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ADVANCES IN PATHOGENESIS AND TREATMENT OF HYPERTENSION

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Abstract:
Background: Tackling hypertension in Saudi Arabia requires a multifaceted approach that includes addressing risk factors, enhancing public health initiatives, and promoting lifestyle changes to improve health outcomes for the population. **Aim:** This review aims to provide a comprehensive synthesis of current research findings, informing clinical practice and guiding future research directions in the understanding and management of hypertension. **Method:** The PubMed and Google Scholar Search Engines were the primary databases used for the search process, with articles collected from 1980 to 2024. **Conclusion:** The epidemiology of hypertension in Saudi Arabia reveals a high prevalence and notable risk factors, highlighting the need for thorough public health initiatives to alleviate its effects on the health of the populace. Understanding alterable and unalterable risk factors is crucial for successfully preventing and managing hypertension. Both changes in lifestyle and pharmaceutical interventions are essential for effectively managing hypertension, with lifestyle modifications acting as the primary approach and medications offering additional assistance when required.

Keywords: Hypertension, Prevalence, Risk factor, Pathophysiology, Diagnosis, Treatment, Device-based therapies

INTRODUCTION TO HYPERTENSION

Hypertension is a significant public health concern in Saudi Arabia, affecting approximately 30% of the adult population, which is one of the highest rates in the Middle East. The condition is closely linked to various risk factors prevalent in the region, including obesity, physical inactivity, and a diet high in salt and sugar. Additionally, cultural and socioeconomic factors, such as limited health education and access to healthcare, exacerbate the situation, making it crucial to address these underlying issues to reduce hypertension prevalence. The Saudi Arabian Ministry of Health has recognized the urgency of this health crisis and has initiated several programs to combat hypertension. These initiatives include public awareness campaigns, screening programs, and improvements in healthcare infrastructure, all designed to enhance the prevention, detection, and management of hypertension. (1, 2)
The epidemiology of hypertension in Saudi Arabia reveals a significant public health challenge, characterized by a high prevalence and a complex interplay of risk factors. Previous studies indicate that approximately 20.8% of the population aged 50-60 years is affected by hypertension, with a notable prevalence among both males (86.2%) and females (88.8%) in this age group. (3) Another national survey of 4,758 adult participants found a prevalence of 25.5%. (4). More recently, a systematic review and meta-analysis of 29 studies involving 278,873 individuals reported a pooled prevalence of 22.66% (95% CI: 18.95-26.60). (5) A study using electronic health records (EHRs) reported a lower prevalence of 13.0% (95% CI: 12.9-13.1) among 650,835 individuals aged 16 years and older. (6) This discrepancy may be attributed to differences in study design, population characteristics, and diagnostic criteria. Overall, these findings underscore the widespread nature of hypertension in the Saudi population. This high

prevalence underscores the urgent need for effective prevention and management strategies. Key risk factors contributing to hypertension in Saudi Arabia include obesity, physical inactivity, and poor dietary habits. These lifestyle factors are critical in understanding the rising rates of hypertension and its associated complications, such as cardiovascular disease, which includes an increased risk of heart attacks and strokes. The relationship between hypertension and these severe health outcomes necessitates a focused approach to public health interventions. Research efforts in Saudi Arabia have been instrumental in advancing knowledge about hypertension, encompassing a range of epidemiological studies and clinical trials.ls

