
Review Article

Hypertension: Unmasking the Silent Epidemic in Developing Countries

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Abstract: *Background:* An estimated 1.28 billion adults aged 30–79 years worldwide have hypertension, about two-thirds of them live in low- and middle-income countries. A systolic blood pressure (BP) > 180 mm Hg or a diastolic BP > 120 mm Hg is considered a "hypertensive crisis." Almost three-quarters of the worldwide deaths due to hypertension are reported in developing countries where hypertension awareness is deficient, and prevalence rates are very high. The aging population, unhealthy diets, and lack of physical activities are some of the factors that are contributing to high levels of hypertension. Resistant hypertension, where a patient fails to respond to three or more different classes of antihypertensive drugs, including a diuretic, is also on the rise. *The Purpose:* This review briefly summarizes the current trends of hypertension in developing countries, its causes, diagnosis, and treatment. It also covers the recent increase in the use of antihypertensive herbs. *Research Methods:* The review critically analyzed recent hypertension trends in developing countries, with a special focus on resistant hypertension diagnosis and treatment. *Conclusion:* Training people to diagnose hypertension in hard-to-reach areas is highly recommended to reduce hypertension cases in developing countries. People should be encouraged to eat healthy diets and actively participate in physical exercises. More research is needed in the development and treatment of resistant hypertension.

Keywords: Resistant Hypertension, Hypertension Treatment, Diagnosis of Hypertension, Hypertension Genetics, Hypertension Herbs

1. Introduction

An estimated 1.28 billion adults aged 30–79 years worldwide have hypertension, most (two-thirds) live in low- and middle-income countries [1]. A systolic blood pressure (BP) > 180 mm Hg or a diastolic BP > 120 mm Hg is considered a "hypertensive crisis" [2]. Almost three-quarters of the worldwide deaths due to hypertension are reported in developing countries [3, 4], where hypertension awareness is deficient, and prevalence rates are very high. Furthermore, hypertension is more common among people of African heritage than Caucasians [5]. As early as 2010, the prevalence of hypertension among adults was more elevated in Low- and Middle-income countries (LMICs) (31.5%, 1.04 billion people) than in high-income countries (HICs; 28.5%, 349 million people) [6]. An increase in the number of patients

effectively treated for hypertension to levels observed in high-income countries could prevent 76 million deaths, 120 million strokes, 79 million heart attacks, and 17 million cases of heart failure between now and 2050 [7].

Uncontrolled hypertension can lead to complications, including congestive heart failure, heart attack, cerebral hemorrhage, aneurysm, vascular dementia, chronic kidney disease, myocardial infarction, and thrombotic stroke [8]. Indeed, high blood pressure is the major contributor to cardiovascular disease, one of the leading causes of mortality. Most strokes and coronary heart diseases are directly linked to high blood pressure [8]. Hypertension as a chronic medical condition increases with age. To make matters worse, there are no clear guidelines on the optimal BP for the older age group due to the mixed evidence in this population [9]. The American Heart Association, American College of Cardiology,

Centers for Disease Control and Prevention, American Society of Hypertension, the International Society of Hypertension, and European Society of Hypertension/European Society of Cardiology Hypertension Guidelines recommend a universal target of <140/90mm Hg for those less than 80 years, <150/90mm Hg for those above 80 years old and, <140/85 mm Hg for patients with diabetes and chronic kidney disease [3]. When the recommended target blood pressure is not achieved with at least three antihypertensive agents, including diuretics, from different classes in the correct combination, the patient is described as having resistant hypertension [6].

Because of the lack of hypertension awareness, efforts to prevent and treat hypertension are not encouraged in African countries, mainly in rural areas. Once one is diagnosed with hypertension, the priority is always to find mechanisms to reduce it to healthy levels, but much more effort should also be placed on its prevention. Even though genetic factors have been implicated in the development of hypertension [10, 11], preventative measures based on changes in lifestyle and nutrition must be prioritized in addition to genetic screening. Indeed, the etiology and non-pharmacological prevention and treatment of hypertension should be highly encouraged. These measures include but are not limited to a consistent intake of low-kilojoule diet (fruits and vegetables), decreasing consumption of saturated fats, cholesterol, and trans-fats, reduction of sodium intake to no more than 2 g per day, reducing alcohol intake, reducing intake of ultra-processed foods [12], and encourage consumption of foods rich in potassium and regular aerobic exercising, has been shown to prevent the development of hypertension [13]. Combining endurance and resistance training is an effective nonpharmacological way of reducing hypertension. Exercise has been proven to regulate shear stress, nitric oxide production, up-regulate antioxidant enzymes, and autonomic nervous system activity, directly reducing hypertension crisis [13]. To reverse the hypertension epidemic in developing countries, there is an urgent need for community-based intervention programs that should encourage hypertension prevention, detection, and treatment. Hypertension tends to be higher in men than women [14]. Furthermore, women are more aware of hypertension than men in developing countries [15].

This review discusses the current epidemiology, etiology, pathophysiology, hypertension genetics, diagnosis, prevention, and treatment of resistant hypertension in developing countries.

1.1. Global Epidemiology and Burden of Hypertension

The global hypertension prevalence is not the same worldwide. In some countries, it is rising at an alarming rate, while in others, it is declining [3]. The aging population, unhealthy diets, and lack of physical activities are some of the factors that are contributing to high levels of hypertension in some countries. Recent studies involving 154 countries with over 8 million participants showed that the mean age-standardized systolic BP was 127.0 mmHg in men and 122.3 mmHg in women. In contrast, the mean

age-standardized diastolic BP was 78.7 mmHg in men and 76.7 mmHg in women [4]. Studies have repeatedly shown that having an optimal blood pressure of SBP <120mmHg and DBP <80mmHg reduces cardiovascular diseases (CVDs) risk [16].

Overall, South Asia, Sub-Saharan Africa, and Central and Eastern Europe have higher mean systolic and diastolic BPs than high-income Western Europe and Asia-Pacific regions (Figure 1) [4]. Economic, social, and environmental factors likely contribute to these regional variations. Some of these variations include limited access to community health workers, health coaches, antihypertensive medications, unhealthy diets including high consumption of salt, low consumption of fresh fruits, a high prevalence of maternal and childhood undernutrition, and lack of physical activity due to a busy lifestyle [4]. One of the reasons that hypertension awareness needs to be improved in developing countries is the wrong perception that it is a disease of affluence and poor diagnosis. Both men and women in Malawi and Mozambique have the highest mean SBP (Figure 1) [3]. Similar trends are only found in Niger and Guinea. In contrast, countries like Brazil and those from Eastern Europe record a higher SBP in men than in women, not in both [3].

Generally, the mean standardized DBP is decreasing in high-income countries while increasing rapidly in Central and Eastern Europe, South Asia, and sub-Saharan Africa (Figure 2). The DBP is the same for both men and women in Malawi. Thus, for a country like Malawi, both the SBP and DBP need to be reduced to manageable levels to decrease untimely deaths associated with high SBP and DBP, which in most cases are misdiagnosed. Although some factors that are leading to the decrease in hypertension in high-income countries are apparent, such as high levels of hypertension awareness, easy availability of treatment options, easy access to fresh fruits and vegetables all year round, and access to social and corporate sports facilities, there are possibilities that there are other obscure factors that may contribute the observed differences in different countries that still need to be understood. Specifically, more hypertension data is required from low-income countries.

An estimated 7.7–10.4 million annual deaths are attributable to high blood pressure. This number is based on CVDs and kidney diseases [17]. In general, hypertension is highly associated with kidney diseases. The low-income and middle-income countries contributed up to 88% of high blood pressure-associated deaths [17]. Even though the high-income countries have the largest elderly population, which is usually prone to high blood pressure, their high blood pressure-associated deaths have been declining in the range of 20–30% annually [17], while the low-income countries with the most significant youth population deaths associated with high blood pressure are on the rise.

1.2. Hypertension and Cardiovascular Disease (CVD)

Extensive cohort studies have demonstrated that high BP is a significant risk factor for heart failure, atrial fibrillation, chronic kidney disease, heart valve diseases, aortic syndromes,

and dementia, in addition to coronary heart disease and stroke [19]. Hypertension accelerates the development of atherosclerosis and vascular lesions [20]. Thus, reducing age-related factors that increase blood pressure can potentially reduce CVD. Indeed, several randomized trials have shown that preventative BP management is associated with a reduced risk of death from CVD and a higher survival rate [20, 21].

