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Uncontrolled Hypertension: Silent but deadly culprit behind a multitude of health woes

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CONTENTS

ABSTRACT

Hypertension is a significant global health concern associated with increased morbidity and mortality. It was major cause of death for women and men in 2019 i.e. 20 % of worldwide fatalities. This review aimed to explore the intricate relationship between hypertension and development of over 15 diseases based. Although effective blood pressure control and appropriate antihypertensive medication can mitigate these risks, but hypertension remains a complex condition involving multiple organs and systems, posing challenges for study and requiring targeted drug development. Hypertension often presents with no symptoms, leading to many individuals being unaware of their condition. Regular health check-ups that includes blood pressure monitoring for effective management and prevention of chronic illnesses are essential. However, relying solely on blood pressure check-ups is inadequate, particularly for individuals with long-term hypertension who face higher risk of associated diseases. To ensure comprehensive health management, physicians should conduct thorough whole-body check-ups to detect early signs of these diseases in hypertensive patients, enabling tailored selection of appropriate antihypertensive medications.

Keywords: Blood pressure control, comprehensive health management, disease development, hypertension, morbidity and mortality.

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1. INTRODUCTION

Hypertension is the leading cause of avoidable deaths worldwide (31), particularly in India where cardiovascular diseases account for a third of all fatalities. Shockingly, only 12 % of the estimated 220 million hypertensive individuals in India have their blood pressure under control. The inadequate management of hypertension is attributed to low awareness, insufficient primary care, and poor follow-up (56). Globally, hypertension was responsible for 20 % of deaths in 2019, ranking as the primary cause among women and the second leading cause among men (42). Hypertension poses significant risks, including diabetes, cardiovascular diseases, organ damage, renal impairment (40), vascular cognitive impairment, Alzheimer's disease (3), and even eye diseases (6). Moreover, it has been identified as a key factor in the severity of Covid-19 cases, increasing the likelihood of critical care, hospitalization, and mortality (33). The pathophysiology of hypertension is complex and not yet fully understood. Further research is necessary to comprehensively elucidate the correlations between pathophysiology, organ changes, and hypertension-related complications (48). Due to its silent nature, hypertension often goes unnoticed (55), emphasizing the importance of regular blood pressure monitoring and routine health check-ups to effectively manage the condition and prevent chronic illnesses (24).

Numerous notable publications have explored the relationship between hypertension and the development of various diseases. In this review, we assess the available evidence and discuss the connections between hypertension and the risks associated with different diseases.

2. DISEASE ASSOCIATED WITH HYPERTENSION

2.1 Gout

Gout patients face a significant complication in the form of hypertension. A nationwide survey in the United States revealed that 65 % of individuals with hypertension also had gout (29). The likelihood of developing gout increases by approximately 88 % for hypertensive individuals, and 18 % of gout patients are at risk of developing hypertension (41). Similar findings were observed in a cohort study conducted in Taiwan's Chinese population, which showed a 32 to 34 % increased risk of gout among both hypertensive men and women (5). Diuretic medications commonly used to treat hypertension have a strong impact on uric acid disposal, making it challenging to manage hyperuricemia. Some antihypertensive drugs, such as β blockers, non-losartan angiotensin II receptor blockers, and angiotensin-converting enzyme inhibitors, have been associated with a higher incidence of gout in hypertensive individuals (7).

2.2 Kidney Disease

Hypertension is highly prevalent among patients with chronic kidney disease (CKD) and its incidence increases as the severity of CKD progresses. A national survey in the United States revealed that 23.3 % of individuals without a history of CKD have hypertension, compared to 84.1 % of stage 4-5 CKD patients, 59.9 % of stage 3 patients, 48.1 % of stage 2 patients, and 35.8 % of stage 1 patients (50). The pathophysiology of hypertension in CKD is complex, involving multiple factors and pathways. Elevated sympathetic nervous system activity and sodium dysregulation play significant roles in the development of hypertension (21).

