ISSN: 2634 - 6796

Journal of Cardiology Research Reviews & Reports

SCIENTIFIC Research and Community

Review Article

Open Access

# Hypertension: A Comprehensive Review

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**ABSTRACT**

Hypertension, often known as high blood pressure, is a prevalent and serious global health problem. It is a chronic disorder characterized by chronically high blood pressure levels, which can lead to serious problems such as cardiovascular disease, stroke, and renal failure. The purpose of this review article is to offer a full overview of hypertension, including epidemiology, etiology, pathophysiology, diagnosis, therapy, and preventative strategies. Furthermore, the study delves into the most recent advances in hypertension research, developing therapy options, and the significance of lifestyle changes in controlling this illness. A solid knowledge of hypertension is essential for healthcare practitioners and researchers in developing effective therapies to control and avoid its negative effects.

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**Received:** December 13, 2024; **Accepted:** December 18, 2024; **Published:** December 31, 2024

## Introduction

### Hypertension

Systemic arterial hypertension is characterized by persistently high blood pressure in the systemic arteries. BP is commonly expressed as the ratio of the systolic BP i.e. the pressure that the blood exerts on the arterial walls when the heart contracts and the diastolic BP i.e. the pressure when the heart relaxes [1].

Hypertension is a common disease seen among the public and the early detection of it is significant for early treatment. There are many risks associated with hypertension.

Hypertension is depicted as systolic blood pressure higher than 120 mmHg or diastolic blood pressure higher than 80 mmHg [2].

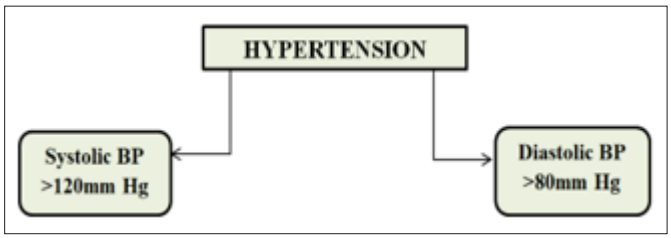


**Figure 1:** Pictorial Description on Hypertension

### Types of Hypertensions

There are two types of hypertensions

- **Primary Hypertension:** High blood pressure that is not related to another medical condition.
- **Secondary Hypertension:** Another medical condition that causes high blood pressure, usually occurring in the kidneys, arteries, heart, or endocrine system.

**Examples include**

- Sleep problems like sleep apnea
- Blocked renal arteries in the kidneys
- Unusual levels of hormones controlling blood pressure [3]

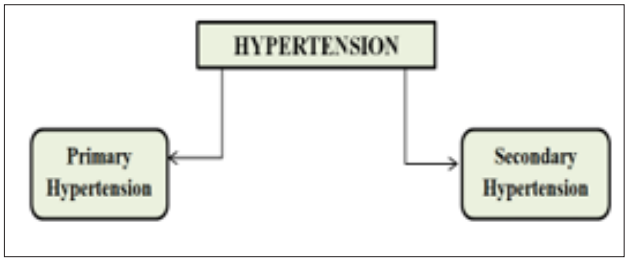


**Figure 2:** Pictorial Description on Types of Hypertensions

### Epidemiology and Global Burden of Hypertension

- Worldwide, 1.28 billion individuals between the ages of 30 and 79 are predicted to have hypertension, while the majority of them residing in countries with low or middle incomes.
- Adults with hypertension are reportedly 46% less likely to be aware of their illness.
- Adults with hypertension are only recognized and treated in 42% of cases.21% of persons who have hypertension have it under control. Around the world, hypertension is a key factor in early mortality.
- The reduction of hypertension prevalence by 33% between 2010 and 2030 is one of the worldwide objectives for non-communicable illnesses [4].

### Risk Factors Associated with Hypertension

- **Obesity:** The more flow of blood you require to provide oxygen and nourishment to your tissues, heftier you are. The pressure inside your arteries rises when more blood is pumped through your blood vessels [5].
- **Eating Too Much Sodium:** Your body might store fluid primarily as a consequence of eating too much salt, which also causes your arteries to narrow. Blood pressure is raised by both circumstances [6].