Nutritional, environmental, and behavioral factors during pregnancy, birth, and old age can contribute to the development of hypertension. Among the high-risk populations, such as those with chronic kidney disease, diabetes, or the elderly, hypertension is the major cause of

CVD [20, 22]. Indeed, among all known risk factors for CVD, hypertension remains the highest risk factor. Thus, the reduction of BP also reduces the incidences of CVD. Multiple clinical trials have shown that a reduction of systolic BP by 3-5 mm Hg reduces stroke risk by 2-3% and has a 16% reduction in coronary disease development [23].

The high-risk individuals should aim to achieve a BP target of less than 130/80 mm Hg to reduce incidences of CVD or stroke. It should also be emphasized that these individuals need regular BP check-ups and appropriate treatment options at the earliest possible stage of diagnosis.

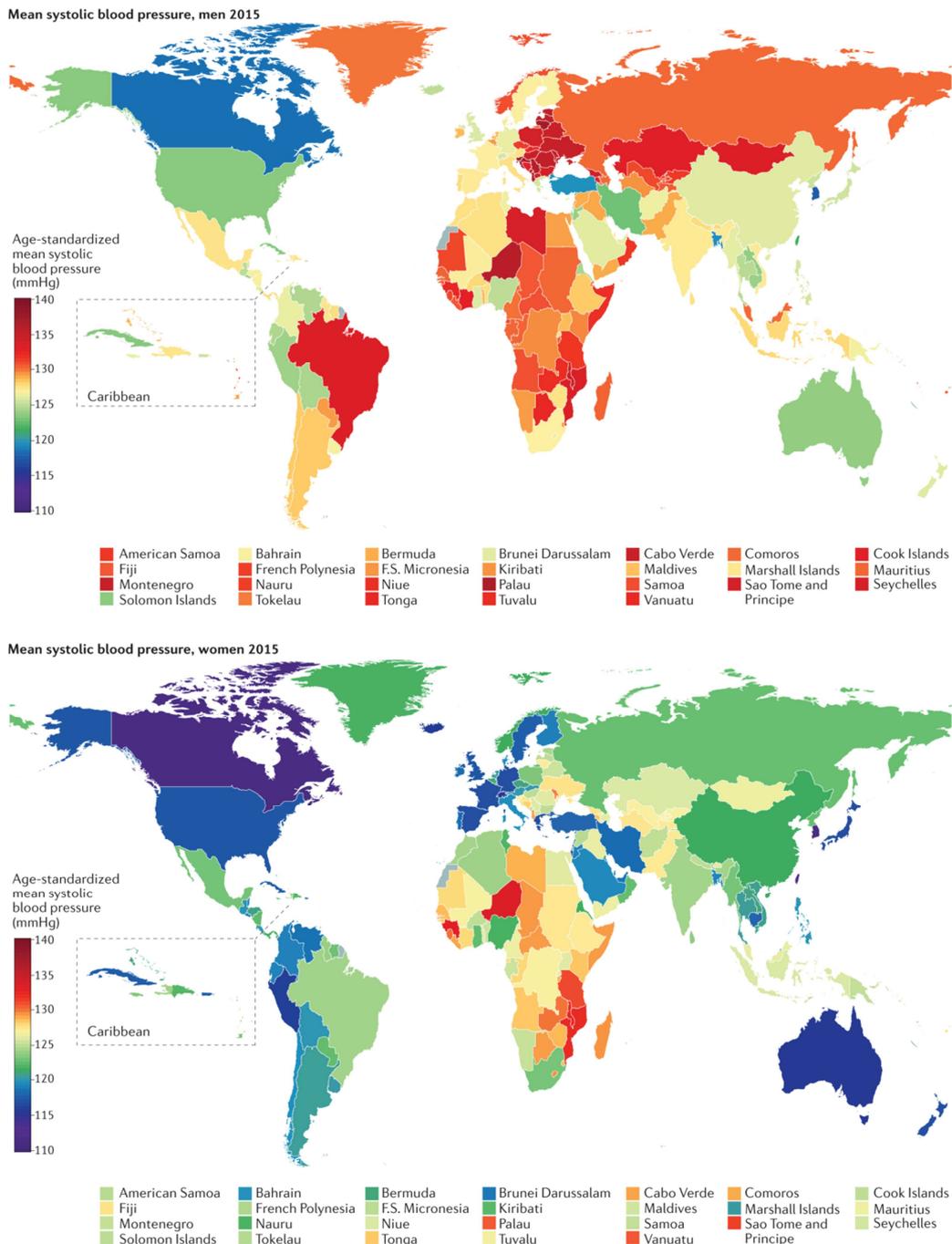
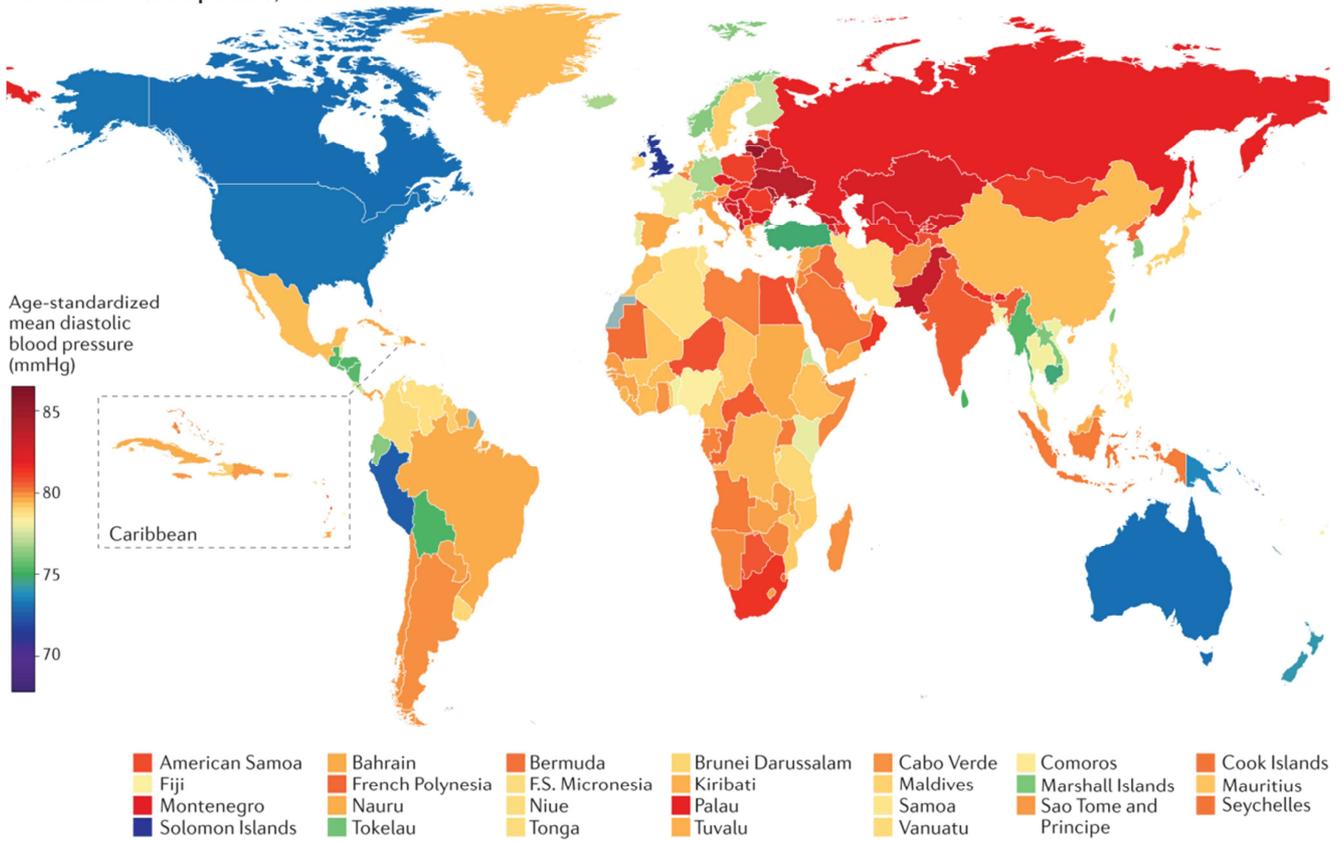


Figure 1. Age-standardized mean systolic blood pressure by country in 2015. Adapted from Zhou et al., 2017 [4], CC BY 4.0 (<https://creativecommons.org/licenses/by/4.0/>).

