Section A-Research paper

Recent Updates About Hypertension and Hypertensive Nephropathy

Mohammed Ghanem Gabr [1], Amir Mohamed Elokely[2], Mabrouk Ibrahim Ismail [2], Nafesa Mohammed Kamal [2], Samia Hassan El-Shishtawy [1]

1 Internal Medicine and Nephrology Department, Faculty of Medicine, Zagazig University, Egypt

2 Internal Medicine and Nephrology Department, Theodor Bilharz Research Institute

Email: Ghanemnephrologist@gmail.com

Article History: Received 10th June, Accepted 5th July, published online 10th July 2023

Abstract

Background: The defining characteristic of systemic arterial hypertension, commonly known as hypertension, is persistently high blood pressure (BP) in the systemic arteries. One common approach to express blood pressure is the ratio of systolic blood pressure to diastolic blood pressure. Systolic blood pressure is the force that the blood applies to the arterial walls when the heart contracts, while the diastolic BP is the pressure when the heart relaxes. Depending on the method of measurement, certain BP cutoffs indicate hypertension. It is generally accepted that chronic kidney disease (CKD) will advance more quickly as a result of elevated systemic blood pressure and that accelerated and malignant types of hypertensions can quickly cause permanent kidney failure. On the other hand, it continues to be debated whether modest to moderate increases in systemic blood pressure frequently cause CKD and subsequently end-stage renal disease (ESRD). Most hypertension patients experience mild-to-moderate hypertensive nephrosclerosis. Nevertheless, when BP values are uncontrolled for a prolonged period of time or kidney disease is present, the proportion of people who develop ESRD drastically rises. The chronological sequence of events (i.e., whether CKD or hypertension occurred first) in the majority of cases of concomitant hypertension and CKD cannot be determined. Hypertensive nephrosclerosis involves hyalinization and sclerosis of interlobular and afferent arterioles, together with glomerular and tubulointerstitial compartments fibrosis. Blood is supplied to afferent arterioles under higher pressure because of ageing and hypertension-related arterial stiffness. Early on, post glomerular vascular hypoxia caused by glomerular ischemia results in primarily monocytic/macrophagic inflammation and epithelial–mesenchymal transition (EMT). For many years, it was believed that hypertensive kidney disease was a condition that only affected the afferent arterioles and glomeruli, and that the pathogenic mechanisms causing the kidney damage were mechanical stress brought on by high blood pressure, RAAS stimulation, and activation of local fibroblasts. Epithelial-mesenchymal transition, podocyte loss, and tubulointerstitial fibrosis have so far been identified as the primary pathways for the development of cytoprotective treatment approaches.

Keywords: Hypertension, Hypertensive Nephropathy

DOI: 10.53555/ecb/2023.12.Si12.271

Introduction

The defining characteristic of systemic arterial hypertension, commonly known as hypertension, is persistently high blood pressure (BP) in the systemic arteries. One common approach to express blood pressure is the ratio of systolic blood pressure to diastolic blood pressure. Systolic blood pressure is the force that the blood applies to the arterial walls when the heart contracts, while the diastolic BP is the pressure when the heart relaxes. Depending on the method of measurement, certain BP cutoffs indicate

hypertension **(1).**

Table (1): Definitions of hypertension based on the 2018 ESH/ESC guidelines **(2).**

Subtype	Systolic BP (mmHg)	Diastolic BP (mmHg)
Optimal BP	<120	<80
Normal BP	120-129	80-84
High normal BP	130-139	85-89
Grade 1 HTN	140-159	90-99
Grade 2 HTN	160-179	100-109
Grade 3 HTN	≥180	≥110
Isolated systolic hypertension	≥140	<90

For the diagnosis of hypertension, systolic blood pressure (BP), diastolic BP, or both have to exceed the reported values. ESC, European Society of Cardiology; ESH, European Society of Hypertension; HTN, hypertension.

White coat hypertension is defined as an office blood pressure reading of at least 130/80 mmHg and less than 160/100 mmHg that drops to at least 130/80 mmHg following at least three months of anti-hypertensive medication. For this diagnosis, ambulatory or at-home blood pressure measurement is usually required **(2).**

Masked hypertension is defined as having a systolic blood pressure of 120 to 129 mmHg in the office and a diastolic blood pressure of less than 80 mmHg but a higher blood pressure on ambulatory or home readings (130/80 mmHg or greater) **(2).**

The relationship between blood pressure and an elevated risk of cardiovascular disease (CVD) is graded and continuous, beginning with blood pressures as low as 115/75 mmHg, considerably within what is considered to be the normotensive range **(3).**

Epidemiology

About 874 million individuals worldwide have systolic blood pressure that is less than 140 mmHg, while 3.5 billion adults have non-optimal systolic blood pressure, which is defined as being >110-115 mmHg. Thus, one in four people suffer from hypertension. Population growth, population ageing, and a rise of 10% in the age-standardized prevalence of hypertension between 1990 and 2015 resulted in a global increase of 43% in the number of healthy life years lost to non-optimal BP. According to the Global Burden of Disease study, high blood pressure continues to be the leading risk factor for the global burden of illness and all-cause mortality, resulting in 9.4 million deaths and 212 million lost healthy life years (8.5% of the total global loss) annually **(3).**

In Egypt, the prevalence of hypertension ranged from 12.1% to 59%. Low levels of awareness (37.5% and 43.9%), diagnosis (42% and 64.7%), therapy (24.4% and 54.1%), and antihypertensive drug adherence (51.9%) were reported in research **(4).**

Causes of hypertension

- *Primary hypertension*

Intricate interactions between environmental and genetic factors result in hypertension. It has been discovered that there are both common genetic variations with little effects on blood pressure and unusual genetic variations with large effects. Genome-wide association studies (GWAS) have also revealed 35 genetic loci linked to blood pressure, 12 of which were newly identified **(5).**