2.3 Alzheimer's Disease (AD)

Hypertension has been found to increase the risk of developing Alzheimer's disease (AD) (1). A case-control study involving over 700 AD patients revealed that hypertension is associated with cognitive decline in AD patients. The risk of increased cognitive decline is approximately 1.5 times higher in AD patients with hypertension compared to those with normal blood pressure. This risk remains significant even when accounting for the underlying AD. The effect of hypertension on AD risk appears to be more pronounced in patients under the age of 65, with a seven-fold higher risk compared to normotensive individuals. The exact mechanism through which hypertension influences AD is not well understood but may involve demyelination or microinfarction of the cerebral white matter. Hypertension can also cause hippocampal atrophy, neurofibrillary tangles, and senile plaques, which are characteristic features of AD (2).Studies have shown that blood pressure starts to increase several years before the onset of AD, and then gradually decreases during the progression of the disease. Hypertension may contribute to cerebrovascular disease, leading to impaired blood flow, ischemia, and hypoxia, which can initiate the pathological processes of AD (47, 49).

2.4 Vascular Dementia

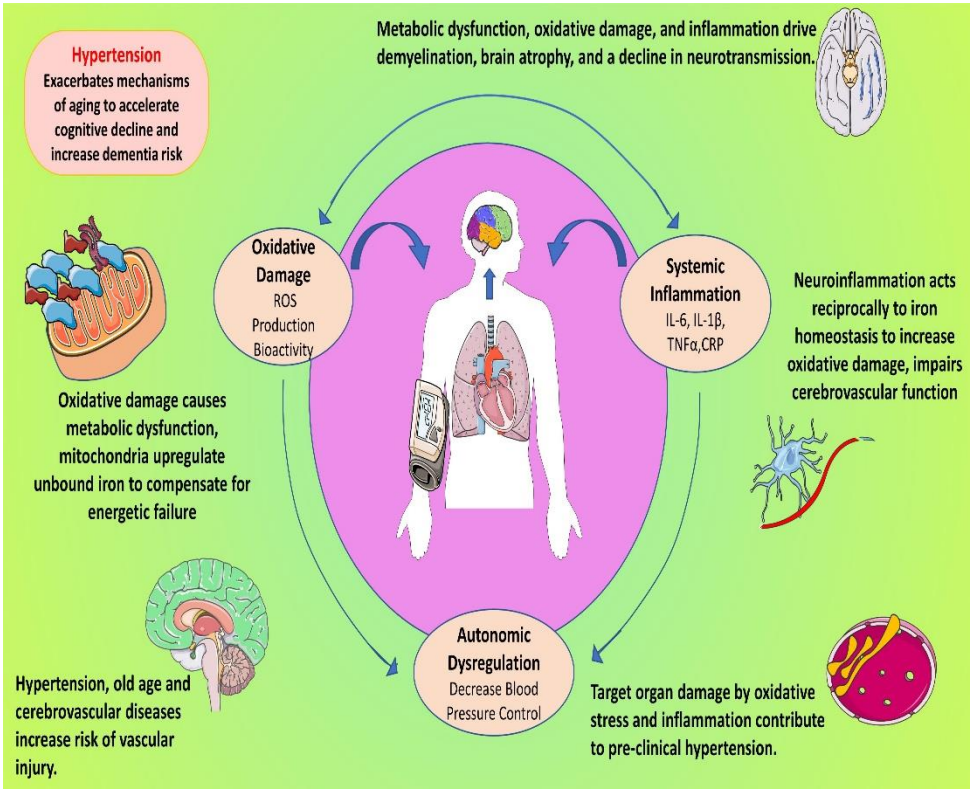

Figure 1. The diagram depicts potential paths for hypertension to increase the risk of cognitive impairment in old age and neurodegenerative disorders.