Mean diastolic blood pressure, men 2015



Mean diastolic blood pressure, women 2015

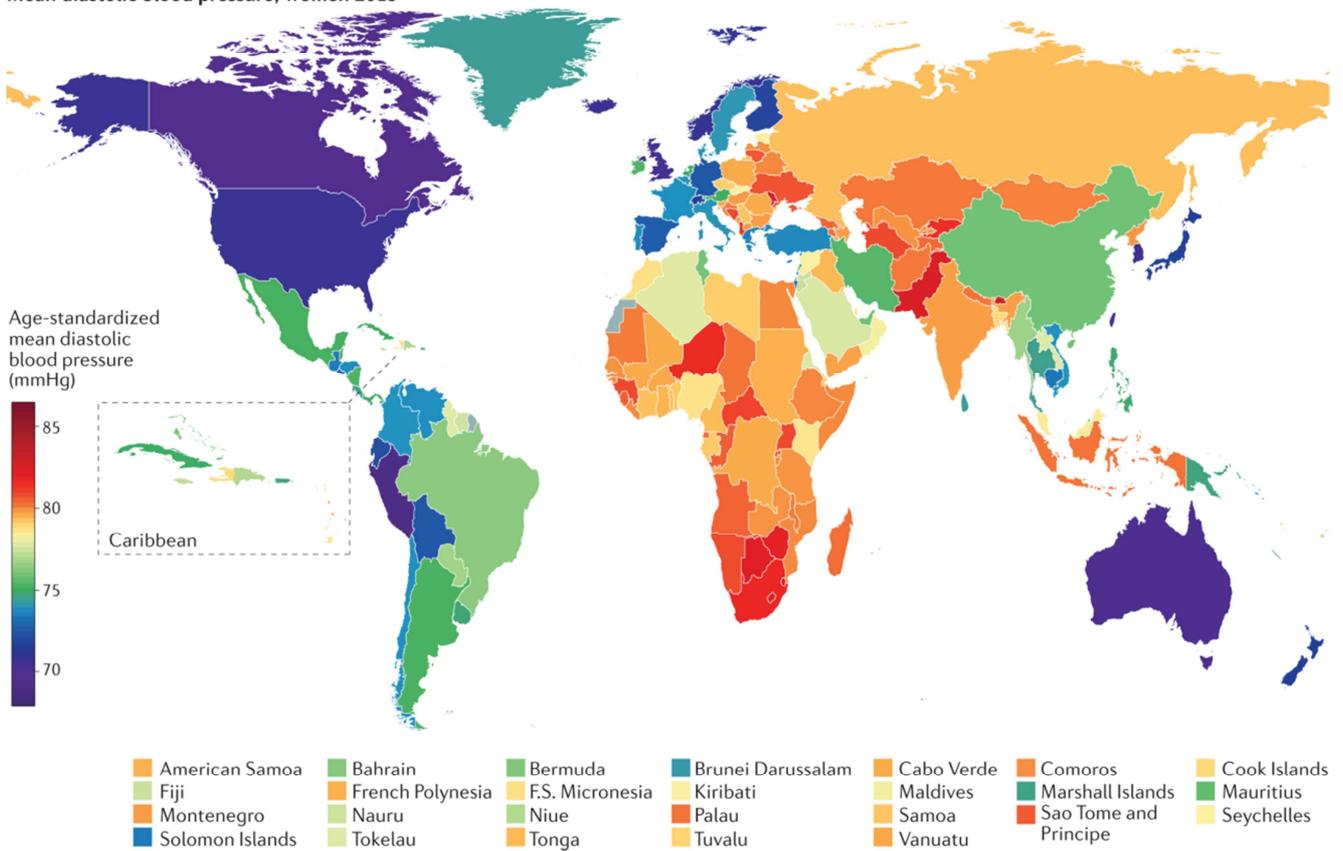
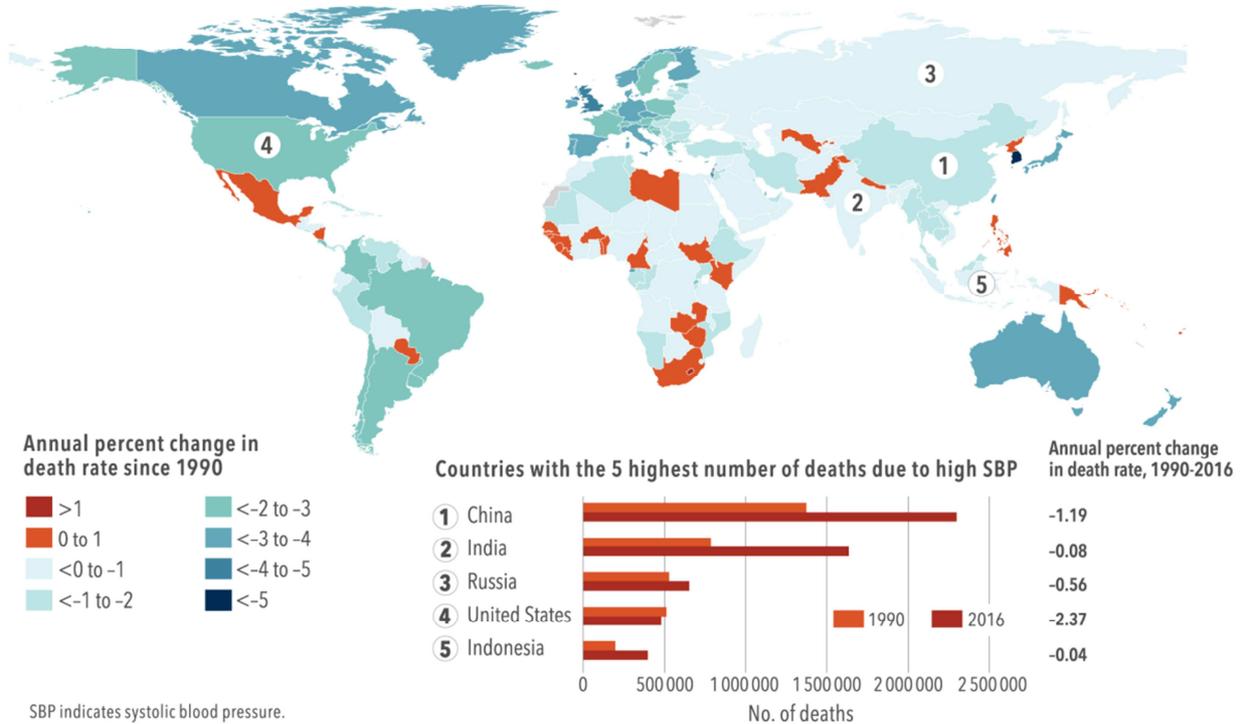


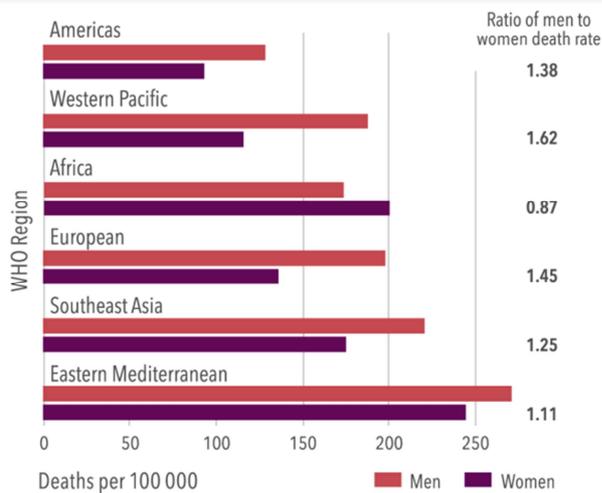
Figure 2. Age-standardized means diastolic blood pressure by country in 2015. Adapted from Zhou et al., 2017 [4], CC BY 4.0 (<https://creativecommons.org/licenses/by/4.0/>).

