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Cognitive impairment in arterial hypertension in Pakistan

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Abstract

Background: The main cause of death and disease on a global scale is high blood pressure, making it a critical issue for public health and a major public health concern.

Objective: This review will identify the available literature and conduct a study to determine the factors which are significantly connected with hypertension based cognitive impairment among the Pakistani population.

Methodology: Data was collected to evaluate the ramifications of this condition. The most significant element in hypertension-related cognitive impairment is the presence of risk factors, including socio-demographic factors, lifestyle hazards, and disease-based risks.

Results: Observational studies imply that therapy with antihypertensives is related to decreased instances of cognitive impairment.

Conclusion: There is a need for additional research to investigate these elements more in-depth and to compile global evidence on the subject.

Keywords: cardiovascular disease; cognitive disability; high blood pressure. treatment; management

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Introduction

There is a correlation between arterial hypertension and cognitive impairment. The key factors that are connected with cognitive disability in hypertension individuals include age, gender, education level, and the presence of other medical conditions. The likelihood of a patient experiencing cognitive impairment due to hypertension rises with the patient's age [1]. The link between blood pressure and cognitive function is mostly non-linear and can be altered by age, ethnicity, education level, and medications that lower blood pressure. The connection between hypertension and cognitive impairment is complicated and involves a number of brain mechanisms, but a full comprehension of this connection is essential for the maintenance of cognitive abilities in hypertensive patients [2]. It is compared to how high blood pressure affects a person's capacity to think, recall, or reason, but researchers are working hard to figure out the connection between the two. Cognitive decline is closely linked to hypertension. It has been observed that blood pressure-lowering medication has a beneficial effect on the preservation of cognitive ability, although the mechanism underlying this benefit is yet unknown [3].

Patients who have hypertension absolutely need to have their blood pressure carefully monitored, brought under control, and treated in order to keep their cognitive abilities intact [4]. One study found that hypertension

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individuals performed poorly on neurocognitive measures like delayed recollection and regional prefrontal skills when equated to control group. The verdicts of neurocognitive testing revealed that hypertensive patients suffer from faulty cognitive abilities and memory loss. Hence, it was determined that these assays were sensitive enough and simple enough to employ in clinical settings [5]. Cognitive performance among young hypertensive patients on tests like attention/executive operating and memory was found to be significantly poor as compared to normotensive people. In contrast, the distinction in cognitive performance of middle-aged hypertensive people is not differentiated from normotensive without having to count, and both groups were independent of psychosocial, demographical, and alcohol-related factors [6]. The findings from different research have disclosed that cognitive performance between young hypertensive patients on tests like attention/executive operating and memory was found.

Research Problem

Elderly patients who have been reported to have mild hypertension and a slight impairment in their cognitive ability are in great danger of developing cardiovascular disease and intense cognitive decline. These patients need to be treated with antihypertensive therapy in order to avoid cardiovascular disorders and a further decline in cognitive function [7]. In industrialized nations, a substantial amount of research has been carried out to evaluate the connection between high blood pressure and cognitive impairment in relation to a variety of factors, including age, gender, educational attainment, and others. In addition, a comprehensive comprehension of the connection between the effects of various antihypertensive treatments for preventing impairments in cognitive ability has been achieved. Therefore this problem has been a sole focus of this project.

Research Focus

The current narrative review focuses on the extraction of studies from the literature review to identify the relation between hypertension and cognitive impairment, its risk factor, condition in Pakistan, current treatment and future perspective.

Research Aim

This review will identify the available literature and conduct a study to determine the factors which are significantly connected with hypertension based cognitive impairment among the Pakistani population

Research Questions

Does cognitive impairment have a significant relation with arterial hypertension in Pakistan?

What are the risk factors of cognitive impairment based hypertension?

What is the current measures of cognitive impairment based hypertension in Pakistan?

Research Methodology

General Background

The primary goals of a narrative review are to provide the author and the reader with a full overview of the subject matter, as well as to draw attention to major areas of research. Narrative reviews can serve to discover problems with the study and aid to improve and establish research topics. A first step in examining the data in a systematic manner and organizing them might be provided by means of a narrative synthesis. At the protocol stage, the procedures that will be used to conduct a narrative synthesis need to be explained. This is because a narrative synthesis will be utilized to a greater or lesser amount in a review.