- **Eating Too Little Potassium:** When sodium levels in your cells are out of balance, potassium helps. Potassium reduces blood pressure by relaxing the smooth muscle cells in your arteries [7].
- **Physically Inactive:** Exercise improves blood flow across all of the body's arteries, which triggers the production of cytokines and natural hormones that relax blood vessels and reduce blood pressure. Being overweight is also a greater possibility when you don't exercise [7].
- **Stress:** A significant yet brief rise in blood pressure can be caused by elevated levels of stress. By increasing your intake, smoking, or drinking alcohol while trying to relax, you can only make your high blood pressure issues worse. Effective blood pressure-lowering methods include meditation and relaxation approaches [8].
- **Decongestants:** Common congestion relievers included in cough and cold medications include pseudo-ephedrine and phenylephrine. These drugs narrow the arteries, which raise blood pressure and heart rate [9].

## Etiology of Hypertension

### Genetic Factors

The heritability of hypertension is widely recognized, and as a result, several investigations ranging from genetic linkage analyses to genome-wide association studies are currently being conducted to better understand the etiology of both monogenic and polygenic forms of hypertension. However, due to the complexity of essential hypertension, single genes regulating blood pressure variability still need to be explored, putting the development of single-gene-focused treatment challenging. Certain genes in your DNA are linked to a higher risk for hypertension. Although there is little we can do to change our genetics, it's important to know about your family history. There are also certain physical conditions that you may be born with that can raise your blood pressure. These include problems with the aorta and other blood vessels, which are usually diagnosed in childhood [10].

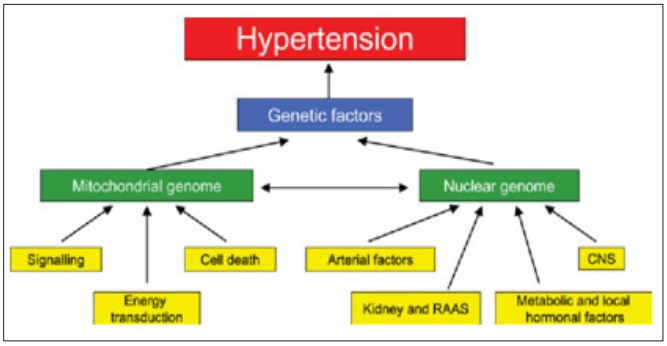


**Figure 3:** Genetic Factors of Hypertension

### Lifestyle Factors

- **Diet:** Unhealthy eating habits and lack of physical exercise are responsible for around 30% of preventable fatalities and morbidity from non-communicable illnesses, including morbidity and mortality from hypertension. Hypertension is a disorder that raises the risk of stroke, heart failure, renal failure, and peripheral vascular disease.
  Excessive consumption of saturated and trans-fatty acids, as well as increased consumption of salt and sugar are risk factors for cardiovascular disease, including hypertension [11].
- **Physical Inactiveness:** Exercise improves blood flow across all of the body's arteries, which triggers the production of cytokines and natural hormones that relax blood vessels and reduce blood pressure. Being overweight is also a greater possibility when you don't exercise [12].
- **Smoking:** Some studies have found that smoking may contribute to hypertension, especially in men over the age of 45.
  Cigarette smoking has a complicated influence on blood pressure, including evidence indicating it raises blood pressure acutely and increases the risk of Reno-vascular, malignant, and hidden hypertension [13].

### Secondary Hypertension and Underlying Medical Condition

- **Kidney Disease:** Kidneys play an important part in maintaining a healthy blood pressure. Kidney disease reduces the ability of the kidneys to assist control blood pressure. Blood pressure rises as a result. If you have chronic renal disease, high blood pressure increases the likelihood that the illness may worsen and lead to cardiac complications.
- **Hormonal Disorders:** Many hormones in our body work together in order to control the blood pressure. When the balance of these hormones is off, we might experience a change in your blood pressure.
  **Example:** Trouble with the thyroid gland and adrenals can lead to high blood pressure [14].