Global Deaths Attributable to High Systolic Blood Pressure, 1990–2016

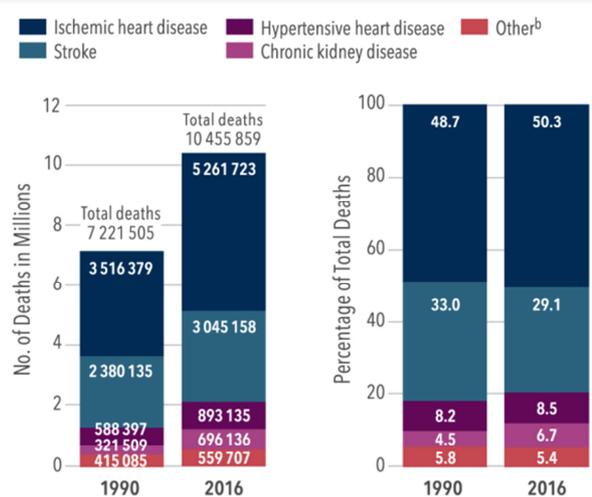
Global Death Rate Due to High SBP (≥ 110 -115 mg/Hg) Declined by 1.35% (Annualized) From 1990 to 2016^a



Death Rates Due to High SBP Greater for Men Than Women in Most Regions in 2016



Ischemic Heart Disease Accounted for the Greatest Proportion of Deaths Due to High SBP



^aDeath rates are age-standardized per 100,000 population for adults 25 years or older. ^bAortic aneurysm, atrial fibrillation and flutter, cardiomyopathy and myocarditis, endocarditis, peripheral artery disease, rheumatic heart disease, and other cardiovascular and circulatory diseases. WHO, World Health Organization.

Authors: Laurie Marczak, PhD; Joan Williams, BA; Michaela Loeffler, BA, for the Institute for Health Metrics and Evaluation

Source: GBD 2016 Risk Factors Collaborators. *Lancet*. 2017;390:139-1422.
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10.1001/jama.2018.5119



Figure 3. Global deaths attributed to high systolic blood pressure. Courtesy of Marczak et al., 2018 [18]. (<https://creativecommons.org/licenses/by/4.0/>).

2. Pathophysiology of Hypertension

Generally, clinical hypertension is categorized into primary (or essential) and secondary hypertension. Most hypertension cases fall under primary hypertension, associated with environmental or genetic causes. Primary hypertension represents between 85% and 95% of human cases [24]. Hypertension cases identified with a known underlying condition are classified as secondary hypertension. These underlying conditions include kidney disease, adrenal disease, hyperparathyroidism, thyroid disease, tightening of the aorta, and obstructive sleep apnea [25].

Several models have been devised to explain the elusive nature

of primary hypertension and sometimes to give more insights into secondary hypertension. Decades of research on hypertension have shown that there are specific perturbations in the renal functions, cardiovascular factors, central nervous system, and endocrine factors that play critical roles in the development of hypertension. Elegant research done by Page and colleagues produced the Mosaic model of hypertension [26]. This model presented the causes of hypertension as multifactorial. Indeed, subsequent research showed that several factors acting on the circulatory system are involved in hypertension. The multifactorial nature of hypertension is best illustrated by Dr. Page's iconic octagonal diagram (Figure 4) [26].

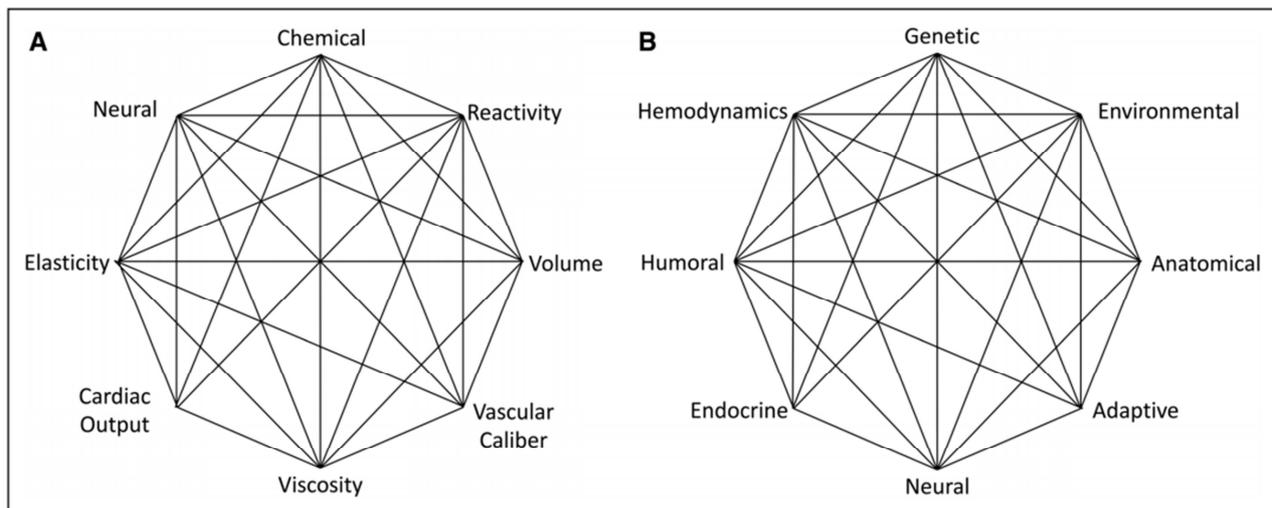


Figure 4. The original (A) and revised (B) Mosaic Theories proposed by Page [26].

Analysis of Figure 4B shows eight factors involved in hypertension development: hemodynamics, genetic, environmental, anatomical, adaptive, neural, endocrine, and humoral. Some of these factors will be discussed in this review. Because of the multifactorial nature of hypertension, tackling one aspect does not always mean a reduction of high BP.

3. Hypertension Genetics

The relationship between genes and hypertension is still an ongoing active research field. Heritable Mendelian forms of hypertension are associated with several single-gene mutations, such as those linked to glucocorticoid remedial hypertension, pseudohyperaldosteronism, aldosterone-producing adenomas, and missense mutations of the mineralocorticoid receptor [27]. Although hypertension has been shown to run in families [10, 11], the genetic basis of this is still unknown. Specific enzymes, channels, and receptors involved in sodium homeostasis and genes involved in the structure and regulation of vascular tone have been implicated in the development of hypertension [28]. Africans tend to have a higher propensity for developing hypertension than other ethnic groups, although the genetic basis behind this is still unknown. Nevertheless, 30 to 50% of blood

pressure is attributed to hereditary [28]. Multiple genetic variants have been identified using the "common disease-common variant" hypothesis and Genome-Wide Association Studies (GWAS). More work is still needed to elucidate more variants that GWAS does not detect. A deeper understanding of rare variants combined with functional studies can improve patient care and antihypertensive treatment outcomes [29].

4. Antihypertensive Drugs

There are many classes of antihypertensive drugs. These include first-line therapies such as thiazide diuretics, β -blockers, ACE inhibitors, angiotensin receptor blockers, and calcium channel blockers. Globally, hypertension treatment is not encouraging, with only 36.9% of the world population able to control both systolic and diastolic BP [3]. This figure is even lower in developing countries, about 8% [30]. Recent studies on hypertension treatment in sub-Saharan Africa showed that 21% of patients received monotherapy, 42.6% two-drug combinations, and 26.6% three-drug combinations [31]. Sub-Saharan Africa has the highest incidence of hypertension in the world. Some of the disparities in the treatment of hypertension are attributed to the

trial-and-error approach for optimal drug regimens. Individualized hypertension management, based on identifying BP levels and other cardiovascular risk factors, is highly recommended with the best doctor-patient relationship. Assessing and monitoring target organ damage for hypertensive patients is essential for better clinical outcomes.

A recent study has shown that starting with a two-drug therapy has a much better treatment outcome than monotherapy [32]. Combined therapy in small doses has fewer side effects than large single doses and easily achieves rapid, effective, well-tolerated, and sustained BP control for individual patients [32].