Each unique genomic locus has a sentinel Single nucleotide polymorphism (SNP) that links DNA methylation at a large number of nearby CpG sites to the gene. These sentinel SNPs are located in genes that influence the function of vascular and renal smooth muscle. DNA methylation may perhaps play a role in the associations between high genetic diversity and a range of disorders, even though the mechanisms behind these correlations are not fully known. The 35 sentinel SNPs (both known and novel) employed in this study's single variant test showed that genetic variants, whether present singly or in combination, raise the likelihood of clinical symptoms related to high blood pressure **(5).**

A significant possibility of acquiring hypertension later in life exists when ageing is mixed with a western diet and lifestyle. There are numerous ways in which the environment affects blood pressure. Eating an excessive amount of salt raises blood pressure in persons who are sensitive to salt; in some cases, obesity and inactivity may also be contributing factors. Although their precise effects are less obvious, additional factors including coffee consumption and a lack of vitamin D may also be involved. Insulin resistance, which is connected to syndrome X (also known as the metabolic syndrome) and is common in obese people, influences hypertension **(2).**

Although the precise processes by which this occurs are still understood, low birth weight, maternal smoking, and not nursing may all be early life events that raise the probability of having essential hypertension in adults. It has been noted that untreated hypertensives had a higher incidence of high blood uric acid than people with normal blood pressure, although it is unclear whether the former is the cause or a sign of poor kidney function. The average blood pressure may be higher in the winter than it is in the summer **(2).**

Secondary hypertension

Kidney dysfunction is the most common secondary cause of hypertension. A few other endocrine conditions that can cause hypertension include amyloidosis, Conn's syndrome or hyperaldosteronism, renal artery stenosis (due to atherosclerosis or fibromuscular dysplasia), hyperparathyroidism, and pheochromocytoma **(2).**

Other causes of secondary hypertension include obesity, sleep apnea, pregnancy, coarctation of the aorta, excessive licorice use, excessive alcohol consumption, some prescription drugs, herbal remedies, and stimulants including caffeine, cocaine, and methamphetamine. Arsenic exposure from drinking water has been shown to be linked to elevated blood pressure. Depression and hypertension have been linked. Being alone is a risky situation. A review from 2018 found that consuming any amount of alcohol increased blood pressure in men, but only one or two drinks did the same for women **(6).**

Mechanisms/pathophysiology

- *Blood pressure regulation*

Blood pressure is regulated by multiple factors, including blood volume, cardiac output, or how much blood the heart pumps out each minute, as well as the balance of arterial tone, which is influenced by both intravascular volume and neurohumoral systems. To maintain normal blood pressure levels, the renin-angiotensin-aldosterone system (RAAS), the actions of natriuretic peptides and the endothelium, the sympathetic nervous system (SNS), and the immune system all interact in complex ways **(1).**

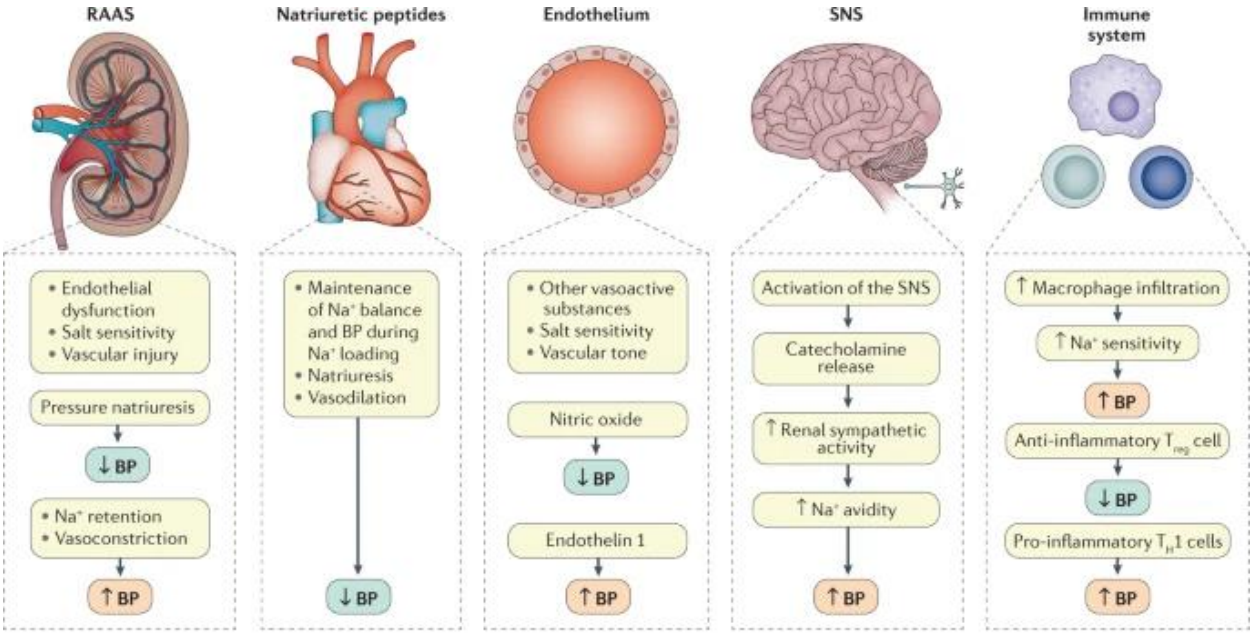

Figure (1): The major neuroendocrine systems involved in the regulation of blood pressure (Neurohumoral, immune, and organ systems involved in the maintenance of blood pressure (BP). Na+, sodium; RAAS, renin–angiotensin–aldosterone system; SNS, sympathetic nervous system **(1).**

Hereditary factors have a role in the complex pathophysiological mechanisms that cause hypertension. Primary hypertension is caused by several different types of genes. Environmental variables such as high sodium intake, poor sleep hygiene or sleep apnea, excessive alcohol consumption, and high mental stress all contribute to the development of hypertension **(1).**

Not the least, the arterial vasculature stiffens with age, raising the risk of hypertension due to, among other things, progressively accumulating alterations in vascular collagen and increases in atherosclerosis. Immunological factors may also be important, especially in the setting of viral or rheumatological diseases like rheumatoid arthritis. The mosaic theory explains the various causes of hypertension **(7).**