PATHOPHYSIOLOGY OF HYPERTENSION

Hypertension is a multifaceted condition characterized by complex pathophysiological mechanisms involving various systems and factors. Central to its development is the dysregulation of the Renin-Angiotensin-Aldosterone System (RAAS), which plays a crucial role in blood pressure regulation through vasoconstriction and sodium retention. (7) Chronic activation of the RAAS not only elevates blood pressure but also contributes to vascular remodeling, a process marked by structural changes in blood vessels that increase peripheral resistance. (8) Endothelial dysfunction is another hallmark of hypertension, characterized by reduced nitric oxide production and increased oxidative stress, leading to vasoconstriction and inflammation. This dysfunction is often exacerbated by sympathetic nervous system activation, which increases heart rate and cardiac output, further perpetuating hypertension. (9, 10) Additionally, aldosterone excess, often resulting from adrenal disorders, leads to sodium retention and volume expansion, compounding the hypertensive state. (11) Inflammation also plays a significant role, as it contributes to oxidative stress and endothelial dysfunction, creating a vicious cycle that exacerbates hypertension. (12) Insulin resistance is another contributing factor, as it can activate the RAAS and impair glucose uptake, linking metabolic disturbances with hypertension. (13) Furthermore, dysregulation of the Epithelial Sodium Channel (ENaC) can lead to increased sodium reabsorption, further elevating blood pressure. Also, the involvement of vasoactive hormones and kidney damage, including nephrosclerosis, underscores the systemic nature of hypertension and its potential to lead to chronic kidney disease. (14)

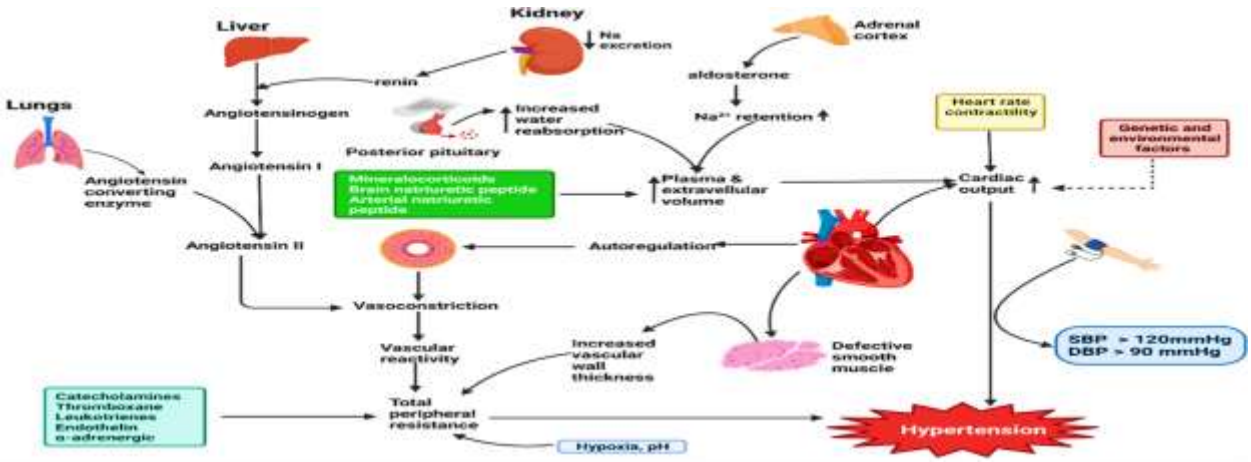

FIGURE (1): ELEMENTS AND FACTORS CONTRIBUTING TO BLOOD PRESSURE REGULATION.

RISK FACTORS OF HYPERTENSION

Hypertension, or high blood pressure, is influenced by a variety of risk factors that can be categorized into modifiable and non-modifiable categories [Figure]. Among the modifiable factors, obesity is a significant contributor, as excess body fat can lead to increased blood pressure and cardiovascular complications. Maintaining a balanced diet and engaging in regular exercise is crucial in mitigating this risk. Similarly, a sedentary lifestyle exacerbates the risk of hypertension by promoting weight gain and reducing cardiovascular fitness, highlighting the importance of physical activity in prevention strategies. (16) Dietary habits also play a critical role; excessive sodium intake is linked to elevated blood pressure, making a low-sodium diet essential for hypertension management. (17) Additionally, chronic stress can elevate blood pressure and heart rate, suggesting that effective stress management techniques, such as meditation, are beneficial. (18) Smoking is another modifiable risk factor, as it damages blood vessels and increases heart rate, thus raising the risk of hypertension. (19) Non-modifiable factors include genetic predisposition and family history, which can significantly increase an individual's likelihood of developing hypertension. Understanding these

genetic and familial links can facilitate early identification and intervention for individuals at high risk. (20, 21) Age is also a critical factor, as blood pressure tends to rise with advancing age, necessitating regular monitoring in older populations. (22) Lastly, ethnicity can influence hypertension risk, with certain groups, such as African Americans, facing higher susceptibility due to a combination of genetic and environmental factors. (23)