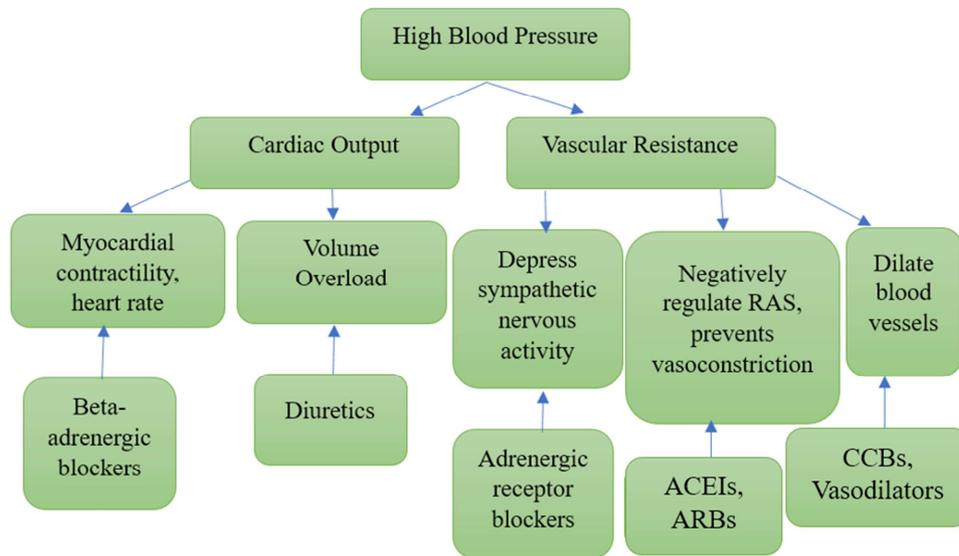


Figure 5. Pharmacological effects of beta-adrenergic blockers, diuretics, adrenergic receptor blockers, angiotensin-converting enzyme inhibitors (ACEI), angiotensin receptor blockers (ARB), and calcium channel blockers (CCBs). Both ACEI and ARB act on the renin-angiotensin-aldosterone system (RAS).

5. Pharmacological Treatment of Hypertension

5.1. Diuretics

Diuretics are highly recommended for treating hypertension in elderly, obese, and female patients [33]. Diuretics includes chlorthalidone and hydrochlorothiazide. They have been grouped into six classes: thiazide diuretics, loop diuretics, potassium-sparing diuretics, aldosterone receptor antagonists, carbonic anhydrase inhibitors, and osmotic diuretics; the last ones are generally not used in hypertension (Table 1). They are relatively cheaper and have high patient tolerance and mild side effects [34]. They generally have a rapid antihypertensive impact. Diuretics help the body to get rid of salt and water.

5.2. Beta-Adrenergic Blockers

Beta-adrenergic blockers (β -blockers) slow down the heart by blocking hormones such as adrenaline [35]. They mainly treat CVD, coronary heart disease, heart failure, arrhythmia, and cardiomyopathy. They are usually not recommended as first-line treatment for hypertension. They have been implicated in significant increases in stroke, mortality, worsening of insulin-dependency diabetes, and poor cardiovascular system protection [35]. The commonly prescribed beta-blockers include atenolol, bisoprolol, carvedilol, labetalol, metoprolol, propranolol, and sotalol.

5.3. Calcium Channel Blockers

Calcium channel blockers (CCB) or calcium channel antagonists are generally better than beta-blockers and are one of the most prescribed antihypertensive drugs [36]. They prevent significant vessel stiffness in elderly patients. CCBs are grouped into dihydropyridine and nondihydropyridine. CCBs act differently on blood vessels and have variable duration of action, selectivity, side effects, and mechanism of action [37].

5.4. Angiotensin-Converting Enzyme Inhibitors

Angiotensin-converting enzyme Inhibitors (ACEIs) drugs act on the Renin-Angiotensin-aldosterone System (RAS), inhibiting the conversion of angiotensin I to angiotensin II, thereby preventing vasoconstriction [38]. Because of their excellent antihypertensive effect, they are recommended as first-line treatment for hypertension in most countries. They also lower CVDs in most hypertensive patients [38]. Some of the prescribed ACEIs and their side effects are presented in Table 1.

5.5. Angiotensin Receptor Blockades

Angiotensin Receptor Blockades (ARBs) are another excellent first-line drug that selectively blocks angiotensin receptor II, inhibits the aldosterone system, reduces sodium and water retention, lowers BP, and protects the nervous and kidney systems [39]. ARBs have fewer side effects compared to ACEIs.

Table 1. List of common drugs and their main adverse reactions in Antihypertensive treatment.

Types of Pharmacological Antihypertensive Drugs	Subtypes	Drug Name	Main Side Effects	References
Diuretics	Aldosterone Receptor Antagonist, mineralocorticoid receptor antagonist (MRA)	Eplerenone, Spironolactone, Finerenone	Increases blood potassium levels, Gynecomastia, Frequent urination	[40]
	Thiazide Diuretic	Hydrochlorothiazide, Metolazone, Chlorthalidone, Methyclothiazide, Indapamide	Urinating more often, Too little sodium in the blood, Hypokalaemia	[41]
	Loop Diuretic	Bumetanide, Ethacrynic acid, Furosemide, Torsemide	Hypokalaemia	[41]
Calcium Channel Blockers (CCBs)	Potassium-Sparing Diuretic	Amiloride, Eplerenone, Spironolactone, Triamterene	Hyperkalemia	[42]
	Dihydropyridine	Nifedipine, Isradipine, Felodipine, Nicardipine, Nisoldipine, Lacidipine, Amlodipine, and Levamlodipine	Edema, Reflex tachycardia, Flushing, Ankle edema	[43]
	Non-dihydropyridine	Diltiazem and Verapamil	Worsening cardiac output, and Bradycardia, Atrioventricular block	[43]
β - Adrenergic blockers		Atenolol, Bisoprolol, Carvedilol, Metoprolol, Nebivolol, Propranolol	Slow heartbeat, Bronchospasm, Dizziness, Tiredness, Blurred vision	[44]
Angiotensin-converting enzyme Inhibitors (ACEIs)		Benazepril, Captopril, Enalapril, Fosinopril, Lisinopril, Moexipril, Perindopril, Quinapril, Ramipril, Trandolapril.	Angioedema Dry cough, Hyperkalaemia, Extreme tiredness or dizziness from blood pressure going too low, Headaches, Loss of taste	[45]
Angiotensin Receptor Blockades (ARBs)		Azilsartan, Candesartan, Eprosartan mesylate, Olmesartan, Irbesarten, losartan potassium, Telmisartan, Valsartan	High potassium levels, Leg swelling	[46]
Combination hypertensive drugs		Diuretic combinations: Amiloride and Hydrochlorothiazide, Spironolactone and Hydrochlorothiazide. Triamterene and Hydrochlorothiazide. Beta blockers and diuretics: Atenolol and Chlorthalidone, Bisoprolol and Hydrochlorothiazide, Metoprolol and Hydrochlorothiazide, Nadolol and Bendroflumethazide, Propranolol and Hydrochlorothiazide, Propranolol ER and Hydrochlorothiazide, Timolol and Hydrochlorothiazide. ACE inhibitors and diuretics: Benazepril and Hydrochlorothiazide, Captopril and Hydrochlorothiazide, Enalapril and Hydrochlorothiazide, Lisinopril and Hydrochlorothiazide, Moexipril and Hydrochlorothiazide. Angiotensin-II receptor antagonists and diuretics: Losartan and Hydrochlorothiazide, Valsartan and Hydrochlorothiazide. Calcium channel blockers and ACE inhibitors: Amlodipine and Benazepril, Diltiazem and Enalapril, Felodipine and Enalapril, Verapamil and Trandolapril	The specific adverse reactions vary in different drug combinations.	[47]

6. Resistant Hypertension

Resistant hypertension happens when patients do not respond effectively to three or more antihypertensive drugs, including diuretics when taken in the correct combination and at tolerable doses [48, 49]. The prevalence of resistant hypertension is estimated in 9–18% of hypertensive patients [48]. The major problem of most resistant hypertension patients is non-adherence to medication and lifestyle changes. Indeed, the research conducted by Galletti and Barbato (2016) showed that 75% of patients diagnosed with resistant hypertension did not adhere to the recommended daily sodium intake [50]. This poses a considerable challenge to medical doctors as it is critically important to rule out “pseudoresistant” hypertension from “true-resistant” hypertension.