- *Sodium homeostasis regulation*

Since sodium promotes fluid (water) retention, which increases blood volume and blood pressure, it is essential for managing blood volume. In individuals with normotension, compensatory hemodynamic changes are made to maintain BP when dietary salt intake increases. Reduced renal and peripheral vascular resistance and enhanced nitric oxide (NO), a vasodilator, endothelial production are two of these alterations. However, BP increases if NO's impact is reduced or eliminated. Salt sensitivity is defined as a significant increase in blood pressure following a salt load of less than 5 g and is characterized by an increase in systolic blood pressure of at least 10 mmHg within a few hours of consumption **(1).**is caused by underlying endothelial dysfunction that can be inherited or triggered by the environment. In response to a high salt load, these persons frequently show overproduction of transforming growth factor (TGF), which increases the risk of fibrosis and oxidative stress, as well as reduced bioavailability of NO. A high salt intake also appears to enhance autoimmunity by activating T helper 17 (TH17) cells **(8).**

Renin–angiotensin–aldosterone system

The RAAS controls blood pressure in a number of ways, including by mediating factors like sodium retention, pressure natriuresis (the process by which increases in renal perfusion pressure (the gradient between renal arterial and venous BP) lead to decreased sodium reabsorption and increased sodium excretion), salt sensitivity, vasoconstriction, endothelial dysfunction, and vascular injury), among others. Additionally, it is important in the pathogenesis of hypertension **(1).**

Renin and prorenin are generated, stored, and released by the kidney's juxtaglomerular cells in response to a wide variety of stimuli. Angiotensinogen is mostly broken down by renin to produce angiotensin I. The conversion of angiotensin I into angiotensin II by an enzyme known as angiotensin-converting enzyme (ACE) is the pathogenetic importance of RAAS in hypertension **(1).**

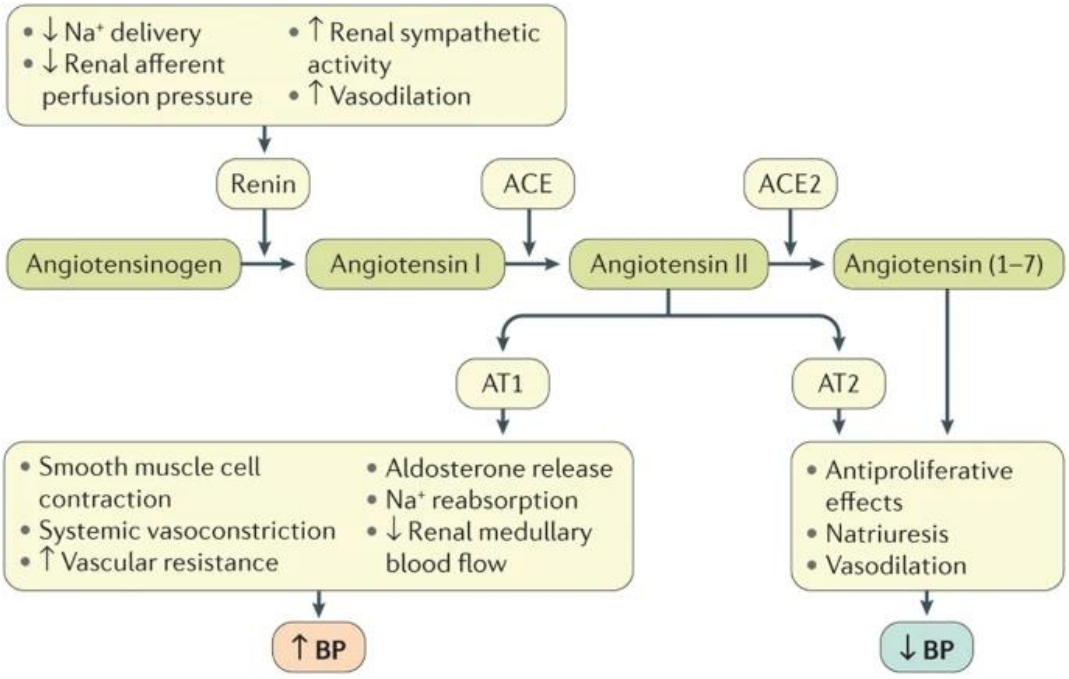

Figure (2): Role of renin–angiotensin–aldosterone system in the regulation of blood pressure **(1).**

ACE2 has emerged as a crucial modulator in the pathogenesis of hypertension, CVD, and renal disease due to its role in the conversion of angiotensin II into angiotensin (1–7). Angiotensin (1–7) induces natriuresis, systemic and localized vasodilation, diuresis and natriuresis. Additionally, it prevents fibroblasts, cardiac myocytes, proximal tubular, glomerular, and smooth muscle cells from proliferating and growing **(9).**

The development of hypertension depends on aldosterone. One of the nongenomic effects of binding to the mineralocorticoid receptor is the activation of the amiloride-sensitive sodium channel, also known as the epithelial sodium channel (ENaC), which stimulates renal sodium reabsorption in the cortical collecting duct. These outcomes happen without directly changing gene expression **(1).**

- *Natriuretic peptides*

Atrial natriuretic peptide (ANP) and brain natriuretic peptide (BNP) have a considerable impact on salt sensitivity and hypertension. The substantial natriuretic and vasodilator characteristics of sodium make it possible to maintain salt balance and blood pressure during sodium loading. ANP and BNP are released as a result of the atrial and ventricular stretch brought on by the administration of a sodium load. This results in systemic vasodilation, a reduction in plasma volume (as a result of fluid shifting from the intravascular to the interstitial compartment), and a lowering of blood pressure **(10).**

Natriuretic peptides boost the efferent arteriolar tone in volume-expanded situations, which in turn raises the glomerular filtration rate. Additionally, they restrict renal salt reabsorption both directly and indirectly. Two examples of direct effects include inhibition of the sodium-glucose cotransporter and Na+/K+-ATPase in the proximal tubule and decreased activity of the ENaC in the distal nephron. Examples of indirect effects include the suppression of renin and aldosterone release **(10).**