Instrument and Procedures

Methodical Approach to the Search engines

Data was collected from Google Scholar, PubMed, and the Medline database for articles available on the current topic. Both the articles' titles with abstracts consisting of keywords such as: blood pressure / hypertens / systolic / antihypertens / diastolic AND post-operative cognitive impairment / POCD / cognitive impairment AND mild cognitive impairment / MCI AND Pakistan studies. After the removal of duplicates, the remaining titles and abstracts of papers were examined by a single investigator to determine whether or not they met the inclusion criteria. The complete texts of the studies were accessed only if it was determined that they had the potential to meet the inclusion criteria or if it looked that they had data on both hypertension and cognitive.

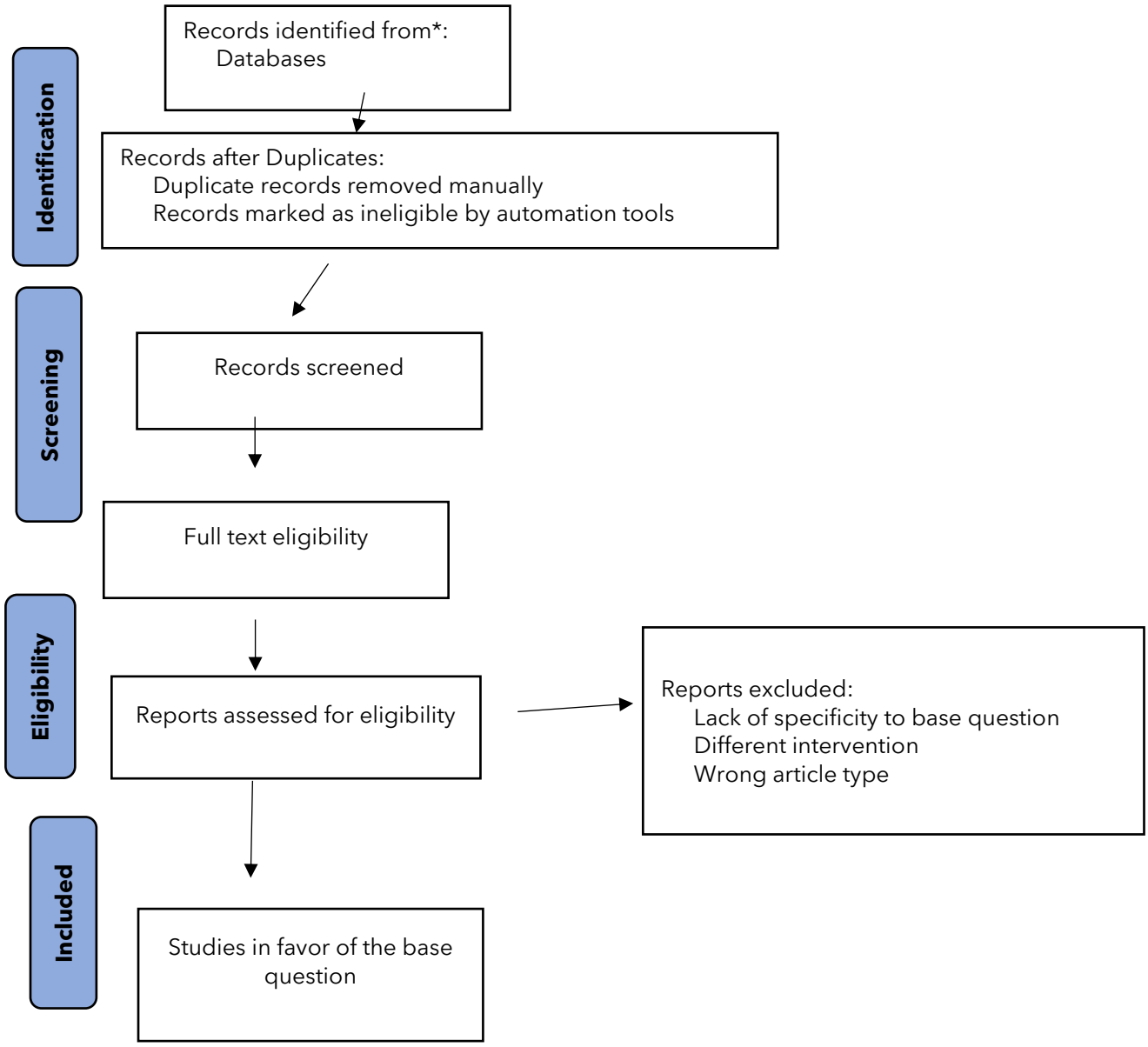
Inclusion and Exclusion Criteria

Only studies that met all of the following requirements were considered for inclusion: i) an investigation into the potential of cognitive based hypertension ii) randomized controlled studuies of people with every age groups related to the topic iii) full text in the English language iv) ascertainment of blood pressure, hypertension, and its relation with cognitive impairement v) disclosing of these exposure factors with risk of cognitive impairment as

relative risks among Pakistanis. Studies on hypotension or those showing correlation with other diseases weren't taken into consideration.