## Pathophysiology of Hypertension

### Renin-Angiotensin Aldosterone System

- The renin-angiotensin-aldosterone system is a set of chemical events that assist control blood pressure.
- When blood pressure drops (to 100 mm Hg or below for systolic), the kidneys release the enzyme renin into the circulation.
- Renin shreds angiotensinogen, a big protein that circulates in the circulation. Angiotensin-1 is one component.
- Angiotensin-converting enzyme, also known as ACE, breaks down angiotensin I, which is generally inactive. One component is angiotensin II, a highly active hormone. Angiotensin II constricts the muscle walls of tiny arteries (arterioles), raising blood pressure. Angiotensin II additionally prompts the adrenal glands to secrete aldosterone and the pituitary gland to release vasopressin (antidiuretic hormone).
- The kidneys retain sodium (salt) when aldosterone and vasopressin are present. Aldosterone also increases potassium excretion in the kidneys. The increased salt induces water retention, which raises blood volume and blood pressure [15].

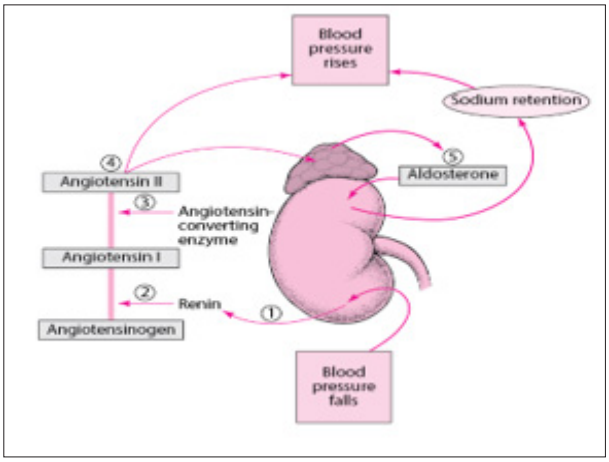


**Figure 4:** RAAS

**Sympathetic Nervous System and Vasoactive Substances**

- A variety of genetic disorders have been linked to the mechanisms of essential hypertension. These genes are linked to vasoactive chemicals. On the other hand, the kidney's responsibilities in the etiology of hypertension have long been recognized.
- Vasoactive chemicals and autonomic nerves have an impact on renal function, namely natriuresis. The autonomic nervous system compensates for blood pressure fluctuations generated by vasoactive drugs. However, those alterations in blood pressure seldom last more than a day. Other processes, such as the central nervous system resetting the baroreceptor response, are required to retain blood pressure at a higher level in order to maintain hypertension.
- That is, vasoactive chemicals may have an effect on the central nervous system. In fact, we discovered that practically all vasoactive drugs have an effect on the central nervous system, causing changes in sympathetic nervous system activity. I evaluated the method by which vasoactive chemicals affect long-term blood pressure levels, which is tied to the central nervous system [16].

**Endothelial Dysfunction and Oxidative Stress**

The involvement of the vascular endothelium in the development of hypertension is not easily defined. In reaction to flowing blood, a quiescent healthy endothelium constantly produces strong vasodilators, which have the ability to directly decrease vascular resistance. Endothelial dysfunction is a disorder that includes both decreased endothelium-dependent vasodilation and increased endothelial inflammatory activity, although endothelial dysfunction is widely established as a predictor of atherosclerosis progression and future cardiovascular events, its significance in hypertension is less clear [17].