- *Endothelium*

The endothelium significantly affects vascular tone and contributes to salt sensitivity via NO. Endothelial cells produce a variety of vasoactive molecules, but NO is the most important for managing blood pressure. Endothelial cells continuously release NO in response to flow-induced shear stress, which activates guanylate cyclase and creates intracellular cyclic GMP45, which relaxes vascular smooth muscle **(11).**

Vasodilators like prostacyclin and endothelium-derived hyperpolarizing factors, as well as vasoconstrictors like endothelin 1 (ET1), locally produced angiotensin II, and the prostanoids thromboxane A2 and prostaglandin A2, are additional vasoregulatory substances secreted by endothelial cells. The potent vasoconstrictor ET1 activates the ETA receptor in vascular smooth muscle **(12).**

- *Sympathetic nervous system*

Baroreceptors, which are mechanoreceptors that detect pressure changes in the circulatory system, are found in significant numbers in the carotid sinus, a dilated area at the base of the internal carotid artery just above the bifurcation of the common carotid artery. When this artery is stretched by increasing blood pressure, nerve bundles that project from the baroreceptors in the carotid sinus communicate with the brain to reduce sympathetic outflow of nerve impulses (nerve traffic) and subsequently, blood pressure **(13).**

Hyperactivity of the SNS is linked to the onset and maintenance of hypertension. The amount of catecholamines released from sympathetic nerves that innervate blood vessels that enter the bloodstream as well as sural nerve activity as measured by microneurography are two additional signs of sympathetic overactivity in normotensive people with a family history of hypertension **(14).**

- *Inflammation and the immune system*

Inflammation has a major impact on both the development of hypertension and damage to target organs. Inflammation is associated with an increase in vascular permeability as well as the development of potent mediators like reactive oxygen species, NO, cytokines, and metalloproteinases. Neo-intima, a newly formed or thicker layer of vascular intima, is influenced by cytokines. Neo-intima causes resistance vessels' lumens to have a smaller diameter, which increases vascular stiffness and resistance. The primary vessels in charge of regulating blood pressure are resistance vessels, which are small arteries and arterioles that receive extensive innervation from autonomic neurons. Cytokines also affect renal tubular function by increasing local angiotensinogen and angiotensin II production, as well as by promoting salt and fluid retention in hypertension **(1).**

By allowing immune cells to pass through the vascular wall and into the interstitium of the injured organs, matrix metalloproteinases degrade the extracellular matrix, promote apoptosis, boost collagen synthesis, and harm the target organ **(1).**

Both innate and adaptive immunological responses in hypertension result in the production of reactive oxygen species and inflammatory changes in the kidneys, blood vessels, and brain. Innate immune-mediated responses, particularly those mediated by macrophages, have been linked to angiotensin II, aldosterone, and NO antagonist-induced hypertension **(15).**

T cell-mediated adaptive immune responses have also been linked to the onset of hypertension and the organ damage they induce. Notably, the Dahl Salt Sensitive rat model of hypertension and kidney damage caused by a high-salt diet was improved by the reduction of mature lymphocytes. Type 1 angiotensin II receptor (AT1) expression by T cells is a mediator of angiotensin II-dependent hypertension **(15).**

Diagnosis, screening

A patient with elevated blood pressure needs to be thoroughly examined for other conditions in addition to hypertension. All patients must have certain standard investigations, but some of them are only

necessary for specific patient groups who can be identified by their medical histories, physical examinations, and normal tests. In uncommon, inherited variations of the disease, a single gene mutation is responsible for the pathophysiology of hypertension **(16).**

In a small percentage of people with a potentially curable cause of hypertension, an accurate diagnosis may lead to a cure or a considerable improvement in blood pressure control with a decrease in the risk of cardiovascular disease (CVD). Consequently, it is appropriate to do a quick secondary hypertension test on all patients **(16).**

The patient's clinical history, a physical examination, and common laboratory tests are the foundation for the screening. Secondary hypertension should also be taken into consideration in situations of sudden worsening of hypertension, insufficient BP response to therapy, or severe target-organ damage that is out of proportion to the duration and severity of hypertension. In certain situations, specific diagnostic tests are suggested **(17).**

The date of the original hypertension diagnosis, previous and current blood pressure readings, and antihypertensive medications must all be included in medical history as hypertension increases the risk of CKD and the consequences of CVD. A woman's history of pregnancy-related hypertension must be taken into account when diagnosing her with hypertension **(17).**

Table (2): Physical examination of patients with hypertensio*n* **(1).**

Signs suggestive of secondary hypertension
• Features of Cushing syndrome • Neurofibromatosis (pheochromocytoma) • Enlarged kidneys (polycystic kidney) • Abdominal bruits (abnormal sound) (renovascular hypertension) • Precordial murmurs (sounds audible via the stethoscope) (aortic coarctation and aortic disease)
Signs of target-organ damage
• Brain: motor or sensory deficit • Retina: hypertensive retinopathy • Heart: atrial fibrillation, arrhythmias, pulmonary congestion and peripheral oedema • Peripheral arteries: absent, reduced or asymmetrical pulses and ischemic skin lesions • Carotid arteries: murmurs
Evidence of obesity
• BMI (body weight/height^2) of >30 kg/m^2 • Waist circumference* of >102 cm in men and of >88 cm in women

BMI, body mass index. *Values might need to be adjusted based on ethnicity or other factors.