Data Analysis

The screening of the relevant data was the first step in the process of conducting the analysis of the data, which was then followed by the organizing the information that was extracted into a table. The articles that had been selected for further review were then evaluated one at a time in order to identify the overarching idea that most effectively illustrates the significance of the research question.



Literature overview

Pathogenesis of Hypertension

Essential hypertension has a complicated and extremely complex pathophysiology. The illness includes the interplay of various organ systems and encompass a wide range of independent or interdependent pathways, and the kidney is both a contributing organ and the target organ of the hypertensive phenomena. Genetics, activation of neurohormonal systems including the sympathetic nervous system and the renin-angiotensin-aldosterone system, obesity, and high sodium consumption are all major factors in the development of hypertension. The condition of persistently elevated systemic blood pressure is known as arterial hypertension (BP). The sum of total peripheral vascular resistance and cardiac output determines blood pressure [8]. The tone of the sympathetic nerve system (SNS) and the parasympathetic neural system affects minute-to-minute fluctuations in blood pressure significantly [9]. Investigations utilizing continuous blood pressure monitoring have shown that the range of values on any given day can be distinct and exhibits a typical circadian pattern, in which

blood pressure decreases at night or during sleeping, correlating with a reduction in SNS tone. Notwithstanding the fact that normal blood pressure is very variable, the majority of authorities describe increased hypertension as having a systolic blood pressure of less than 140 mmHg or a diastolic blood pressure of less than 90 mmHg, or both, measured when seated and relaxed [10].

When blood pressures are below 140/90 mmHg for more than 25% of measurements in any 24-hour period, hypertension is often considered to exist [11]. Just 5–10% of the US populace had blood pressure readings in that range when the 140/90 mmHg limit was chosen in the early 1900s [8]. Additionally, it was known from the beginning that hypertension in the hypertensive spectrum were almost always associated by small vessel disorder of the arterioles also known as arteriolosclerosis and kidneys that were massively contracted and "granular" in presence, with glomerular, and much more frequently tubular, modification on microscopic analysis [12].

Cognitive Impairment and its pathologic basis

One of the most prevalent clinical symptoms affecting the elderly is mild cognitive impairment (MCI), which is quickly rising in prevalence. It is unclear whether molecular and pathologic factors contribute to MCI in patients. It is crucial to describe the neuropathology alterations in the brains of patients who underwent autopsy with a well-defined diagnostic technique of MCI since MCI is a human-specific condition where neither clinical and nor neuropathological development appears to follow a clear linear route. A broad range of cellular molecular and biochemical deficits, many of which are related to cognitive impairment as well as compensatory reactions to the advancing disease process, must be considered when determining the pathologic substrate of MCI. These deficits must be considered in addition to the conventional plaque and coiled pathology. There may not be a singular incident that triggers this prodromal stage of AD due to the complexity of the neuronal detachment condition linked to MCI. In reality, at this point of the dementing chronic illness, it can be claimed that neuronal degeneration, which began at various stages of the neurological system, drives cognitive decline as a concluding common pathway [13, 14].

Research Results

By considering inclusion criteria in mind, 15 studies was extracted out. Some studies extracted the epidemiological of hypertension based cognitive impairment in Pakistan [15] and worldwide [16]. The results also identified the pathological relation between hypertension and cognitive impairment [17, 18]. Preclinical studies that have shown neuroinflammation among hypertension patient [19, 20]. Results alos demonstrated risk factors for hypertension based cognitive impairment include stress, smoking, disease based and age [21-30]. Research on hypertension based cognitive impairment data has been limited due to socio-economic factors. However, some studies [31-34] have demonstrated that there is a relationship between hypertension and cognitive impairment due to socio-demographic characteristics, comorbidities, or a previous history of hospitalization.