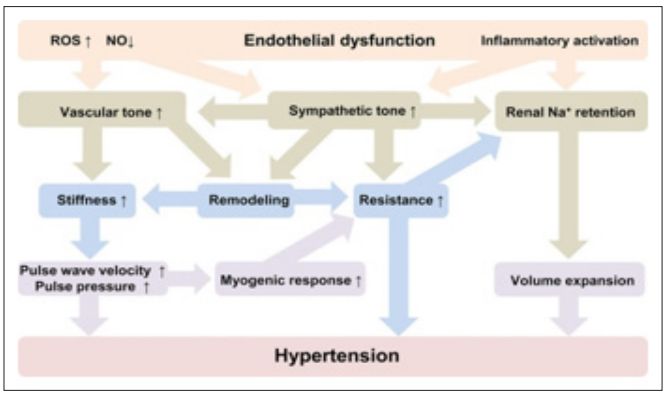


**Figure 5:** Role of Endothelial Dysfunction in Hypertension.

**Inflammation and Immune System Involvement**

In recent decades, research has revealed that a weakened immune system and inflammation play a role in hypertension. Experiments on animal models have revealed that immune cells such as dendritic cells, macrophages, and lymphocytes have a role in the development and maintenance of hypertension. In hypertension, infiltrating inflammatory immune cells in the kidney induce salt retention, renal fibrosis, glomerular damage, and chronic kidney disease, all of which lead to high blood pressure. Similarly, immune cells and inflammatory cytokines have a role in the structural and functional alterations of blood arteries associated with hypertension.

A weakened immune system and persistent low-grade systemic inflammation increase SNS activity, which leads to high blood pressure through its effects on blood vessel tone, the kidneys, and the immune system [18].

**Diagnosis**

**Mercury Sphygmomanometer**

- **Patient Condition:** BP should be taken in a calm, warm environment. Sitting pressures are advised for routine follow-up; the patient should sit quietly for five minutes with the back supported and the arm supported at the level of the heart. Caffeine and exogenous adrenergic stimulants should be avoided for an hour before the reading, and smoking should be avoided for 30 minutes beforehand. If feasible, the blood pressure should be checked 30-60 minutes before taking antihypertensive medicines to estimate the trough or nadir impact.
- **Equipment:** Mercury sphygmomanometers give the most precise blood pressure reading. The bladder should wrap and cover two-thirds of the length of the arm; if not, position the bladder over the brachial artery to prevent excessive readings from a bladder that is too small.
- **Technique & Guidelines:** When taking blood pressure, the cuff ought to be inflated to a pressure roughly 30 mmHg higher than systolic, as determined by palpation of the pulse in the brachial artery. Palpation-based systolic pressure estimate reduces possible difficulties with an auscultatory gap. As the cuff is deflated, the Korotkoff noises go away. After the cuff has been suitably inflated, proceed as follows:

1. Because excessive pressure might enhance turbulence and prolong the disappearance of sound, the stethoscope should be positioned softly over the brachial artery. As a result, the diastolic pressure measurement may be artificially decreased by up to 15 mmHg. The patient's arm should always be supported at the level of the heart when taking their blood pressure. Allowing the patient's arm to dangle down when sitting or standing results in the brachial artery being 15 cm below the heart. As a result of the extra hydrostatic pressure caused by gravity, the measured BP will be raised by 10-15 mmHg.
2. The cuff should be gently deflated at a rate of 2 to 3 mmHg each heartbeat. The systolic pressure is the pressure at which the brachial pulse may be palpated for the first time when blood flow is restored through the previously compressed artery; it is also the pressure at which the pulse is first heard by auscultation (Korotkoff phase 1).
3. The pulse continues to be heard as the cuff is deflated below the systolic pressure until there is abrupt muffling (phase 4) and, approximately 8 to 10 mmHg later, disappearance of sound (phase 5), although the point of muffling sound should be used in patients with a difference of more than 10 mmHg between phases 4 and 5.
4. Initially, the blood pressure should be monitored in both arms. If there is a discrepancy owing to a unilateral artery lesion, employ the arm with the higher pressure.
5. Each visit, the blood pressure should be measured at least twice, with one or two minutes between measures to allow trapped blood to be released. If the second value deviates from the first by more than 5 mmHg, more measures should be taken until a stable value is obtained. The figure entered on the patient's chart should be the average of the previous two measurements [19].

**Figure 6:** Diagnosis of BP.

**Ambulatory Monitoring**

A longer blood pressure monitoring test may be done to check blood pressure at regular times over six or 24 hours. This is called ambulatory blood pressure monitoring. However, the devices used for the test aren't available in all medical centers.