Table (3): *Identifiable Hypertension and Screening Tests* **(18).**

Condition	Screening Test
Chronic kidney disease	Estimated glomerular filtration rate
Coarctation of the aorta	Computed tomography angiography
Cushing syndrome; other states of glucocorticoid excess (e.g., chronic steroid therapy	Dexamethasone suppression test
Drug-induced/drug-related hypertension*	Drug screening
Pheochromocytoma	24-hour urinary metanephrine and normetanephrine
Primary aldosteronism, other states of mineralocorticoid excess	Plasma aldosterone to renin activity ratio. If abnormal, refer for further evaluation such as saline infusion to determine if aldosterone levels can be suppressed, 24-hour urinary aldosterone level, and specific mineralocorticoid tests
Renovascular hypertension	Doppler flow ultrasonography, magnetic resonance angiography, computed tomography angiography
Sleep apnea	Sleep study with oxygen saturation (screening would also include the Epworth Sleepiness Scale [ESS])
Thyroid/parathyroid disease	Thyroid stimulating hormone level, serum parathyroid hormone level

Hypertensive nephropathy

It is generally accepted that chronic kidney disease (CKD) will advance more quickly as a result of elevated systemic blood pressure and that accelerated and malignant types of hypertensions can quickly cause permanent kidney failure. On the other hand, it continues to be debated whether modest to moderate increases in systemic blood pressure frequently cause CKD and subsequently end-stage renal disease (ESRD) **(19).**

Most hypertension patients experience mild-to-moderate hypertensive nephrosclerosis. Nevertheless, when BP values are uncontrolled for a prolonged period of time or kidney disease is present, the proportion of people who develop ESRD drastically rises. The chronological sequence of events (i.e., whether CKD or hypertension occurred first) in the majority of cases of concomitant hypertension and CKD cannot be determined **(19).**

Epidemiology

According to epidemiological data, arterial hypertension is the primary cause of renal failure in 30% of dialysis patients in the United States and 13% of patients in Europe In *Egypt*, the prevalence of CKD among hypertensive, non-diabetic patients were 33% according to a recently published study **(20).**

Pathophysiology

The main risk factors for the development of hypertensive nephropathy include RAAS activation, inappropriately elevated sympathetic nervous activity, increased arterial stiffness, impaired salt and water excretion by the kidney, and genetic susceptibility. Hypertensive nephrosclerosis involves hyalinization and sclerosis of interlobular and afferent arterioles, together with glomerular and tubulointerstitial

compartments fibrosis. Blood is supplied to afferent arterioles under higher pressure because of ageing and hypertension-related arterial stiffness. Early on, post glomerular vascular hypoxia caused by glomerular ischemia results in primarily monocytic/macrophagic inflammation and epithelial–mesenchymal transition (EMT). For many years, it was believed that hypertensive kidney disease was a condition that only affected the afferent arterioles and glomeruli, and that the pathogenic mechanisms causing the kidney damage were mechanical stress brought on by high blood pressure, RAAS stimulation, and activation of local fibroblasts. Epithelial-mesenchymal transition, podocyte loss, and tubulointerstitial fibrosis have so far been identified as the primary pathways for the development of cytoprotective treatment approaches **(21).**

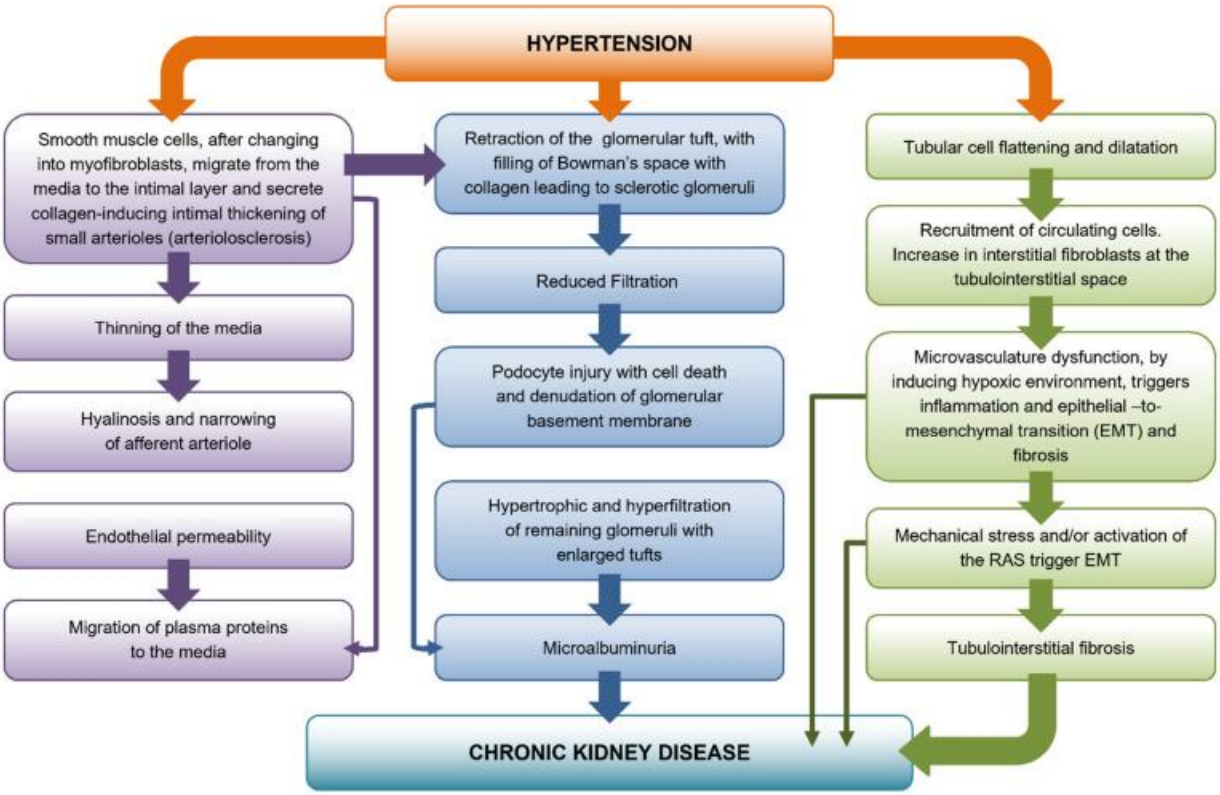

Figure (3): Histopathology and molecular mechanisms underlying nephropathy in primary (essential) hypertension **(21).**

Diagnosis of hypertensive nephropathy (HN)