Table 1. The extracted information from screened studies

Extracted information	Reference
Hypertension is leading problem worldwide	[15]
Hypertension impairs several aspects of cognitive functioning	[16]
pathophysiological effects of hypertension-induced BBB disruption	[17, 18]
pathogen-based molecular sequences can enter the neural parenchyma through a disrupted BBB, where they induce neuroinflammation by activating microglia	[19, 20]
oxidative stress have directly role in neuroinflammation	[20]
risk variables include getting older, disease, stress, and smoking	[23]
Persistent stress is considered as an important factors that might donate to the onset of hypertension and other cardiovascular diseases.	[35, 36]
Underlie chronic stress's impact on hypertension and cognitive performance is an increase in the production of inflammatory cytokines by endothelial cells.	[37]
Tobacco use affects cognitive function and hypertension.	[38-41]
Smoking cause damage to the heart muscle, brain cell and cognition.	[42-47]
Diabetes has role in the progression of hypertension and cognitive diease	[24, 29, 30]
Estrogen-induced central suppression of sympathetic outflow in the case of hypertension.	[48-52]
Antihypertensive drugs have an impact on hypertensive Pakistani patients' cognitive function	[31]

Hypertension and impaired cognitive performance have a significant impact in Pakistani patients aged 70 or older.	[53]
A Pakistan and US study with similar findings identified low socioeconomic status as the cause of cognitive impairment in older people	[32, 33]
Cognitive impairment leads to depression among hypertenion's patients	[34]
Having hypertension have a huge impact on the quality of lifestyle and cognitive activities	[50-52]
Diuretics, dihydropyridine calcium channel blockers (CCBs), and inhibitors of the renin-angiotensin system can be helpful against cognitive impairment based on hypertension.	[54-56]
Pharmacological-based treatment of hypertension could result in a decline in cognitive impairment	[57]

Discussion

In order to prevent and treat age-related cognitive impairment (also referred as ARCI), it is important to have a thorough understanding of the interrelated risk factors, particularly how a person's genetic makeup affects their risk. Those who have heart illness or hypertension are at higher risk of developing aortic arch calcification. Moreover, a majority of the risk factors linked to the emergence of hypertension are also linked to the development of ARCI. These risk variables include getting older, disease, stress, and smoking [23].

Epidemiology

It is estimated that hypertension based adults aged prevalence of 65–74 year old in the United States is 76%, while the hypertension based adults aged prevalence of 75 years and above is 82%. In the 37 studies that were taken into consideration, the total prevalence of hypertension ranged anywhere from 3.0 to 77.5%. It ranged anywhere from 3.0 to 65.1% in research that used cross-sectional designs and from 27.5 to 77.5% in studies that used case-control designs. Even though more people are becoming aware of the harmful effects of hypertension, the rate at which blood pressure is controlled is still not as good as it could be [15]. At the end of the eighteenth century, the detrimental influence of hypertension on cognitive performance were identified [58]. Research conducted in the 1960s and 1970s gave evidence that hypertension impairs several aspects of cognitive functioning. After that, numerous prospective longitudinal investigations have shown that there is a significant connection among hypertennsion and the occurrence of cognitive impairment [16].

Pathophysiology basis of hypertension-based cognitive impairment

Cognitive decline is linked to lacunar infarcts, cerebral microhemorrhages, and white matter injury, are brought on by pathological changes in cerebral microvessels that harm the network signalling, microvascular structure, and function. Neuroinflammation, synapse loss, and impaired synaptic function are pathophysiological effects of hypertension-induced BBB disruption [17, 18]. IgG, fibrinogen, thrombin, and other inflammation of pathogen-based molecular sequences can enter the neural parenchyma through a disrupted BBB [18], where they induce neuroinflammation by activating microglia [19]. Preclinical studies that have shown that arterial rigidity causes microglia activation driven by oxidative stress have directly demonstrated the crucial role that haemodynamic variables play in neuroinflammation. Moreover, BBB disruption causes a rise in serum amyloid A levels in the brain, which plays a part in neuroinflammation with neurodegeneration [20].

Risk factors associated with hypertension-based cognitive impairment

Chronic Stress links to Blood Pressure and Brain Health: Persistent stress is considered as an important factors that might donate to the onset of hypertension [29] and other cardiovascular diseases [36]. It is well known that both short- and long-term stress can raise blood pressure by activating the sympathetic nervous system, which causes the sympathetic nerve terminals to produce norepinephrine. Vasoconstriction results from this, which also activates the hypothalamic-pituitary-adrenal axis or HPA. The activation of the HPA leads to the discharge of corticotrophin-releasing factor (CRF) from neurons in the para-ventricular nucleus. As a result, the anterior pituitary releases more adrenocorticotropic hormone (ACTH), and the adrenal gland releases more catecholamines and glucocorticoids. Moreover, the mineralocorticoid aldosterone is released [24]. Endothelial cells lining blood vessels can endure long-term damage due to sustained shear stress if the HPA axis is continuously stimulated and activated. Damage of this kind leads to an increase in the production of inflammatory cytokines by endothelial cells, such as IL-6, C-reactive protein (CRP), IL-8, and PAI-1, as well as reactive oxygen species [ROS], which in turn causes modifications in vascular function, neovascularization, and the evolution of atherosclerosis [21, 22].