Pseudoresistant hypertension is associated with poor adherence to antihypertensive therapy, lifestyle changes, and high sodium intake. In most cases of true resistant hypertension, there are myriad underlying medical conditions such as blood pressure-associated hormonal abnormality, renal artery stenosis (artery-clogging plaque in blood vessels), obstructive sleep apnea, obesity, and heavy intake of alcohol [51] (Figure 6). It is very important to screen for secondary hypertension when diagnosing resistant hypertension. Secondary hypertension traits include obstructive sleep apnea, primary aldosteronism, chronic kidney disease, pheochromocytoma, and cushing syndrome.

Patients with resistant hypertension need strict lifestyle changes and medication adherence [49].

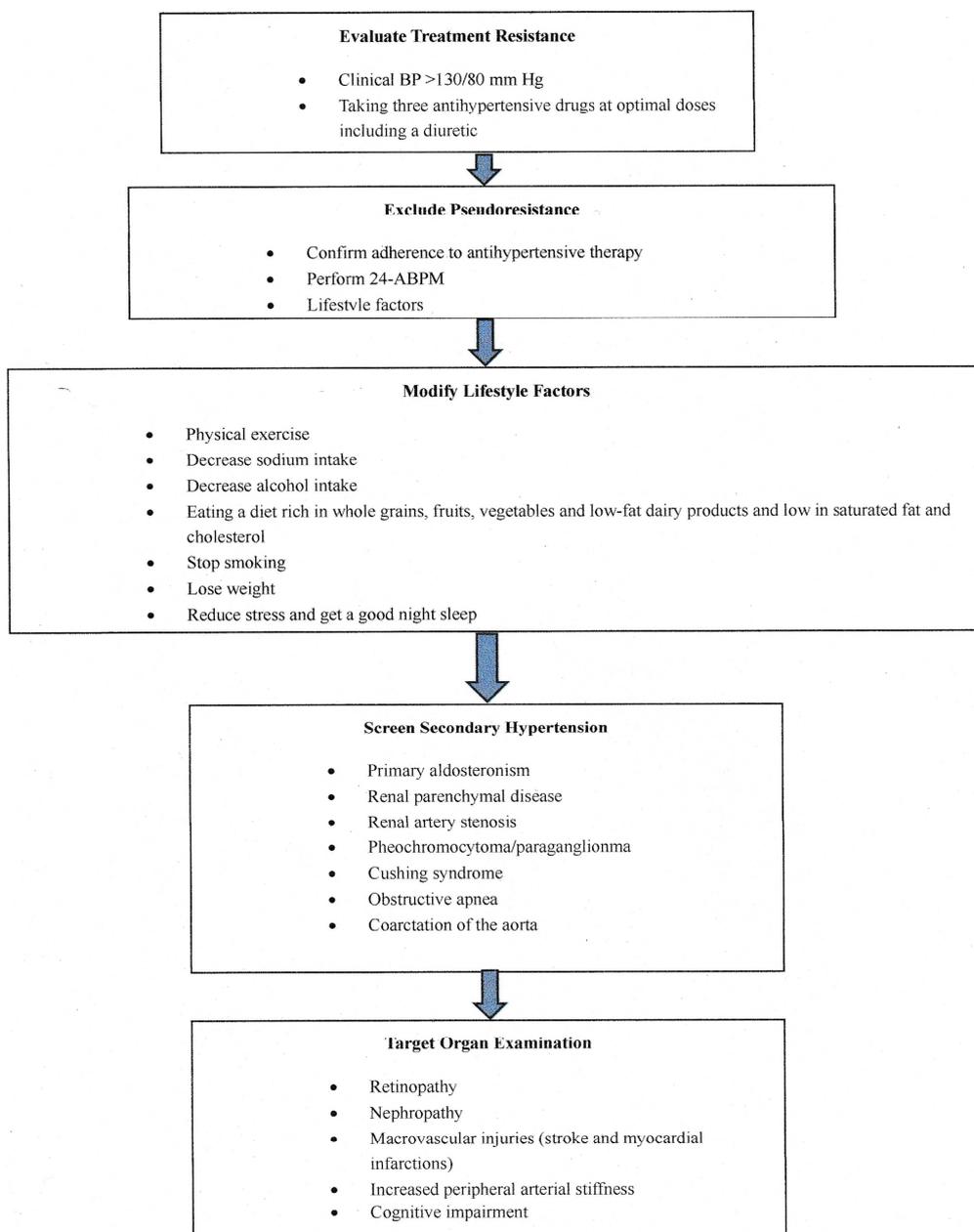


Figure 6. Diagnosis of resistant hypertension. ABPM indicates ambulatory blood pressure monitoring.

7. Herbs for Hypertension

Several plants have been recommended to treat hypertension, although their mode of action, safety, and efficiency are unknown [52-54]. They are popular in most developing countries because most people cannot afford

pharmaceutical drugs or have no access to medical doctors, devices, or training to check their blood pressure regularly. Some herbs used for treating hypertension and their mode of action are given in Table 2. More studies are needed on these plants to identify their active ingredients [55, 56].

Table 2. Medicinal plants in treating hypertension and their proposed mode of action.

Antihypertensive Herbs	Molecular Mechanism of Action	Antihypertensive Effects	References
<i>Apium graveolens</i>	Blocking calcium channels	Reduce blood pressure Decrease vascular resistance	[57]
<i>Coptis chinensis</i>	Increases HO ¹ enzyme amelioration of oxidative stress elevates the expression of eNOS with a concomitant rise in NO release	Hypotensive effect Relaxing arterial tissues Vasorelaxant activities Vasodilation	[58]
<i>Coriandrum sativum</i>	Decreases NF-Kb antioxidant activities	Reduction in SBP, DBP, and mean arterial blood pressure Diuretic effects Vasorelaxant activities	[59]
<i>Hibiscus sabdariffa</i>	Lowers uric acid concentration Reduces plasma Na ⁺ levels Inhibition of ACE activity Increases free radical scavenging	blood pressure-lowering effects vasorelaxant activities Diuretic action	[60]
<i>Bidens pilosa L</i>	Calcium channel antagonism Inhibits NF-κB and TNF-alpha activation	Prevent and attenuate high blood pressure Vasorelaxant responses Vasodilation	[61]
<i>Camelia sinensis</i>	Increases antioxidant enzymes an augmented release of NO	Reduces both SBP and DBP Vasorelaxant responses Endothelial dependent dilation	[62]
<i>Nigella sativa</i>	Decrease inflammatory mediators (TNFα, IL-6) generation of TNF-α and NF-κB an endogenous inhibitor of Enos increases HO ¹ enzyme expression	Improvement in renal function and antioxidant activity Reduces both SBP and DBP Vasorelaxant responses Diuretic action	[63]
<i>Salvia miltiorrhiza</i>	Activating eNOS-NO signaling	relaxes the vasculature via endothelium-dependent and endothelium-independent mechanisms Lowers blood pressure	[64]
<i>Tribulus terrestris</i>	NO release membrane hyperpolarization Stimulate angiogenesis inhibit Ang II-induced production of H ₂ O ₂	Lowers blood pressure Diuretic action	[65]
<i>Allium sativum</i>	Inhibits Angiotensin Converting Enzyme (ACE) Increases NO, eNOS, H ₂ S,	Reduction of either SBP, DBP, or both Vasodilation Vasorelaxant activities	[66]

8. Conclusion

Hypertension as a chronic medical condition increases with age. In developing countries, not only the elderly but also the youths are affected by hypertension at alarming rates. Some causes of hypertension include limited access to community health workers, health coaches, antihypertensive medications, unhealthy diets including high consumption of salt, low consumption of fresh fruits, a high prevalence of maternal and childhood undernutrition, and lack of physical activity due to a busy lifestyle.

Cases of resistant hypertension complicate matters and need special attention and further medical research.

Although some plants have shown antihypertensive activities, their safety, efficiency, and mode of action need further research.