Kidney disease that develops as a result of HTN is referred to be HN. When long-term HTN with organ destruction predominates in the clinical picture, this syndrome is typically recognized in patients with CKD of uncertain etiology in clinical practice. It should be noted that HTN is the most common sign of CKD, especially in the advanced stages (stages 4-5 CKD) **(19).** It appears excessively simplistic to assume that HTN is the only factor causing decreased glomerular filtration because there are no other known causes of renal failure. Studies have shown a relationship between blood pressure readings and the severity of renal disease, yet severe HTN related to later stages of CKD is extremely common and typical **(22).**

Microproteinemia

Microalbuminuria (MA), which is defined as an albumin excretion of greater than >30 to 299 mg/day or 20 to 200 g/min, is not a sign of renal disease as was previously thought, but rather a sign of endothelial dysfunction and an independent risk marker for CV events. Since the kidney is one of the most vascular organs in the body, increases in MA over time are a sign of deteriorating endothelial function, which is

linked to deteriorating renal function. Macroalbuminuria, also referred to as proteinuria, is characterized by a protein excretion rate of greater than >300 mg per day or >200 g per minute. It is unmistakably connected to podocyte dysfunction and has a higher CV risk than MA. It does signify the existence of CKD, and the degree of albuminuria is closely related to the development of ESRD **(23).**

Unfortunately, the available clinical criteria for clinical diagnosis of HN are of low specificity. The results of making a diagnosis of HN based solely on clinical criteria without confirmation by a renal biopsy could lead to incorrect epidemiological etiology of ESRD. This could negatively impact the evaluation and management of patients with renal disorders **(24).**

Table (4): Diagnostic criteria of HN **(25).**

Schlessinger criteria:
(1) Family history of hypertension
(2) Long-term primary arterial hypertension
(3) Moderate proteinuria or renal impairment
(4) Left ventricular hypertrophy or hypertensive retinopathy
(5) Absence of nephrotoxin exposure or other renal disease
(6) Renal size reduction in imaging studies
African American Study of Kidney Disease (AASK) criteria for HN:
(1) Urine protein to urine creatinine ratio < 2.0
(2) Absence of other renal disease

Renal histopathology

If no other disease process is found in affected people, the renal pathologic hallmarks of arteriolar nephrosclerosis identify high blood pressure as a potential cause. These features include the involvement of arteries, arterioles, glomeruli, and the tubulointerstitial. Atherosclerosis and arterioles are the primary lesions. Muscular hypertrophy and the accumulation of plasma protein insudates between endothelial cells and the muscularis cause the walls of arterioles to thicken. The majority of the proteins are complement (C3), and their accumulation causes hyalinosis, a process that mostly concerns the afferent arterioles, which gives the morphological appearance of smooth, homogenous material. Lumina are narrowed, sometimes significantly. Both intimal fibroblastic thickening (fibrosis) and medial (muscular) hypertrophy in arteries are indicative of luminal narrowing. Interstitial fibrosis and tubular atrophy, two types of chronic tubular and interstitial lesions, are also present **(26).**

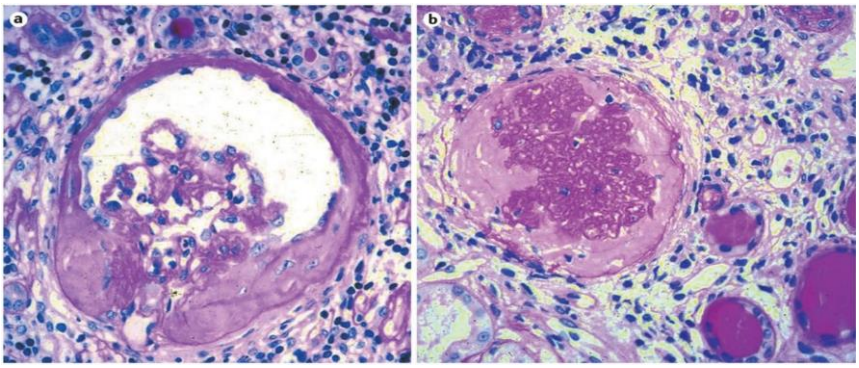

Figure (4): a. Chronic glomerular ischemia with capillary wall collapse and collagen deposition in the urinary space. B. Late phase of complete ischemic glomerulosclerosis with extensive collagen deposition in the

urinary space and thickening of the Bowman capsule Periodic acid–Schiff stain **(26).**

Along with this tubulointerstitial and vascular involvement, glomerular changes—traditionally characterized as full sclerosis brought on by prolonged ischemia—occur. Chronic ischemic wrinkling, capillary wall collapse, and eventually disintegration and consolidation of the capillary tufts characterize these changes, a concomitant buildup of collagen in the urinary space results in the creation of a solid mass **(26).**

Management of hypertension

- *Nonpharmacologic management of hypertension*

Losing weight, consuming a heart-healthy diet, boosting potassium intake, getting physical activity, and lowering alcohol use are all well-established nonpharmacologic therapies for the prevention and management of hypertension. Behavior change is possible, while being challenging to implement and maintain, especially in motivated clients receiving professional counselling and reinforcement from a clinician. Each of these therapies has the potential to lower mean SBP by around 5 mm Hg in individuals with hypertension and by about 2 to 3 mm Hg in adults without the condition. When lifestyle changes are coupled, greater blood pressure reductions are feasible for individuals with higher initial blood pressure. Even in patients with drug-resistant hypertension, nonpharmacologic therapies help pharmacologic medicines reduce blood pressure **(27).**

Implementing the interventions most likely to be effective, based on the patient's willingness to adopt the interventions and the lifestyle characteristics that are most suboptimal, is a reasonable strategy **(28).**

- *Pharmacologic treatment of hypertension*

The ideal blood pressure target for an individual maintains a balance between the advantages of lowering BP to prevent CVD events and the dangers of adverse consequences at that level of BP. Evidence in favor for most individuals having an SBP target of less than 130 mmHg. For adults under the age of 65, a DBP value of less than or equal to 80 mm Hg is suggested as a target. The ideal blood pressure target for individuals with hypertension is therefore less than 130/80 mm Hg, with the exception of adults 65 years of age or above, for whom the target is SBP less than 130 mm Hg without regard to DBP **(29).**