Ambulatory blood pressure monitoring takes 24-hour measures of your blood pressure (BP), whether you're awake or asleep. This occurs outside of your doctor's office, as you go about your normal activities. A cuff on your arm and a tiny gadget linked to a strap or belt are worn [20].

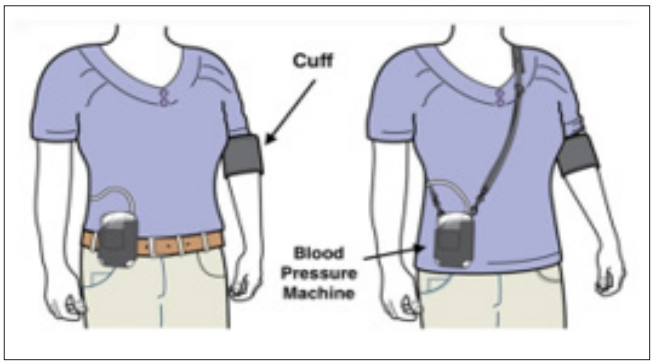


**Figure 7:** Ambulatory BP Monitoring

**Lab Tests**

Blood and urine tests are done to check for conditions that can cause or worsen high blood pressure. For example, tests are done to check your cholesterol and blood sugar levels. You may also have lab tests to check your kidney, liver and thyroid function [21].

**Electrocardiogram**

This quick and painless test measures the heart's electrical activity. It can tell how fast or how slow the heart is beating. During an ECG, sensors called electrodes are attached to the chest and sometimes to the arms or legs. Wires connect the sensors to a machine, which prints or displays results [22].

**Echocardiogram**

This noninvasive exam uses sound waves to create detailed images of the beating heart. It shows how blood moves through the heart and heart valves [23].

**Complications of Hypertension**

Hypertension, among other issues, can cause catastrophic heart damage. Excessive pressure can harden arteries, reducing blood and oxygen flow to the heart. This increased blood pressure and decreased blood flow can result in:

- **Cardiovascular Diseases:** High blood pressure (BP) is a major risk factor for cardiovascular disease (CVD), which is the main cause of death. High blood pressure is responsible for around 54% of strokes and 47% of coronary heart disease globally [24].
- **Cerebrovascular Disease:** Hypertension increases the risk of stroke by worsening atherosclerosis in the aortic arch and cervicocerebral arteries, causing arteriosclerosis and lipohyalinosis in the small-diameter penetrating cerebral end arteries, and promoting heart disease, which can be complicated by stroke [25].
- **Renal Complications:** High blood pressure can constrict and restrict blood vessels, causing them to become damaged and weak throughout the body, including the kidneys. Blood flow is reduced because to the constriction. If the blood arteries in your kidneys are damaged, they may no longer function correctly [26].

**Treatment of Hypertension**

**Lifestyle Modifications**

Lifestyle modifications that effectively lower blood pressure is

- **DASH Diet:** The DASH diet emphasizes on fruits, vegetables, and whole grains. Dairy items that are fat-free or low-fat, fish, poultry, beans, and nuts are all included. The diet restricts meals high in salt, often known as sodium. It also restricts additional sugar and saturated fat, which are commonly found in fatty meats and full-fat dairy products.
- Increased physical activity
- Weight loss
- Limited alcohol consumption
- Relaxation techniques of Yoga, Acupuncture
- Mindfulness-based stress-reduction program [27].

**Pharmacological Treatment**

Drug therapy is needed if lifestyle modifications cannot adequately bring BP to goal.

First-line medications used in the treatment of hypertension include diuretics, angiotensin-converting enzyme (ACE) inhibitors or angiotensin receptor blockers (ARBs), beta-blockers, and calcium channel blockers (CCBs).

**Diuretics**

Diuretics help rid your body of sodium and water. Most work by making your kidneys release more sodium into the urine. The sodium then takes water with it from your blood decreasing the amount of fluid flowing through your blood vessels hence lowering blood pressure. Diuretics are used effectively in the management of hypertension, and are typically prescribed because of their efficacy, low cost, and low side effects profile. Diuretics are known for their ability to increase the formation and excretion of urine. The increase in excretion allows for more water and sodium to be removed, and ultimately affects the vascular system by leading to a decrease in fluid volume. The decrease in fluid volume affects blood pressure directly, which is why they are effective in reducing high blood pressure.