Smoking: It is also known that smoking leads to an increase in the amount of chronic inflammation that occurs in the vasculature as well as an increase in the number of cell adhesion molecules [38]. These two elements raise

the risk of cardiovascular disease and hypertension, respectively. Increases in IL-6 levels, as well as aqueous ICAM-1 as well as MCP-1, have repeatedly been demonstrated to be strongly associated with cigarette usage [25, 26]. In the Framingham Heart Study, those who smoked had levels of soluble ICAM-1 that was 25% greater than nonsmokers [39]. Many research have been carried out to examine how long-term tobacco use affects cognitive function, and the majority of these studies have discovered a clear link between contemporary smoking and cognitive function [40, 41]. The connection between smoking and one's level of cognitive function was investigated over a span of 5.5 years in a study that involved 5705 individuals from the Rotterdam study [42, 43]. There are studies that suggest that the cellular mechanisms which are involved in the chronic effects of smoking on the damage done to the heart, blood vessels, and lungs are also involved in the damaging effects that smoking has on brain function and cognition [43]. This is in addition to the effects that smoking has on the cardiovascular and pulmonary systems. It has been established that smoking lowers performance on tests of executive function, memory and learning, attention, and processor speed [44]. These investigations were conducted on younger persons who did not have any underlying disorders that were readily apparent. According to magnetic resonance imaging (MRI) results, long-term cigarette smoking is substantially associated with reductions in gray and white matter volume and density [45, 46].

Diabetes: Throughout the past several decades, a significant amount of research has been conducted to investigate gender variations in the role that diabetes has on the progression of hypertension and cognitive diease [24, 29, 30]. Pre-menopausal women had a lower rate of hypertension as compared to men of the same age [59], despite the fact that both men-women have age-related rises in blood pressure as they get older. The risk of developing hypertension in women dramatically rises beyond the age of 55, with approximately 70 percent of women over the age of 65 in the United States being diagnosed with the condition. It is considered that premenopausal women who still have ovarian hormones in their bodies are provided some kind of defense against the risk of developing cardiovascular disease as well as high blood pressure [46, 47]. The idea that an estradiol-induced considerable increase in vascular endothelial nitric oxide secretion and vasodilation is one of the processes that contribute to ovarian hormone protection has been put forth as a possibility [48], improvements in endothelial function [49], and estrogen-induced central suppression of sympathetic outflow [50, 51] in the case of hypertension.

Cognitive impairment based hypertension in Pakistan

According to a study, antihypertensive drugs have an impact on hypertensive Pakistani patients' cognitive function [31]. Patients with hypertension taking beta-blockers had a higher percentage of cognitive impairment than patients taking diuretics, who had a lower percentage. Those receiving ACEI monotherapy and the calcium channel blocker/ARB combination also showed significantly less cognitive impairment than those receiving beta-blocker monotherapy. Similar studies have shown that calcium channel blockers and ACE inhibitors are more efficient than beta blockers as well as diuretics at postponing cognitive deterioration [48]. Although this link weakens with advancing age, cognitive loss or disability is strongly associated with elevated blood pressure, especially in a middle-aged sample [49]. The findings of the current investigation demonstrated that senior hypertensive patients who were older than 60 had a comparatively greater level of cognitive impairment. Similar results from a different study suggested a link between hypertension and impaired cognitive performance, particularly in patients aged 70 or older[53]. More literate adults had sharper minds than those who were less literate. The current investigation results indicated that low-educated hypertensive patients had a moderate level of cognitive impairment. Also, the current study found a link between hypertension patients' work status and cognitive function. It was shown that hypertension patients who had better-paying jobs and were employed exhibited superior cognitive function over those who were unemployed. When compared towards housewives of the same age, highly educated women in better professional positions displayed comparable signs of less cognitive deterioration. Furthermore, a strong correlation between the level of income and cognitive impairment was found in the current study. In patients with hypertension, lower income was associated with higher cognitive decline. A Pakistan and US study with similar findings identified low socioeconomic status as the cause of cognitive impairment in older people [32, 33]. Another Pakistan-based research revealed the cognitive impairment leads to depression among hypertenion's patients. According to the findings, there is a relationship between hypertension and depression, and this association exists regardless of socio-demographic characteristics, comorbidities, or a previous history of hospitalisation [34]. Many research describe that participants having hypertension have a huge impact on the quality of lifestyle and cognitive activities [50-52].