In developing countries, it is imperative to increase the awareness of hypertension and the availability of hypertension drugs. For communities located in inaccessible rural areas, training and equipping community leaders in hypertension

awareness and measurement can assist most people in these communities and hopefully reduce fatal hypertension cases.

Conflicts of Interest

The author has no commercial or financial conflicts of interest or any funding sources to disclose.

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References

- [1] World Health Organization (WHO). Hypertension fact sheet. <https://www.who.int/news-room/fact-sheets/detail/hypertension>. Accessed 17th October 2023.

- [2] Naranjo M, Chauhan S, Paul M. Malignant Hypertension. In StatPearls. StatPearls Publishing, 2023.
- [3] Mills KT, Stefanescu A, He J. (2020). The global epidemiology of hypertension. *Nature reviews. Nephrology*, 2020; 16 (4): 223–237.
- [4] Zhou B, Bentham J, Di Cesare M, Bixby H, Danaei G, Cowan MJ, *et al.* Worldwide trends in blood pressure from 1975 to 2015: a pooled analysis of 1479 population-based measurement studies with 19·1 million participants. *The Lancet*, 2017; 389 (10064): 37-55.
- [5] Ogunniyi MO, Commodore-Mensah Y, Ferdinand KC. Race, Ethnicity, Hypertension, and heart disease: JACC Focus Seminar 1/9. *J Am Coll Cardiol.*, 2021; 78 (24): 2460-2470.
- [6] Doroszko A, Janus A, Szahidewicz-Krupska E, Mazur G, Derkacz A. Resistant Hypertension. *Advances in Clinical and Experimental Medicine: Official Organ Wroclaw Medical University*, 2016; 25 (1): 173–183.
- [7] World Health Organization (WHO). First WHO report details devastating impact of hypertension and ways to stop it. <https://www.who.int/news/item/19-09-2023-first-who-report-detailed-devastating-impact-of-hypertension-and-ways-to-stop-it> Accessed 17 October 2023.
- [8] Oparil S, Acelajado MC, Bakris G, Berlowitz, DR, Cifková R, Dominiczak AF, Grassi G, Jordan J, Poulter NR, Rodgers A, Whelton PK. *Hypertension. Nature Reviews Disease Primers*, 2018; 4: 18014.
- [9] Odden MC, Beilby PR, Peralta CA. Blood Pressure in Older Adults: The Importance of Frailty. *Curr Hypertens Rep.* 2015; 17 (7): 55.
- [10] Metoki H, Kuriyama S. Combination of genetic and environmental factors for childhood hypertension: a simple indicator of family history remains useful. *Hypertens Res.* 2023; 46 (4): 1061-1063.
- [11] Jang S, Kim ST, Kim YK, Song YH. Association of blood pressure and hypertension between parents and offspring: The Korea National Health and Nutrition Examination Survey. *Hypertension Research: official journal of the Japanese Society of Hypertension*, 2023; 46 (2): 368–376.
- [12] Wang Z, Lu C, Wang Y, *et al.* Association between ultra-processed foods consumption and the risk of hypertension: An umbrella review of systematic reviews. *Hellenic J Cardiol.*, 2023; S1109-9666(23)00137-9.
- [13] Zhou L, Feng W, Xiang N, *et al.* Association between physical activity dimensions and the risk of hypertension among middle and older adults: A cross-sectional study in China. *Front Public Health*, 2022; 10: 995755.
- [14] Ohldeck AE, Kringeland E, Midtbø H, Tell GS, Gerds E. High-normal blood pressure in midlife is a stronger risk factor for incident hypertension 26 years later in women than men: the Hordaland Health Study. *Blood Press.* 2023; 32 (1): 2179337.
- [15] Everett B, Zajacova A. Gender differences in hypertension and hypertension awareness among young adults. *Biodemography Soc Biol.*, 2015; 61 (1): 1-17.
- [16] Park S. Ideal Target Blood Pressure in Hypertension. *Korean Circ J.*, 2019; 49 (11): 1002-1009.
- [17] Zhou B, Perel P, Mensah GA, Ezzati M. Global epidemiology, health burden and effective interventions for elevated blood pressure and hypertension. *Nat Rev Cardiol.*, 2021; 18 (11): 785-802.
- [18] Marczyk L, Williams J, Loeffler M, for the For the Institute for Health Metrics and Evaluation. Global Deaths Attributable to High Systolic Blood Pressure, 1990-2016. *JAMA*, 2018; 319 (21): 2163.
- [19] Fuchs FD, Whelton PK. High blood pressure and cardiovascular disease. *Hypertension*, 2020; 75 (2): 285-292.
- [20] Poznyak AV, Sadykhov NK, Kartuesov AG, *et al.* Hypertension as a risk factor for atherosclerosis: Cardiovascular risk assessment. *Front Cardiovasc Med.*, 2022; 9: 959285.
- [21] Canoy D, Nazarzadeh M, Copland E, Bidel Z, Rao S, Li Y, Rahimi K. How Much Lowering of Blood Pressure Is Required to Prevent Cardiovascular Disease in Patients with and Without Previous Cardiovascular Disease? *Current Cardiology Reports*, 2024; 24 (7): 851–860.
- [22] Kamalumpundi V, Shams E, Tucker C, Cheng L, Peterson J, Thangavel S, Ofori O, Correia M. Mechanisms and pharmacotherapy of hypertension associated with type 2 diabetes. *Biochemical Pharmacology*, 2022; 206: 115304.
- [23] McFarlane SI, Jean-Louis G, Zizi F, *et al.* Hypertension in the high-cardiovascular-risk populations. *Int J Hypertens.*, 2011; 2011: 746369.
- [24] Çakıcı EK, Yazılıtaş F, Kurt-Sukur ED, Güngör T, Çelikkaya E, Karakaya D, Bülbül M. Clinical assessment of primary and secondary hypertension in children and adolescents. *Archives De Pediatrie: Organe Officiel De La Societe Francaise De Pediatrie*, 2020; 27 (6): 286–291.
- [25] Charles L, Triscott J, Dobbs B. (2017). Secondary Hypertension: Discovering the Underlying Cause. *American Family Physician*, 2017; 96 (7): 453–461.
- [26] Harrison DG, Coffman TM, Wilcox CS. Pathophysiology of Hypertension: The Mosaic Theory and Beyond. *Circulation Research*, 2021; 128 (7): 847–863.
- [27] Raina R, Krishnappa V, Das A, *et al.* Overview of Monogenic or Mendelian Forms of Hypertension. *Front Pediatr.* 2019; 7: 263.
- [28] Padmanabhan S, Dominiczak AF. Genomics of hypertension: the road to precision medicine. *Nat Rev Cardiol.*, 2021; 18 (4): 235-250.
- [29] Garimella PS, du Toit C, Le NN, Padmanabhan S. A genomic deep field view of hypertension. *Kidney International*, 2023; 103 (1): 42–52.
- [30] Schutte AE, Srinivasapura Venkateshmurthy N, Mohan S, Prabhakaran D. Hypertension in Low- and Middle-Income Countries. *Circ Res.*, 2021; 128 (7): 808-826.
- [31] Cavagna P, Leplay C, N'Guetta R, Kramoh KE, Diop IB, Balde DM, Mipinda JB, Azizi M, Jouven X, Antignac M. Hypertension treatment in sub-Saharan Africa: a systematic review. *Cardiovascular Journal of Africa*, 2023; 34: 1–11.
- [32] Marinier K, Macouillard P, de Champvallins M, Deltour N, Poulter N, Mancina G. Effectiveness of two-drug therapy versus monotherapy as initial regimen in hypertension: A propensity score-matched cohort study in the UK Clinical Practice Research Datalink. *Pharmacoepidemiol Drug Saf.*, 2019; 28 (12): 1572-1582.