Examples: Bumetanide , Furosemide, Torsemide etc [28].

**ACE Inhibitors**

Angiotensin-converting enzyme (ACE) inhibitors are medications that help relax the veins and arteries to lower blood pressure. ACE inhibitors prevent an enzyme in the body from producing angiotensin II, a substance that narrows blood vessels. This

narrowing can cause high blood pressure and forces the heart to work harder. Angiotensin II also releases hormones that raise blood pressure [28].

Examples of ACE inhibitors include
- Benazepril
- Captopril
- Enalapril
- Eosinophil
- Lisinopril
- Moexipril
- Perindopril
- Quinapril
- Ramipril

**Angiotensin Receptor Blocker**
Angiotensin II receptor blockers help relax your veins and arteries to lower your blood pressure and make it easier for your heart to pump blood.

Angiotensin is a chemical in your body that narrows your blood vessels. This narrowing can increase your blood pressure and force your heart to work harder.

Angiotensin II receptor blockers block the action of angiotensin II. As a result, the medication allows your veins and arteries to widen (dilate).

Examples of angiotensin II receptor blockers include
- Azilsartan
- Candesartan
- Eprosartan
- Irbesartan
- Losartan
- Olmesartan
- Telmisartan
- Valsartan

**Beta Blockers**
Beta blockers also known as beta-adrenergic blocking agents, are medications that reduce blood pressure. Beta blockers work by blocking the effects of the hormone epinephrine, also known as adrenaline.

Beta blockers cause the heart to beat more slowly and with less force, which lowers blood pressure.

Beta blockers also help widen veins and arteries to improve blood flow.

Examples of beta blockers taken by mouth include
- Acebutolol
- Atenolol
- Bisoprolol
- Metoprolol
- Nebivolol
- Propranolol

**Calcium Channel Blockers**
Calcium channel blockers are medications used to lower blood pressure. They work by preventing calcium from entering the cells of the heart and arteries. Calcium causes the heart and arteries to squeeze (contract) more strongly. By blocking calcium, calcium channel blockers allow blood vessels to relax and open. Some calcium channel blockers can also slow the heart rate, which can further lower blood pressure. The medications may also be prescribed to relieve chest pain (angina) and control an irregular heartbeat.

Calcium channel blockers are also called calcium antagonists.

Examples of calcium channel blockers include
- Amlodipine
- Diltiazem
- Felodipine
- Isradipine
- Nicardipine
- Nifedipine
- Nisoldipine
- Verapamil [30].

**Combination Therapies and Personalized Treatment Approaches**
Hypertension is a key risk factor for atherosclerosis and ischemic heart disease that may be avoided. Despite the availability of contemporary and effective antihypertensive medications, most patients continue to have inadequate blood pressure management. To reach therapeutic goals, most hypertension patients will require a combination of antihypertensive medications.

Most antihypertensive drugs combination whether fixed dosage and free combination contain a diuretic. These combinations have been demonstrated to reduce blood pressure more effectively than mono-therapies. Combinations of a calcium antagonist and a renin-angiotensin system inhibitor, whether an Angiotensin Converting Enzyme Inhibitor or an Angiotensin Receptor Blocker, have also been found to be useful and safe in the therapy of hypertensive patients [31].

More personalized therapy options add the most benefit to patients for whom straightforward, low-information-burden treatments are ineffectual. The increased complexity of new information can be valuable if it enhances the possibility of excellent decision-making and improved results [11].

