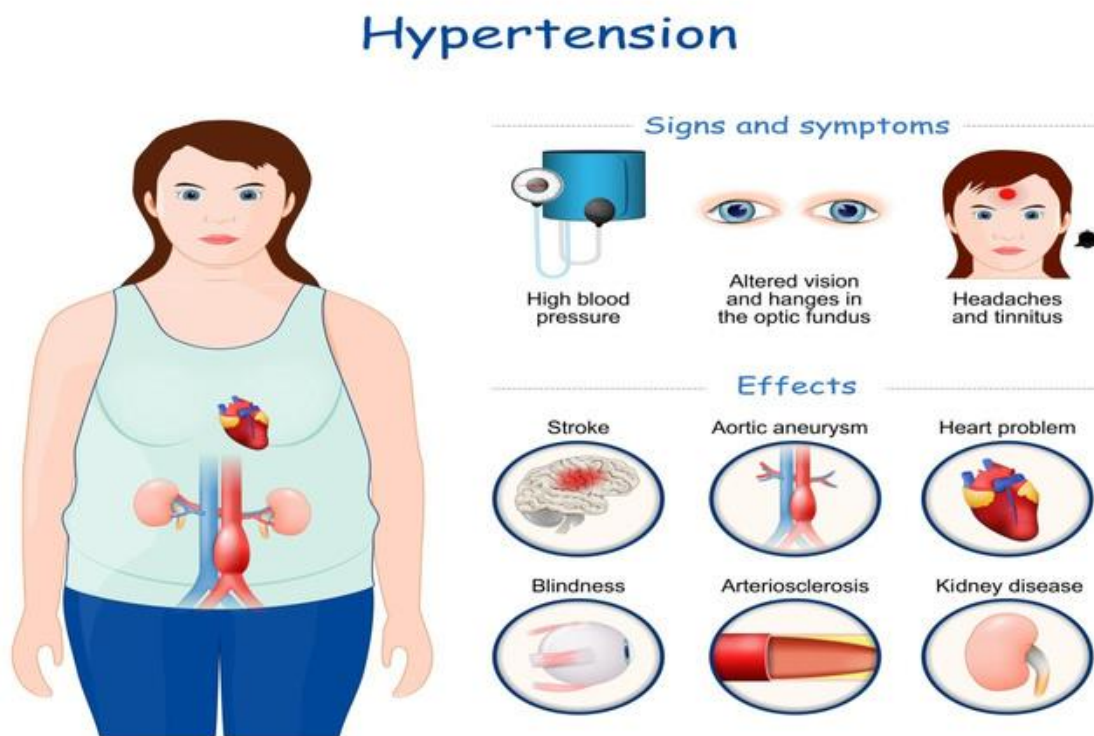
Medication as well as substances can provoke development of secondary hypertension, such as birth control pills, corticosteroids, NSAIDs, and alcohol consumption. Clinical presentation in secondary hypertension can vary compared to primary hypertension. The disease can be characterized by the abrupt development of high blood pressure, unresponsiveness to conventional treatments for hypertension, or markedly elevated blood pressure at an early age. Clinical manifestations can also provide clues about the cause of hypertension, like obesity and full moon face in Cushing's syndrome and heart palpitations and excessive sweating in pheochromocytoma. Diagnosis entails identifying the etiology behind hypertension using various laboratory and radiologic assessments and physical examination. Management primarily aims to treat the underlying disorder, as this would significantly improve or even eliminate hypertension. Anti-hypertensive medications only serve as a supplementary management approach. In summary, secondary hypertension is a critical medical problem since it can be cured when its root causes are identified and managed early.