The evidence suggests a strong association between hypertension and the development of Vascular Dementia (VaD). Individuals with hypertension, both currently or in their midlife history, have a twofold increased risk of acquiring VaD. However, the relationship between hypertension and cognitive decline may change with age, as the risk of high blood pressure-related cognitive decline appears to decrease with advancing years (51).The prevalence of VaD tends to peak around the age of 75, with a higher incidence in patients aged 70-79 compared to those aged 60-69 (47). Hypertension is a significant risk factor for dementia and vascular cognitive impairment in the aging population (45). While antihypertensive medication is associated with a moderate reduction in dementia risk, strict blood pressure management, including during sleep, may have a neuroprotective effect and lower the risk of developing dementia (3). Ongoing blood pressure control is essential as part of a global strategy to combat dementia (37), considering the projected increase in the number of individuals living with this condition (35).

2.5 Obesity

Population studies have indicated that individuals with hypertension have a higher likelihood of weight gain compared to those without hypertension, suggesting a connection between hypertension and obesity (10). Data from studies like Tecumseh and Framingham show that hypertensive individuals are more prone to future weight gain, even if they are not obese initially (38). It has been observed that hypertensive individuals face difficulties in losing weight and are more likely to regain lost weight (28). Additionally, research has found that adolescents whose mothers had gestational hypertension are at increased risk of developing high blood pressure and being overweight or obese. However, the exact mechanism linking hypertension and obesity requires further investigation for a better understanding of their relationship (27).

2.6 Erectile Dysfunction in Male

The risk of developing sexual dysfunction in men with hypertension compared to those without hypertension varies across countries, age groups, and study designs, ranging from 25 % to 75 % (16). Vascular abnormalities in the penile tissue, caused by both functional and structural impairments of the penile vessels, are the primary contributors to erectile dysfunction in hypertensive men (53). Long-standing or severe hypertension is associated with a higher prevalence and severity of erectile dysfunction. Hypertension can lead to smooth muscle hypertrophy, blood flow obstruction, and atherosclerosis-related lesions, which affect penile vasculature and impair erectile function (53). Chronic hypertension also negatively impacts smooth and neurogenic muscle-induced relaxation in response to nitric oxide, an essential factor for maintaining and achieving an erection. Various hormones and vasoactive substances have been implicated in the pathophysiology of hypertension-related erectile dysfunction, but their exact roles require further investigation (30). Studies suggest that hypertensive patients are up to seven times more likely to develop erectile dysfunction compared to normotensive individuals. Future research is needed to better understand the mechanisms and factors contributing to erectile dysfunction in hypertensive men (39).

2.7 Female Sexual Dysfunction

The study revealed that women with hypertension experience reduced sexual function, with a roughly 2.7-folds increased risk of sexual dysfunction compared to

normotensive women (8). Sexual dysfunction is a significant concern for hypertensive women (11), and the use of hypertensive medications may help alleviate its severity. Changes in blood flow caused by hypertension affect the physiological aspects of the sexual response cycle in women, leading to interference with sexual desire, arousal, and orgasm (44). Elevated blood pressure impairs blood flow to the vaginal organs and pelvic region, resulting in decreased peripheral vascular circulation (32). This can lead to vaginal and clitoral vascular insufficiency and vasculogenic female sexual dysfunction. Factors such as insufficient blood pressure management, increasing age, duration of hypertension, higher systolic blood pressure, and β-blocker treatment have been identified as risk factors for sexual dysfunction. Research suggests that hypertension treatment can affect female sexual function, with certain medications like valsartan improving sexual fantasies and desire while others like atenolol significantly reducing these aspects. It is important to note that the occurrence of female sexual dysfunction decreases with age, but the exact reasons for variations in findings require further exploration (12).