Office-based blood pressure monitoring is best when used in conjunction with out-of-office measurements, such as home BP monitoring recordings made by a patient who has received proper instruction and performs the right technique and sends cumulative BP data to the clinician's office **(30).**

Many drug classes of antihypertensive drugs are used for management of hypertension, Owing to their different mechanisms of actions, side effects and patients' comorbidities, treatment plan should be tailored for every patient individually **(31).**

- *Management of hypertensive nephropathy*

According to the most recent research, non-pharmacologic interventions including sodium restriction, weight loss, and moderately vigorous physical exercise are not only supplementary but also insufficient for the treatment of hypertensive nephropathy. The increased salt and water retention found in patients with advanced nephropathy necessitates special focus on the advice for sodium restriction **(32).**

According to recommendations, treatment of hypertensive nephropathy should concentrate on lowering blood pressure and albuminuria. To reach BP targets, initial treatment with RAAS blockers, such as ACE inhibitors or angiotensin receptor blockers (ARBs), is advised, typically in conjunction with either diuretics or calcium antagonists **(33).**

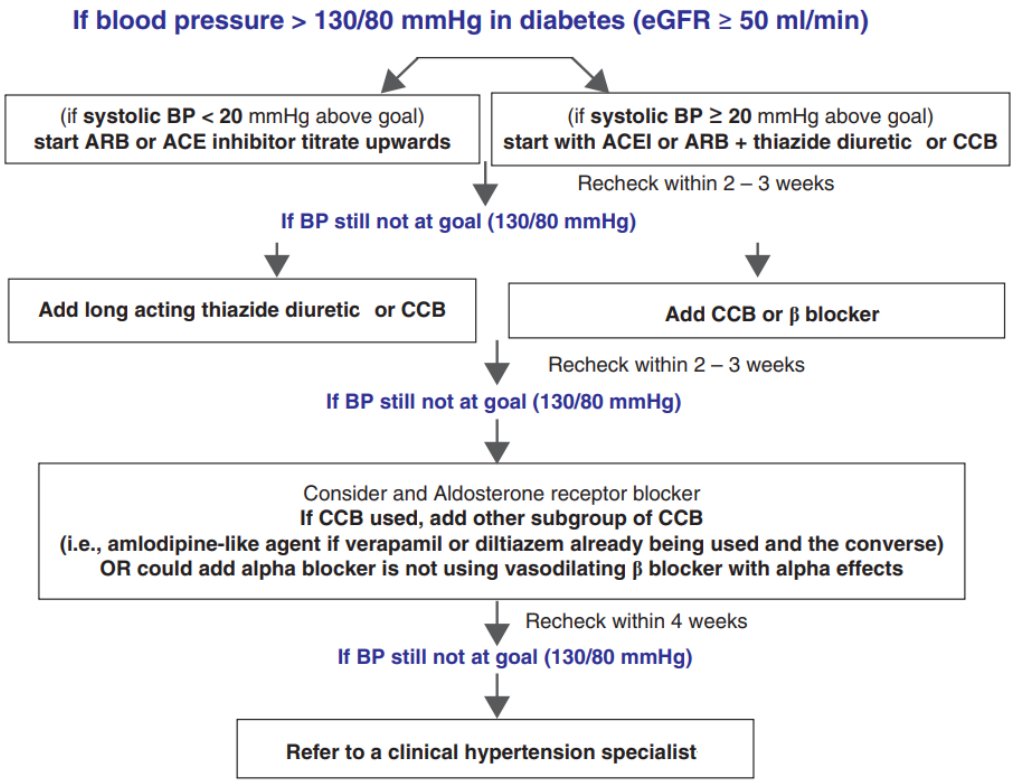

Figure (5): A suggested algorithm to achieve the BP goal of < 130/80 mmHg in patients with diabetes and/or albuminuria **(34).**

References

1. Oparil, S., Acelajado, M.C., Bakris, G.L., Berlowitz, D.R., Cífková, R., Dominiczak, A.F., et al. (2018): 'Hypertension', Nature Reviews Disease Primers, 4 (1): 18014.
2. Iqbal, A.M. and Jamal, S.F. (2023): Essential Hypertension. Treasure Island (FL): StatPearls Publishing.
3. Forouzanfar, M.H., Liu, P., Roth, G.A., Ng, M., Biryukov, S., Marczak, L., et al. (2017): 'Global Burden of Hypertension and Systolic Blood Pressure of at Least 110 to 115 mm Hg, 1990-2015', JAMA, 317 (2): 165.
4. Reda, A., Ragy, H., Saeed, K. and Alhussaini, M.A. (2021): 'A semi-systematic review on hypertension and dyslipidemia care in Egypt—highlighting evidence gaps and recommendations for better patient outcomes', Journal of the Egyptian Public Health Association, 96 (1): 32.
5. Kato, N., Loh, M., Takeuchi, F., Verweij, N., Wang, X., Zhang, W., et al. (2015): 'Trans-ancestry genome-wide association study identifies 12 genetic loci influencing blood pressure and implicates a role for DNA methylation', Nature Genetics, 47 (11): 1282–1293.
6. Roerecke, M., Tobe, S.W., Kaczorowski, J., Bacon, S.L., Vafaei, A., Hasan, O.S.M., et al. (2018): 'Sex-Specific Associations Between Alcohol Consumption and Incidence of Hypertension: A Systematic Review and Meta-Analysis of Cohort Studies', Journal of the American Heart Association, 7 (13): doi:10.1161/JAHA.117.008202.
7. Mikael, L. de R., Paiva, A.M.G. de, Gomes, M.M., Sousa, A.L.L., Jardim, P.C.B.V., Vitorino, P.V. de O., et al. (2017): 'Vascular Aging and Arterial Stiffness', Arquivos Brasileiros de Cardiologia [Preprint]. doi:10.5935/abc.20170091.
8. Wilck, N., Matus, M.G., Kearney, S.M., Olesen, S.W., Forslund, K., Bartolomaeus, H., et al. (2017): 'Salt-responsive gut commensal modulates TH17 axis and disease', Nature, 551 (7682): 585–589.