Treatment

Because of the use of different drug combinations within and among trials, it is impossible to make conclusions in relation to individual drug classes. This is especially true when considering the low number of participants in the recently included research. It was hypothesised in the 1998 issue of Syst Eur that the neuroprotective properties of the CCB nitrendipine could make the prevention of dementia more feasible. According to the findings of one meta-analysis, diuretics, dihydropyridine calcium channel blockers (CCBs), and inhibitors of the renin-angiotensin system may have distinct effects on the body. Possible impacts that vary according to class have

been discussed elsewhere [54-56], and additional research is now being conducted. These studies showed that pharmacological-based treatment of hypertension could result in a decline in cognitive impairment. It is essential to stress that cardiovascular outcomes, including cerebrovascular outcomes, were the primary objectives in the vast majority of the research investigations included in this analysis, with cognitive function and dementia serving as secondary endpoints. After it became clear that there would be improvements for the key endpoints, the previous trials were stopped. It is probable, as a result, that significant effects on cognitive control were not observed before the improvements in cardiovascular health became apparent [57].

Current situation and future perspective

Working in public health in identifying patient populations that are at high risk and in developing appropriate treatment and prevention methods. It is necessary to do more study in order to investigate the direct and indirect validating assumptions that relate particular important denominators with hypertension. The prioritization of medical treatment for hypertension patients residing in Pakistan will be made possible as a result of this, which is a significant step towards accomplishing the objective and will help bring Pakistan closer to its goal. The research also underlines the low quality of the evidence that is currently accessible, particularly with regard to the subject of hypertension and broadly speaking with regard to the overall research and policy on healthcare system in Pakistan. There is no effective government healthcare credentialing system, no evidence-based recommendations for public health practices, and no regulation of rigorous regulations for public health, the inappropriate use of pharmaceuticals, patient safety, and the responsibility of healthcare professionals and organizations. In Pakistan, there are no standardized guidelines or instruments that clarify what constitutes proper clinical practice or research on the public health system. Public health boards and other local government entities in Pakistan have taken dramatic measures to encourage a culture of public health, get medical doctors involved in research, and build evidence-based clinical processess.

We learned that cognitive impairment based on hypertension can be prevented and treated if you know how the different risk factors work together, especially how a person's genes affect their risk. Those who have heart disease or high blood pressure are more likely to get aortic arch calcification. Also, most of the risk factors for developing hypertension are also risk factors for developing cognitive impairment based hypertension. Some of these risk factors are getting older, getting sick, being stressed out, and smoking. More research needs to be done to find out the direct and indirect validating assumptions that link important denominators with high blood pressure. This will make it possible to prioritize medical care for people with high blood pressure who live in Pakistan. This is an important step toward achieving the goal and will help Pakistan get closer to its goal. The research also shows that the evidence we have right now isn't very good, especially when it comes to hypertension and, more generally, the research and policy on the healthcare system in Pakistan as a whole.

Conclusions and Implications

According to the findings of this research :

1. A number of socio-demographic, pathophysiological, risk factors strongly correlate with hypertension.
2. To avoid and cure age-related cognitive impairment (also known as ARCI), it is critical to comprehend the interconnected risk factors, especially how a person's genetic composition impacts their risk.
3. Those with cardiac disease or hypertension are more likely to acquire aortic arch calcification.
4. Furthermore, the bulk of the risk factors associated with the onset of hypertension are also associated with the development of ARCI.
5. These risk factors include aging, illness, worry, and smoking. These associations might go either advantageously or adversely.
6. More research is required to study the direct and indirect causal inferences.
7. There are no established standards in Pakistan for what constitutes appropriate clinical practise or research on the public health system.
8. In Pakistan, public health boards and other local governmental bodies have taken significant steps to promote a culture of public health, involve clinicians in research, and develop evidence-based clinical procedures.
9. Some key denominators with hypertension bases studies are needed, so that Pakistani hypertensive patients can be given priority for medical care.
10. This would allow Pakistan to concentrate medical treatment for hypertensive patients.

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Declaration of interest: No conflict of interest is declared by authors.

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