2.8 Hypertensive Retinopathy

The occurrence of hypertensive retinopathy is directly related to the duration and severity of hypertension. The prevalence of hypertensive retinopathy varies between studies, ranging from 22 % to 60 % (14, 52). Individuals with severe hypertension have a higher prevalence rate (84.6 %) (34), compared to those with mild (25.3 %) or moderate (34.5 %) hypertension (25). The frequency of hypertensive retinopathy in individuals with hypertension is estimated to be between 40 % and 90 % (25). Long-term observational studies have shown that successful hypertension treatment can lead to regression or elimination of hypertensive retinopathy, while elevated blood pressure is associated with its progression. Hypertensive retinopathy is linked to an increased risk of ocular conditions such as age-related maculopathy, retinal vein occlusion, glaucoma, and optic neuropathy. Genetic factors, such as certain genotypes and the deletion of the angiotensin-converting enzyme allele, are associated with a higher risk of hypertensive retinopathy (20). Smoking is also believed to have a significant correlation with severe or malignant hypertensive retinopathy (34). Target-based treatment for hypertension has been associated with lower rates of hypertensive retinopathy compared to those with poorly managed hypertension (26).

2.9 Cataract

The studies revealed that hypertension is associated with an increased risk of developing cataracts (58). High blood pressure is linked to all three types of cataracts, and the prevalence of cataracts is higher in individuals with metabolic syndrome components, higher systolic blood pressure, and elevated blood glucose levels (43). The presence of both cataracts and high blood pressure significantly increases the likelihood of developing cataracts. Severe hypertension and longer duration of hypertension further increase the risk (46). Hypertension-induced cataract formation involves pathophysiological pathways such as systemic inflammation, altered lens capsule conformation, disrupted lens short-circuit current, and nitric oxide imbalance. Hypertension is often associated with dyslipidemia and diabetes mellitus, which can worsen the deleterious effects on cataract development (36). Certain anti-hypertension drugs may have a role in cataract development, while others, such as angiotensin-converting enzyme inhibitors and thiazide diuretics, may have

preventive benefits. Lowering blood pressure could potentially reduce the prevalence of cataracts and related surgical costs (58).

2.10 Glaucoma

Recent research indicates that glaucoma is more prevalent in individuals with either high or low blood pressure (23). Hypertension and glaucoma are closely related, with a higher incidence of glaucoma among hypertensive individuals (9). Aggressive use of antihypertensive medications, resulting in a significant reduction in ocular perfusion pressure, has been associated with an increased risk of developing glaucoma (23). The relationship between blood pressure and glaucoma appears to be age-dependent, with high blood pressure being beneficial in younger individuals but potentially harmful as blood vessels age and become narrower. A 'U'-shaped connection has been observed between glaucoma prevalence and diastolic blood pressure. Ocular hypertension is another modifiable risk factor for glaucoma, and lowering intraocular pressure can reduce the risk. Factors such as higher IOP and older age contribute to the conversion of ocular hypertension to glaucoma (18).

2.11 Covid-19

Hypertensive patients with COVID-19 have a higher mortality rate and are more likely to experience severe cases (17). The presence of hypertension is associated with a longer illness duration in COVID-19 patients (13). COVID-19 can increase blood pressure and may even lead to new-onset hypertension (57). Laboratory findings reveal elevated levels of certain biomarkers in hypertensive individuals, indicating a more severe disease course (54). Corticosteroid use is more common among hypertensive patients (4). Overall, hypertension is a significant risk factor for poor clinical outcomes in COVID-19 patients, supported by laboratory testing results showing decreased blood oxygen levels in hypertensive individuals (57).

2.12 Cancer

Hypertension is associated with an increased risk of kidney carcinoma, with a higher risk observed in Afro-Americans compared to Caucasians. The duration of hypertension correlates with the incidence of kidney cancer (22), indicating that hypertension plays a role in its development. Digestive system, endometrial, and breast cancers have also been linked to high blood pressure. The association between hypertension and cancer is more pronounced in older individuals, particularly in men (15). Antihypertensive medication may complicate the relationship, as some medications increase the risk of tumor development. The use of certain hypertension medications has shown positive effects in breast cancer therapy. The exact mechanisms underlying the link between hypertension and cancer are unclear but may involve oxidative stress, hypoxia-inducible factors, and biochemical abnormalities. Other factors such as lifestyle, age, obesity, and smoking may contribute to the association. Overall, systolic hypertension is associated with a 23 % higher risk of cancer death, particularly in the case of renal cell cancer (19).