- [33] Kehrenberg MCA, Bachmann HS. Diuretics: a contemporary pharmacological classification? *Naunyn-Schmiedeberg's Archives Of Pharmacology*, 2022; 395 (6): 619–627.
- [34] Reinhart M, Puil L, Salzwedel DM, Wright JM. First-line diuretics versus other classes of antihypertensive drugs for hypertension. *Cochrane Database Syst Rev.*, 2023; 7 (7): CD008161.
- [35] Frishman WH, Saunders E. β -Adrenergic blockers. *Journal of Clinical Hypertension (Greenwich, Conn.)*, 2011; 13 (9): 649–653.
- [36] Antza C, Stabouli S, Kotsis V. Combination therapy with lercanidipine and enalapril in the management of the hypertensive patient: an update of the evidence. *Vascular Health and Risk Management*, 2016; 12: 443–451.
- [37] Fici F, Robles NR, Tengiz I, Grassi G. Beta-Blockers, and Hypertension: Some Questions and Answers. *High Blood Pressure & Cardiovascular Prevention: the official journal of the Italian Society of Hypertension*, 2023; 30 (3): 191–198.
- [38] Ahmad H, Khan H, Haque S, Ahmad S, Srivastava N, Khan A. Angiotensin-Converting Enzyme and Hypertension: A Systemic Analysis of Various ACE Inhibitors, Their Side Effects, and Bioactive Peptides as a Putative Therapy for Hypertension. *Journal of The Renin-Angiotensin-Aldosterone System: JRAAS*, 2023; 7890188.
- [39] Park CS, Kim B, Rhee TM, *et al.* Association between renin-angiotensin-aldosterone system blockade and clinical outcomes in patients with hypertension: real-world observation from a nationwide hypertension cohort. *Clin Res Cardiol*, 2023.
- [40] Maron BA, Leopold JA. Aldosterone receptor antagonists: effective but often forgotten. *Circulation*. 2010; 121 (7): 934-939.
- [41] Sica DA, Carter B, Cushman W, Hamm L. Thiazide and loop diuretics. *J Clin Hypertens (Greenwich)*. 2011; 13 (9): 639-643.
- [42] Martins, V. M., Ziegelmann, P. K., Ferrari, F., Bottino, L. G., Lucca, M. B., Corrêa, H. L. R., Blum, G. B., Helal, L., Fuchs, S. C., & Fuchs, F. D. (2023). Thiazide diuretics alone or combined with potassium-sparing diuretics to treat hypertension: a systematic review and network meta-analysis of randomized controlled trials. *Journal of hypertension*, 41 (7), 1108–1116.
- [43] Li JF, Chen YQ, Wang L, Cao YS, Yuan JX. Editorial: Calcium and pulmonary hypertension. *Frontiers in Physiology*, 2022; 13: 1019158.
- [44] Pathak A, Mrabeti S. β -Blockade for Patients with Hypertension, Ischemic Heart Disease or Heart Failure: Where are We Now? *Vasc Health Risk Manag.*, 2021; 17: 337-348.
- [45] Sharifan A, Bahreini M, Ashraf H, Najmeddin F. Blood Pressure Control Following Angiotensin-Converting Enzyme Inhibitors and Angiotensin II Receptor Blockers: Insights from a Triple-Blind, Randomized, Clinical Trial. *J Clin Pharmacol.*, 2023; 10.1002/jcph.2294.
- [46] Rao GA, Mann JR, Shoaibi A, *et al.* Angiotensin receptor blockers: are they related to lung cancer? *J Hypertens*. 2013; 31 (8): 1669-1675.
- [47] Skolnik NS, Beck JD, Clark M. Combination antihypertensive drugs: recommendations for use. *Am Fam Physician*, 2000; 61 (10): 3049-3056.
- [48] Shalaeva EV, Messerli FH. (2023). What is resistant arterial hypertension? *Blood Pressure*, 2023; 32 (1): 2185457.
- [49] Carey RM, Calhoun DA, Bakris GL, Brook RD, Daugherty SL, Dennison-Himmelfarb CR, *et al.* Resistant Hypertension: Detection, Evaluation, and Management: *A Scientific Statement from the American Heart Association*. *Hypertension (Dallas, Tex.: 1979)*, 2018; 72 (5): e53–e90.
- [50] Galletti F, Barbato A. Prevalence and determinants of resistant hypertension in a sample of patients followed in Italian hypertension centers: results from the MINISAL-SIIA study program. *Journal of human hypertension*, 2016; 30 (11): 703-708.
- [51] Rimoldi SF, Messerli FH, Bangalore S, Scherrer U. Resistant hypertension: what the cardiologist needs to know. *Eur Heart J*. 2015; 36 (40): 2686-2695.
- [52] Tabassum N, Ahmad F. Role of natural herbs in the treatment of hypertension. *Pharmacogn Rev.*, 2011; 5 (9): 30-40.
- [53] Kamyab R, Namdar H, Torbati M, Ghojzadeh M, Araj-Khodaei M, Fazljou SMB. Medicinal Plants in the Treatment of Hypertension: A Review. *Advanced Pharmaceutical Bulletin*, 2021; 11 (4): 601–617.
- [54] Verma T, Sinha M, Bansal N, Yadav SR, Shah K, Chauhan NS. Plants Used as Antihypertensive. *Nat Prod Bioprospect.*, 2021; 11 (2): 155-184.
- [55] Al Disi SS, Anwar MA, Eid AH. Anti-hypertensive Herbs and their Mechanisms of Action: Part I. *Front. Pharmacol.*, 2016; 6: 323.
- [56] Anwar MA, Al Disi SS, Eid AH. Anti-Hypertensive Herbs and Their Mechanisms of Action: Part II. *Front. Pharmacol.*, 2016; 7: 50.
- [57] Shayani Rad M, Moohebaty M, Mohajeri SA. Effect of celery (*Apium graveolens*) seed extract on hypertension: A randomized, triple-blind, placebo-controlled, cross-over, clinical trial. *Phytother Res.*, 2022; 36 (7): 2889-2907.
- [58] Song D, Hao J, Fan D. Biological properties and clinical applications of berberine. *Front Med.*, 2020; 14 (5): 564-582.
- [59] Wang X, Liu Y, Wang Y, *et al.* Protective Effect of Coriander (*Coriandrum sativum L.*) on High-Fructose and High-Salt Diet-Induced Hypertension: Relevant to Improvement of Renal and Intestinal Function. *J Agric Food Chem.*, 2022; 70 (12): 3730-3744.
- [60] Serban C, Sahebkar A, Ursoniu S, Andrica F, Banach M. Effect of sour tea (*Hibiscus sabdariffa L.*) on arterial hypertension: a systematic review and meta-analysis of randomized controlled trials. *J Hypertens.*, 2015; 33 (6): 1119-1127.
- [61] Tcheutchoua YC, Bilanda DC, Dzeufiet PDD, *et al.* Preventive Potential of the Aqueous Extract of the Mixture of *Bidens pilosa* (Asteraceae) and *Cymbopogon citratus* (Poaceae) Aerial Parts on Hypertension Induced by a Chronic Salt and Alcohol Consumption on the Rats. *Evid Based Complement Alternat Med.*, 2022; 2022: 1980622.
- [62] Chiang SS, Chen LS, Chu CY. Active food ingredients production from cold pressed processing residues of *Camellia oleifera* and *Camellia sinensis* seeds for regulation of blood pressure and vascular function. *Chemosphere*, 2021; 267: 129267.

- [63] Maideen NMP, Balasubramanian R, Ramanathan S. *Nigella Sativa* (Black Seeds), A Potential Herb for the Pharmacotherapeutic Management of Hypertension - A Review. *Current Cardiology Reviews*, 2021; 17 (4): e230421187786.
- [64] Wu R, Zhou Y, Xu H, et al. Aqueous extract of *Salvia miltiorrhiza Bunge* reduces blood pressure through inhibiting oxidative stress, inflammation and fibrosis of adventitia in primary hypertension. *Front Pharmacol.*, 2023; 14: 1093669.
- [65] Abbas K, Rizwani GH, Qadir MI, Younis M, Qaisar MN, Siddique FA, Aamir MN, Wazir A, Shaheer T. (2023). Herbal Formulation Comprised of Methanol Extracts of *Tribulus terrestris L.* and *Zingiber officinale Roscoe* Has Antihypertensive Effects. *Alternative Therapies in Health and Medicine*, 2023; 29 (4): 234–239.
- [66] Serrano JCE, Castro-Boqué E, García-Carrasco A, et al. Antihypertensive Effects of an Optimized Aged Garlic Extract in Subjects with Grade I Hypertension and Antihypertensive Drug Therapy: A Randomized, Triple-Blind Controlled Trial. *Nutrients*, 2023; 15 (17): 3691.