**Non-Pharmacological Interventions**
Non-pharmacological treatments are an important aspect of hypertension care.
- **Device Based Therapies:** Efforts to enhance blood pressure regulation have expanded beyond traditional measures of lifestyle modification and pharmacological therapy in the last decade to include interventional therapies. Based on animal and human research that clearly show a role for the sympathetic nervous system in the etiology of hypertension, recent technologies that have developed are mostly directed at neuro-modulation of peripheral nervous system targets. Renal denervation, baro-reflex activation therapy, endovascular baro-reflex amplification therapy, carotid body ablation, and pacemaker-mediated programmable hypertension management are examples of these treatments [32].
- **Renal Denervation:**With a recent series of proof-of-concept trials demonstrating the safety and efficacy of radiofrequency and, more recently, ultrasound-based renal denervation, this technology is poised to become available as a viable treatment option for hypertension in the near future [33].

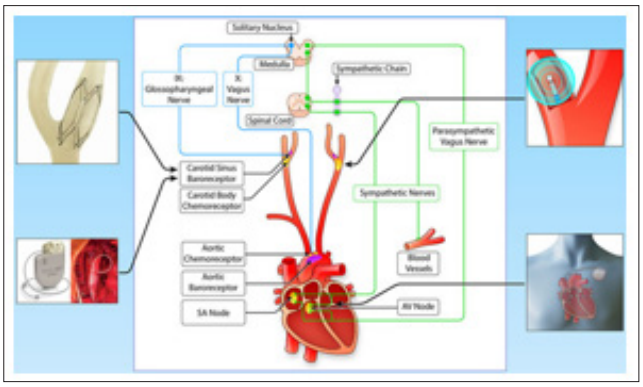


**Figure 8:** Device based therapies for HT.

**Prevention and Management**

Prevention encompasses a wide variety of actions known as "interventions" that try to reduce health risks or dangers.

- **Early Detection and Screening Programs:** Office blood pressure measurement (OBPM) should be used for first hypertension screening. A manual or automated sphygmomanometer is most typically used in the office to assess blood pressure. Various OBPM procedures are available; however, in the studies examined by the OBPM was taken at the brachial artery (upper arm) after 5 minutes of rest, with the patient most usually sitting and medical professionals present during measurement. Before beginning therapy, ambulatory blood pressure monitoring (ABPM) and home blood pressure monitoring (HBPM) with approved and accurate equipment should be utilized outside of a clinical context to confirm a diagnosis of hypertension [34].
- **Public Health Strategies for Hypertension Prevention:** Lifestyle modification methods are used in combination with antihypertensive drugs in the treatment of hypertension. Weight control, the adoption of specialized food plans, dietary salt reduction, physical exercise, and limitation of alcoholic intake is the key lifestyle changes to lower and manage blood pressure. Implementing and sticking to these techniques can successfully and dramatically lower blood pressure levels, as well as the risks of hypertension-related diseases in the population [35].
- **Patient Education and Self-Management Techniques:** Multiple studies have indicated that Hypertension Self-Management (HSM), in which individuals measure their blood pressure (BP) in nonclinical situations, is better than typical office-based hypertension care. HSM leads to more frequent blood pressure measurements, which allows healthcare personnel to better determine the severity of a patient's hypertension. Combining HSM with team care, in which BP data from home monitoring is relayed to healthcare practitioners on a frequent basis, resulting in even better BP management [36].
- **Telemedicine and Digital Health Solutions:** Blood pressure tele-monitoring (BPT) is a specialized use of telemedicine for hypertension treatment that permits remote data transfer of BP and associated information on patients' health status from their home or community setting to the doctor's office or the hospital [37].

**Figure 9:** Tele-Monitoring of Blood Pressure.

**Emerging Trends and Future Directions**

- **Precision Medicine and Genetic Profiling:** Personalized illness management that takes into account significant patient characteristics allows for optimal therapy rather than management based on an average patient. Precision hypertension management is critical since both susceptibility to problems and responsiveness to therapy differ between people. While the use of genetic and proteomic personal traits for broad precision hypertension care is impractical, other factors such as age, ethnicity, and cardiovascular disease have been included in hypertension management recommendations. More blood-pressure-related clinical and physiological data in the patient's profile can be used in precision medicine to determine the hypertension threshold and effective therapy. Several non-invasive and simple-to-use approaches for measuring hypertension-related physiological parameters are proposed for use in hypertension precision treatment [38].