Key points:

1. Hypertension is the main preventable risk factor responsible for cardiovascular diseases and early mortality across the globe.
2. There are increasing rates of the incidence and the prevalence of hypertension, especially in low- and middle-income countries (LMICs).
3. There are inadequate efforts toward awareness, treatment, and management of hypertension, especially in LMICs.
4. Efforts toward risk reduction, which include high sodium intake, low potassium intake, obesity, alcohol intake, physical inactivity, and unhealthy diets, are encouraged to manage and prevent hypertension.
5. There should be a multi-faceted approach to the implementation of hypertension prevention and management strategies to address the challenges in patients, providers, systems, and communities.
6. There is a need for assessments to measure the economic impact of hypertension around the world.
7. Hypertension is a disease condition involving sustained elevation of blood pressure within arteries.
8. It is referred to as the "silent killer" since it may not exhibit any symptom for many years.

9. The normal BP ranges at 120/80 mmHg.
10. Hypertension is considered present where the BP is $\geq 140/90$ mmHg or $\geq 130/80$ mmHg.
11. Hypertension is generally divided into primary and secondary types.
12. Primary hypertension has no known cause and accounts for 90-95% of cases.
13. Secondary hypertension arises as a result of other diseases, e.g., kidney diseases.
14. Major risk factors are genetics, obesity, stress, and age-related.
15. Hypertension due to lifestyles such as excessive salt and alcohol intake.

HYPERTENSION –INTEGRATED DIAGRAM



Diagnosis:

The determination of the presence of hypertension is largely dependent on the accurate measurement of blood pressure through standardized measurement methods rather than one time only measurement. In accordance with the recommendations of groups like the American Heart Association and the World Health Organization, hypertension is diagnosed when systolic blood pressure readings have been consistently ≥ 140 mm Hg and/or diastolic blood pressure readings ≥ 90 mm Hg in repeat measurements performed during separate

visits. Standardized methods used for the measurement include the use of a calibrated sphygmomanometer with the patient comfortably seated after five minutes of rest.

In order to enhance accuracy and to exclude white coat hypertension, which refers to falsely high readings due to anxiety, ABPM or HBPM may be employed. The former is characterized by the recording of blood pressure readings at certain intervals throughout 24 hours, whereas the latter makes it possible for patients to self-monitor blood pressure in a comfortable setting over several days. Both types of procedures are effective means of confirming sustained hypertension and excluding masked hypertension. In addition to taking blood pressure measurements, the clinical approach to the diagnosis of hypertension is of great importance. Medical history is carefully taken in order to determine risk factors, such as family history, smoking, drinking, obesity, and physical inactivity. Physical examination implies taking body mass index, heart rate, and checking for signs of target organ damage. Laboratory investigation comprises various tests of blood and urine, as well as electrocardiography.

Treatment of Hypertension:

Hypertension Management aims at lowering blood pressure levels in order to avoid any adverse effects, including heart conditions, stroke, and kidney problems. The approach depends on the patient's level of severity and risk factors, where a combination of lifestyle adjustments and medication is used. Lifestyle interventions are considered the first step and apply to all individuals, regardless of whether medications are necessary or not. Such interventions involve minimizing sodium content in the diet, attaining an ideal weight, exercising, avoiding excessive alcohol intake, smoking cessation, and following a proper diet, such as the DASH diet, which includes fruits, vegetables, whole grain foods, and low-fat milk. In the case where changes in lifestyle are not enough for the management of blood pressure, medicines become necessary. Various antihypertensive medicines are available depending on the profile of the patient and other health conditions. Some of the frequently used medicines are diuretics, which aid in the removal of excess sodium and water from the body; angiotensin-converting enzyme (ACE) inhibitors and angiotensin II receptor blockers, which target the renin-angiotensin system and dilate blood vessels; calcium channel blockers, which lower blood vessel resistance through calcium channel blockade; and beta-blockers, which lower heart rate and heart output. The management of hypertension is personalized based on several factors like age, presence of diabetes, kidney problems, or heart complications. Monitoring and maintaining proper medication intake is very important for its

management. Education of the patient becomes very crucial in the management of hypertension. Therefore, successful treatment of hypertension needs an ongoing effort from the patient.