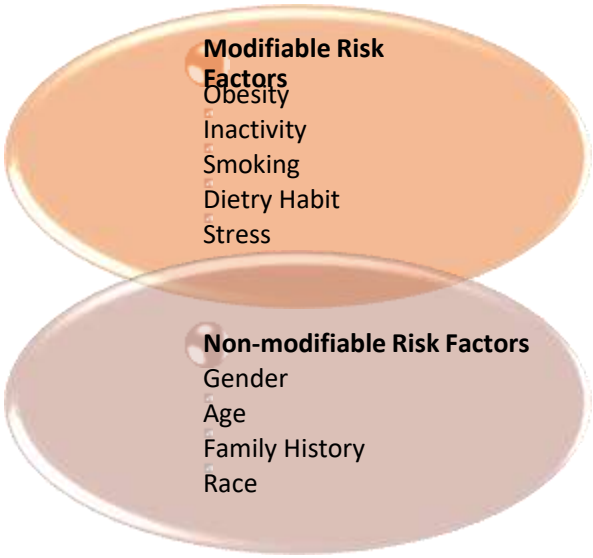

FIGURE (2): MODIFIABLE AND NON-MODIFIABLE RISK FACTORS OF HYPERTENSION.

DIAGNOSTIC APPROACHES

Hypertension diagnosis can be approached through various innovative diagnostic techniques, each providing unique insights into cardiovascular health. One prominent method is Ambulatory Blood Pressure Monitoring (ABPM), which measures blood pressure at regular intervals over 24 hours. This technique is particularly effective in identifying masked hypertension and offers a comprehensive view of blood pressure variations throughout the day and night, enhancing diagnostic accuracy and cardiovascular risk prediction. (24) Another significant approach is Central Blood Pressure Measurement, which assesses blood pressure directly in the aorta. This method is more indicative of cardiovascular risk than traditional brachial measurements, allowing for better identification of individuals at high risk for cardiovascular diseases. (25) Additionally, Pulse Wave Velocity (PWV) serves as a non-invasive marker of arterial stiffness, which is crucial for evaluating hypertension and associated cardiovascular risks. (26)
Echocardiography is also vital in diagnosing hypertension, as it can reveal left ventricular hypertrophy, a common complication of high blood pressure. (27) Other diagnostic methods include 24-Hour Urinary Sodium Excretion, which helps assess sodium intake and its relationship with hypertension. (28) and the Renal Resistive Index, which measures blood flow resistance in the kidneys, potentially indicating underlying kidney disease. (29) Advanced imaging techniques like Cardiac Magnetic Resonance Imaging and Blood Oxygen Level-Dependent Magnetic Resonance Imaging provide detailed insights into cardiac structure and function, further aiding in hypertension diagnosis. (30) Together, these diagnostic approaches enhance the understanding and management of hypertension, ultimately improving patient outcomes.