3. FUTURE LINES OF WORK

High blood pressure, often called the "silent killer," can lead to various serious health problems such as heart failure, stroke, and heart attack. It is also associated with

several other diseases including gout, kidney disorders, neurodegenerative diseases, eye disorders, sexual dysfunction, diabetes, cancer, obesity, pulmonary hypertension, OSA, and fatty liver diseases. Regular monitoring of blood pressure is crucial, and healthcare professionals should conduct thorough assessments to evaluate risks and related issues. Long-standing hypertension requires annual health check-ups to prevent complications. Hypertensive medications can sometimes contribute to the development of other diseases, underscoring the importance of comprehensive health examinations and considering alternative therapies with minimal side effects. Further research is needed to explore the risks associated with hypertensive medication.

AUTHOR'S CONTRIBUTION

In the present review, Vishnu explains uncontrolled hypertension and was the most important contribution in making the manuscript. A. Mazumder, S. Das, and A. Kanda performed the systemic evaluation and elaborated on the conclusion. All authors read and approved the final manuscript.

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DECLARATION

We declare that all authors of this manuscript have made substantial contributions. We have not excluded any author that substantially contributed to this manuscript. We have followed our ethical norms established by our respective institutions.

REFERENCES

1. Bajwa, E. and Klegeris, A. (2022). Neuroinflammation as a mechanism linking hypertension with the increased risk of Alzheimer's disease. *Neural Regeneration Research* **17**: 2342.
2. Bellew, K.M., Pigeon, J.G., Stang, P.E., Fleischman, W., Gardner, R.M. and Baker, W.W. (2004). Hypertension and the rate of cognitive decline in patients with dementia of the Alzheimer type. *Alzheimer Disease & Associated Disorders* **18**: 208-213.
3. Canavan, M. and O'Donnell, M.J. (2022). Hypertension and Cognitive Impairment: A Review of Mechanisms and Key Concepts. *Frontiers in Neurology* **13**: 45.
4. Chen, J., Liu, Y., Qin, J., Ruan, C., Zeng, X., Xu, A., Yang, R., Li, J., Cai, H. and Zhang, Z. (2022). Hypertension as an independent risk factor for severity and mortality in patients with COVID-19: a retrospective study. *Postgraduate Medical Journal* **98**: 515-522.
5. Chen, J.H., Yeh, W.T., Chuang, S.Y., Wu, Y.Y. and Pan, W.H. (2012). Gender-specific risk factors for incident gout: A prospective cohort study. *Clinical Rheumatology* **31**: 239-245.
6. Cheung, C.Y., Biousse, V., Keane, P.A., Schiffrin, E.L. and Wong, T.Y. (2022). Hypertensive eye disease. *Nature Reviews Disease Primers 2022* **8**: 1-18.
7. Choi, H.K., Soriano, L.C., Zhang, Y. and GarciáRodriǵuez, L.A. (2012). Antihypertensive drugs and risk of incident gout among patients with hypertension: population based case-control study. *British Medical Journal* **344**: 1-9.
8. Choy, C.L., Sidi, H., Koon, C.S., Ming, O.S., Mohamed, I.N., Guan, N.C. and Alfonso, C.A. (2019). Systematic review and meta-analysis for sexual dysfunction in women with hypertension. *The Journal of Sexual Medicine* **16**: 1029-1048.
9. Cui, Y., Kun, Pan, L., Lam, T., Wen, C. Yi, Do, C. and Wai, C. (2021). Mechanistic links between systemic hypertension and open angle glaucoma. *Clinical and Experimental Optometry* **105**: 362-371.