Complications:

Hypertension, popularly referred to as high blood pressure, is usually referred to as a “silent killer” owing to the possibility of damage caused by the condition to various organs without presenting any signs or symptoms. The heart is one of the primary organs affected by high blood pressure. Continuous high blood pressure causes the heart to strain and become enlarged, less efficient, and ultimately fail. High blood pressure also increases the likelihood of developing coronary artery disease that may lead to angina and myocardial infarction. The brain is yet another significant organ affected by long-term hypertension. High blood pressure damages the brain blood vessels, causing stroke by either blocking or bursting the blood vessels. High blood pressure may also increase the likelihood of vascular dementia through poor blood supply to brain tissues. Renal impairment is a typical and serious complication that occurs. As a result of high pressure in the blood vessels of the kidneys, their function deteriorates over time, resulting in chronic renal disease, and ultimately kidney failure that needs dialysis or transplantation. The name for this disorder is hypertensive nephropathy. Another organ that can be affected by high blood pressure is the eye, and this happens through a condition called hypertensive retinopathy. The damage caused to the fine blood vessels of the retina leads to visual impairment and even blindness in advanced stages. Furthermore, hypertension causes peripheral arterial disease through the constriction and thickening of blood vessels in the arms and legs, leading to pain, decreased movement ability, and impaired wound healing. Furthermore, hypertension raises the risk of developing an aortic aneurysm and dissection, which are fatal due to a weakened or torn aortic wall. Thus, hypertension causes extensive harm to blood vessels, affecting several bodily systems and increasing the likelihood of death if it is left untreated.

CONCLUSION:

Hypertension plays a significant role as a predictor of morbidity and mortality from cardiovascular disease, in particular, among older adults. Clinical trials have established not only the safety of the treatment of hypertension among older patients but also the fact that such therapy is capable of reducing the occurrence of stroke, HF, myocardial infarction, and mortality among those older patients. Moreover, treatment of hypertension leads to a reduced

occurrence of cognitive disorders and dementia in old age. Healthy living constitutes one of the basic principles of hypertension treatment. Research has shown that several antihypertensive medications are capable of reducing cardiovascular diseases; however, typically, no one medication can effectively reduce BP among older hypertensive patients. The association of depression with BP is indeed a complicated matter. In fact, studies have shown that depressed individuals show elevated BP values, increased incidence of hypertension, hypotension, and circadian rhythm disturbances. There have been several reasons cited for this phenomenon, which include autonomic nervous system disturbance, as well as genetic mechanisms recently reported. Obviously, there is much significance to this topic because the occurrence of depression may lead to poor BP management among hypertensive individuals, resulting in possible complications. Moreover, depressed hypertensive patients should also be more cautious in using antidepressants due to their adverse effect on BP. Hypertension is the number one cause for physician office visits in the United States,¹ and the extensive use of drugs to control hypertension is one of the main reasons for the reduction in the prevalence rates of stroke and heart disease over the past three decades.² Nevertheless, the proportion of people whose hypertension is well-controlled (a systolic blood pressure below 140 mm Hg and a diastolic blood pressure below 90 mm Hg) is considered very poor, and it may even be lower in recent years than it was in 1990.³ The figures often quoted based on NHANES III Phase II (1992-1994) show that 32% of hypertensive individuals are unaware of the existence of their hypertension and are not receiving any medical treatment, 15% are aware of their hypertension but do not receive any medication, and 26% are under treatment but their hypertension is uncontrolled, while only 27% have controlled hypertension. It is now known that alterations in lifestyle behavior, such as dietary modification lowering body weight, body fat, and alcohol consumption, increasing the intake of potassium and calcium, and exercise, can decrease or bring BP to normal levels in individuals. The discovery of the genetic constellation behind the inheritance of essential hypertension would result in more successful prevention or treatment of hypertension. This might be achieved through the use of particular interventions targeting individuals at risk for CVD due to their genetics, through pharmacogenomic intervention.

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