9. Varagic, J., Ahmad, S., Nagata, S. and Ferrario, C.M. (2014): 'ACE2: Angiotensin II/Angiotensin- (1–7): Balance in Cardiac and Renal Injury', Current Hypertension Reports, 16 (3): 420.

10. Kerkelä, R., Ulvila, J. and Magga, J. (2015): 'Natriuretic Peptides in the Regulation of Cardiovascular Physiology and Metabolic Events', Journal of the American Heart Association, 4 (10).

11. Khaddaj Mallat, R., Mathew John, C., Kendrick, D.J. and Braun, A.P. (2017): 'The vascular endothelium: A regulator of arterial tone and interface for the immune system', Critical Reviews in Clinical Laboratory Sciences, 54 (7–8): 458–470.

12. Kohan, D.E. and Barton, M. (2014): 'Endothelin and endothelin antagonists in chronic kidney disease', Kidney International, 86 (5): 896–904.

13. de Leeuw, P.W., Bisognano, J.D., Bakris, G.L., Nadim, M.K., Haller, H. and Kroon, A.A. (2017): 'Sustained Reduction of Blood Pressure With Baroreceptor Activation Therapy', Hypertension, 69 (5): 836–843.

14. Grassi, G., Mark, A. and Esler, M. (2015): 'The Sympathetic Nervous System Alterations in Human Hypertension', Circulation Research, 116 (6): 976–990.

15. Rodriguez-Iturbe, B. (2016): 'Autoimmunity in the Pathogenesis of Hypertension', Hypertension, 67 (3): 477–483.

16. Maass, P.G., Aydin, A., Luft, F.C., Schächterle, C., Weise, A., Stricker, S., et al. (2015): 'PDE3A mutations cause autosomal dominant hypertension with brachydactyly', Nature Genetics, 47 (6): 647–653.

17. Muntner, P. and Whelton, P.K. (2017): 'Using Predicted Cardiovascular Disease Risk in Conjunction With Blood Pressure to Guide Antihypertensive Medication Treatment', Journal of the American College of Cardiology, 69 (19): 2446–2456.

18. Chobanian, A. V., Bakris, G.L., Black, H.R., Cushman, W.C., Green, L.A., Izzo, J.L., et al. (2003): 'Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure', Hypertension, 42 (6): 1206–1252.

19. Griffin, K.A. (2017): 'Hypertensive Kidney Injury and the Progression of Chronic Kidney Disease', Hypertension, 70 (4): 687–694.

20. Nagib, S.N., Abdelwahab, S., Amin, G.E.E.D. and Allam, M.F. (2023): 'What is the prevalence of chronic kidney disease among hypertensive non-diabetic Egyptian patients attending primary healthcare?', Clinical and Experimental Hypertension, 45 (1).

21. Costantino, V.V., Gil Lorenzo, A.F., Bocanegra, V. and Vallés, P.G. (2021): 'Molecular Mechanisms of Hypertensive Nephropathy: Renoprotective Effect of Losartan through Hsp70', Cells, 10 (11): 3146.

22. Ameer, O.Z. (2022): 'Hypertension in chronic kidney disease: What lies behind the scene', Frontiers in Pharmacology, 13.

23. Athavale, A. and Roberts, D.M. (2020): 'Management of proteinuria: blockade of the renin-angiotensin-aldosterone system.', Australian prescriber, 43 (4): 121–125.

24. Hull, K.L., Adenwalla, S.F., Topham, P. and Graham-Brown, M.P. (2022): 'Indications and considerations for kidney biopsy: an overview of clinical considerations for the non-specialist', Clinical Medicine, 22 (1): 34–40.

25. Kubiak, M., Januszko-Giergielewicz, B., Moczulska, B. and Gromadziński, L. (2014): 'Hypertensive nephropathy – A yet unsolved problem', Polish Annals of Medicine, 21 (2): 147–151.

26. Freedman, B.I. and Cohen, A.H. (2016): 'Hypertension-attributed nephropathy: what's in a name?', Nature Reviews Nephrology, 12 (1): 27–36.

27. Tsao, C.W., Aday, A.W., Almarzooq, Z.I., Alonso, A., Beaton, A.Z., Bittencourt, M.S., et al. (2022): 'Heart Disease and Stroke Statistics—2022 Update: A Report From the American Heart Association', Circulation, 145 (8).

28. Carey, R.M., Moran, A.E. and Whelton, P.K. (2022): 'Treatment of Hypertension', JAMA, 328 (18): 1849.

29. Whelton, P.K., Carey, R.M., Aronow, W.S., Casey, D.E., Collins, K.J., Dennison Himmelfarb, C., et al. (2018):

'2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines', Hypertension, 71 (6):

30. Bello, N.A., Schwartz, J.E., Kronish, I.M., Oparil, S., Anstey, D.E., Wei, Y., et al. (2018): 'Number of Measurements Needed to Obtain a Reliable Estimate of Home Blood Pressure: Results From the Improving the Detection of Hypertension Study', Journal of the American Heart Association, 7 (20).

31. Goit, L.N. and Yang, S. (2019): 'Treatment of Hypertension: A Review', Yangtze Medicine, 03 (02): 101–123.

32. Bucharles, S.G.E., Wallbach, K.K.S., Moraes, T.P. de and Pecoits-Filho, R. (2019): 'Hypertension in patients on dialysis: diagnosis, mechanisms, and management', Brazilian Journal of Nephrology, 41 (3): 400–411.

33. Banerjee, D., Winocour, P., Chowdhury, T.A., De, P., Wahba, M., Montero, R., et al. (2022): 'Management of hypertension and renin-angiotensin-aldosterone system blockade in adults with diabetic kidney disease: Association of British Clinical Diabetologists and the Renal Association UK guideline update 2021', BMC Nephrology, 23 (1): 9.

34. Hart, P.D. and Bakris, G.L. (2010): 'Hypertensive nephropathy: prevention and treatment recommendations', Expert Opinion on Pharmacotherapy, 11 (16): 2675–2686.