10. DeMarco, V.G., Aroor, A.R. and Sowers, J.R. (2014). The pathophysiology of hypertension in patients with obesity. *Nature Reviews Endocrinology* **10**: 364-376.
11. Doumas, M. and Douma, S. (2006). Sexual dysfunction in essential hypertension: Myth or Reality? *The Journal of Clinical Hypertension* **8**: 269-274.
12. Doumas, M., Tsiodras, S., Tsakiris, A., Douma, S., Chounta, A., Papadopoulos, A., Kanellakopoulou, K. and Giamarellou, H. (2006). Female sexual dysfunction in essential hypertension: A common problem being uncovered. *Journal of Hypertension* **24**: 2387-2392.
13. Ebinger, J.E., Driver, M., Joung, S., Tran, T., Barajas, D., Wu, M., Botting, P.G., Navarrette, J., Sun, N. and Cheng, S. (2022). Hypertension and excess risk for severe COVID-19 illness despite booster vaccination. *Hypertension* **79**: E132-E134.
14. Erden, S. and Bicakci, E. (2012). Hypertensive retinopathy: Incidence, risk factors and co-morbidities. *Clinical and Experimental Hypertension* **34**: 397-401.
15. Fan, Y., Khan, N.H., Khan, M.F.A., Ahammad, M.F., Zulfiqar, T., Virk, R. and Jiang, E. (2022). Association of hypertension and breast cancer: Antihypertensive drugs as an effective adjunctive in breast cancer therapy. *Cancer Management and Research* **14**: 1323-1329.
16. Flynn, K.E., Lin, L., Bruner, D.W., Cyranowski, J.M., Hahn, E.A., Jeffery, D.D., Reese, J.B., Reeve, B.B., Shelby, R.A. and Weinfurt, K.P. (2016). Sexual satisfaction and the importance of sexual health to quality of life throughout the life course of U.S. Adults. *The Journal of Sexual Medicine* **13**: 1642-1650.
17. Gao, Q., Hu, Y., Dai, Z., Xiao, F., Wang, J. and Wu, J. (2020). The epidemiological characteristics of 2019 novel coronavirus diseases (COVID-19) in Jingmen, Hubei, China. *Medicine* **99**: 23.
18. Garcia-Villanueva, C., Milla, E., Bolarin, J.M., García-Medina, J.J., Cruz-Espinosa, J., Benítez-del-Castillo, J., Salgado-Borges, J., Hernández-Martínez, F.J., Bendala-Tufanisco, E., Andrés-Blasco, I., Gallego-Martinez, A., Zanón-Moreno, V.C. and Pinazo-Durán, M.D. (2022). Impact of systemic comorbidities on ocular hypertension and open-angle glaucoma, in a population from Spain and Portugal. *Journal of Clinical Medicine* **11**: 5649.
19. Grossman, E., Messerli, F.H., Boyko, V. and Goldbourt, U. (2002). Is there an association between hypertension and cancer mortality? *The American Journal of Medicine* **112**: 479-486.
20. Grosso, A., Veglio, F., Porta, M., Grignolo, F.M. and Wong, T.Y. (2005). Hypertensive retinopathy revisited: Some answers, more questions. *British Journal of Ophthalmology* **89**: 1646-1654.
21. Hamrahian, S.M. and Falkner, B. (2017). Hypertension in chronic kidney disease. *Advances in Experimental Medicine and Biology* **956**: 307-325.
22. Hasan Khan, M., Pathak, S., Yadav, U., Rochlani, Y. and Aronow, W.S. (2022). Hypertension in cancer survivors. *Current Hypertension Reports* **24**: 435-443.
23. He, Z., Vingrys, A.J., Armitage, J.A. and Bui, B. v. (2021). The role of blood pressure in glaucoma. *Clinical and Experimental Optometry* **94**: 133-149.
24. Jeong, Y.W., Jung, Y., Jeong, H., Huh, J.H., Sung, K.C., Shin, J.H., Kim, H.C., Kim, J.Y. and Kang, D.R. (2022). Prediction model for hypertension and diabetes mellitus using Korean public health examination data (2002-2017). *Diagnostics* **12**: 1967.
25. Khalid, A., Rafique, R., Arshad, M., Hamdani, M., Pirzada, M., Ali, S. and Hussain, S. (2022). Duration of the hypertension and prevalence of retinopathy in hypertensive patients. *Journal of Pakistan Society of Internal Medicine* **3**: 45-48.
26. Kolman, S.A.M., Van Sijl, A.M., Van Der Sluijs, F.A. and Van De Ree, M.A. (2017). Consideration of hypertensive retinopathy as an important end-organ damage in patients with hypertension. *Journal of Human Hypertension* **31**: 121-125.
27. Kuciene, R. and Dulskiene, V. (2022). Associations of maternal gestational hypertension with high blood pressure and overweight/obesity in their adolescent offspring: A retrospective cohort study. *Scientific Reports* **12**: 1-9.
28. Lasser, V.I., Raczynski, J.M., Stevens, V.J., Mattfeldt-Beman, M.K., Kumanyika, S., Evans, M., Danielson, E., Dalcin, A., Batey, D.M., Belden, L.K. and Brewer, A.A. (1995). Trials of *Hypertension Prevention*, phase II structure and content of the weight loss and dietary sodium reduction interventions. *Annals of Epidemiology* **5**: 156-164.
29. Liu, K., Yao, Y., Chen, W., Mao, Y., Ye, D. and Wen, C. (2022). Modifiable risk factors and incidence of gout: Estimation of population attributable fraction in the US. *Seminars in Arthritis and Rheumatism* **55**: 152040.
30. Manolis, A. and Doumas, M. (2009). Hypertension and sexual dysfunction. *Archives of Medical Science Special Issues* **2009**: 350-350.