MANAGEMENT OF HYPERTENSION

The management of hypertension can be approached through both lifestyle modifications and pharmacological treatments, each playing a crucial role in effective blood pressure control. Lifestyle modifications are essential in the management of hypertension. The Dietary Approaches to Stop Hypertension (DASH) diet, which emphasizes whole grains, fruits, vegetables, and low-fat dairy products, has been shown to significantly lower blood pressure in individuals with prehypertension and stage 1 hypertension. Sodium restriction is another critical component, with guidelines suggesting an intake of less than 2,300 milligrams per day to mitigate hypertension risk. (31) Furthermore, potassium supplementation can counteract the effects of sodium and promote vasodilation, thereby aiding in blood pressure reduction. (32) Regular aerobic exercise, recommended at 150 minutes per week, also helps lower blood

pressure and improve cardiovascular health. Additionally, weight loss, particularly a reduction of 5-10% of body weight, can lead to substantial improvements in blood pressure levels. (33) Stress management techniques, such as meditation and yoga, are also beneficial in lowering blood pressure by promoting relaxation and reducing stress. (34) Pharmacologically, several classes of medications are utilized. Drugs such as angiotensin-converting enzyme (ACE) inhibitors, calcium channel blockers, diuretics, and beta blockers are commonly prescribed. ACE inhibitors work by blocking the enzyme that constricts blood vessels, thereby lowering blood pressure. Calcium channel blockers relax blood vessels by preventing calcium from entering the cells of the heart and blood vessel walls. Diuretics help reduce blood pressure by increasing urine production, which removes excess fluid and sodium from the body. Beta blockers decrease heart rate and the force of heart contractions, making them particularly useful in patients with heart disease. (35) While pharmacological treatments are essential, they are most effective when combined with lifestyle changes, creating a comprehensive approach to managing hypertension. For patients with resistant hypertension, combination therapy—using two or more medications—has become standard practice. This approach can enhance blood pressure control while minimizing side effects. (36) Furthermore, alpha blockers and vasodilators are also effective, particularly in specific populations such as those with kidney disease or severe hypertension. (37)

DEVICE-BASED THERAPIES

Device-based therapies for hypertension represent a significant advancement in the management of resistant hypertension, a condition that is notoriously difficult to control with traditional medications and lifestyle changes. These innovative approaches include renal denervation, baroreflex activation therapy, carotid body stimulation, and vagus nerve stimulation, each targeting different physiological mechanisms to regulate blood pressure. Renal denervation is a minimally invasive procedure that utilizes radiofrequency ablation to reduce sympathetic nerve activity in the kidneys, thereby effectively lowering blood pressure in patients with resistant hypertension. Similarly, baroreflex activation therapy (BAT) stimulates baroreceptors in the carotid sinus, leading to a sustained reduction in blood pressure. This therapy has been shown to be well-tolerated and effective, particularly in patients with chronic kidney disease (CKD). Carotid body stimulation is another promising technique that enhances the body's natural reflexes to regulate blood pressure through increased afferent traffic in the carotid sinus nerve. Vagus nerve stimulation, which targets the vagus nerve to restore cardiac autonomic balance, has also demonstrated efficacy in managing hypertension by modulating inflammatory responses. Additionally, therapies such as CVRx's Barostim Neo and ReSet Therapeutics' ROX Coupler utilize baroreflex activation to achieve similar outcomes, highlighting the versatility of device-based interventions in hypertension management. (38) These therapies not only provide alternative options for patients who do not respond to conventional treatments but also highlight the ongoing research and development in the field of hypertension management. As the prevalence of resistant hypertension continues to rise, these device-based therapies offer hope for improved patient outcomes and better blood pressure control.

CONCLUSION

The epidemiology of hypertension in Saudi Arabia reveals a high prevalence and notable risk factors, highlighting the need for thorough public health initiatives to alleviate its effects on the health of the populace. A deep understanding of alterable and unalterable risk factors is crucial for successfully preventing and managing hypertension. Both changes in lifestyle and pharmaceutical interventions are essential for effectively managing hypertension, with lifestyle modifications acting as the primary approach and medications offering additional assistance when required.

Conflict of Interest

The authors declare that they have no conflicts of interest, personal, financial and otherwise.

Author contributions

The work is overseen, important revisions are made, and the final manuscript is approved for submission by the corr esponding author.Each author accepted submission of the finished work after reading it and committing to full respo nsibility for it. The original author develops the concept and writes the first draft of the text.

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Ethical Approval

Not Applicable

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