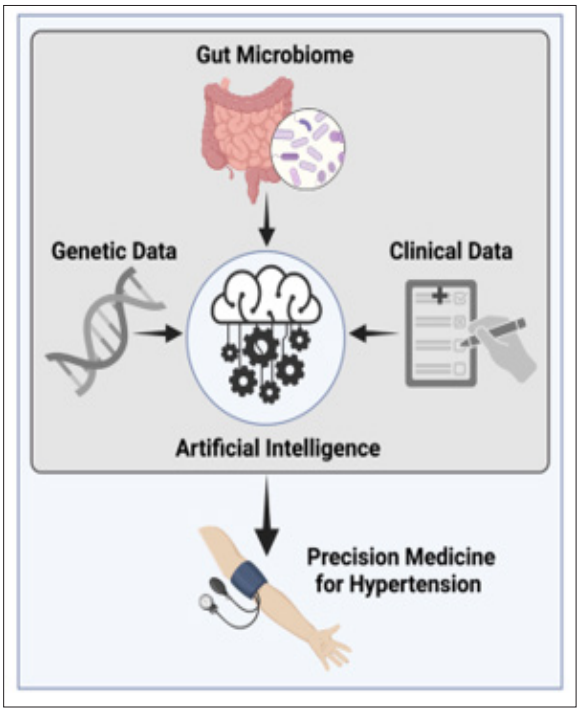


**Figure 10:** Precision Medicine.

- **Novel Therapeutic Targets and Drug Development:** Hypertension is a common cardiovascular condition that can occur on its own or as a result of other disorders. It is a significant risk factor for coronary artery disease, myocardial infarction, congestive heart failure, renal failure, and stroke.

The results of novel approaches revealed various targets that might be investigated as prospective treatment possibilities. Toll-like receptor 4, which is a key regulator of angiotensin II-induced hypertension; protease-activated receptor 2, which promotes collagen deposition and inflammatory responses; chemerin, which causes metabolic and obesity-related hypertension; apelin receptor; transient receptor potential melastatin; urotensin-II; and Tie2 receptor are among them [39].

- **Artificial Intelligence and Machine Learning Applications:** Hypertension is becoming more common as the world's population ages, resulting in millions of premature deaths each year. The biggest barriers to efficient hypertension care are a lack of awareness of blood pressure (BP) increase and an inadequate hypertension diagnosis. However, the emergence of artificial intelligence (AI) illuminates new tactics for hypertension care, such as remote telemedicine support and big data-derived prediction. There is substantial evidence that AI applications in hypertension control are feasible. A foreseen trend was the integration of blood pressure measures with different wearable sensors and cellphones, allowing for continuous and simple monitoring. In the meanwhile, more research is needed to verify the innovative prediction and prognostic techniques. Revolutionary breakthroughs have moved us closer to the future model [40].

**Figure 11:** Role of AI in Hypertension.

- **Wearable Devices and Remote Monitoring:** Out-of-office blood pressure measurement is regarded as an essential component of hypertension diagnosis and therapy. A plethora of wearable blood pressure measurement gadgets have been produced in the digital age. As the necessity of getting a correct diagnosis of hypertension has become clear, these digital blood pressure monitors allow for regular BP measures with minimum irritation to the patient, while also promising significant increases in diagnostic accuracy. These monitors provide reliable detection of several clinical phenotypes, such as hidden hypertension and pathological BP fluctuation, that appear to have a detrimental influence on cardiovascular prognosis by increasing the number of BP recordings in diverse situations [37].


**Figure 12:** Wearable Devices for Hypertension.

## Conclusion

This review paper provides a comprehensive analysis of hypertension, covering various aspects such as etiology, pathophysiology, diagnosis, treatment, and prevention. By highlighting recent advancements and emerging trends, this paper aims to contribute to the existing knowledge base and facilitate the development of effective strategies to combat the global burden of hypertension. It emphasizes the significance of a holistic approach encompassing lifestyle modifications, pharmacotherapy, and targeted interventions for managing hypertension and its associated complications.

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