31. Marklund, M., Cherukupalli, R., Pathak, P., Neupane, D., Krishna, A., Wu, J.H.Y., Neal, B., Kaur, P., Moran, A.E., Appel, L.J. and Matsushita, K. (2023). Hypertension treatment capacity in India by increased workforce, greater task-sharing, and extended prescription period: A modelling study. *The Lancet Regional Health - Southeast Asia* **10**: 100124.
32. Maseroli, E., Scavello, I. and Vignozzi, L. (2018). Cardiometabolic Risk and Female Sexuality-Part I. Risk factors and potential pathophysiological underpinnings for female vasculogenic sexual dysfunction syndromes. *Sexual Medicine Reviews* **6**: 508-524.
33. McFarlane, E., Linschoten, M., Asselbergs, F.W., Lacy, P.S., Jedrzejewski, D. and Williams, B. (2022). The impact of pre-existing hypertension and its treatment on outcomes in patients admitted to hospital with COVID-19. *Hypertension Research* **45**: 834-845.
34. Modi, P. and Arsiwalla, T. (2022). Hypertensive retinopathy. *Ophthalmology Clinics of North America* **11**: 535-558.
35. Mogi, M. (2022). Hypertension management to prevent dementia. *Hypertension Research* **45**: 573-575.
36. Mylona, I., Dermenoudi, M., Ziakas, N. and Tsinopoulos, I. (2019). Hypertension is the prominent risk factor in cataract patients. *Medicina* **55**: 430.
37. Nagai, M., Hoshide, S. and Kario, K. (2010). Hypertension and dementia. *American Journal of Hypertension* **23**: 116-124.
38. Narkiewicz, K. (2006). Obesity and hypertension-the issue is more complex than we thought. *Nephrology Dialysis Transplantation* **21**: 264-267.
39. Nicolosi, A., Moreira, E.D., Shirai, M., bin Mohd Tambi, M.I. and Glasser, D.B. (2003). Epidemiology of erectile dysfunction in four countries: Cross-national study of the prevalence and correlates of erectile dysfunction. *Urology* **61**: 201-206.
40. Nii, R., Lamptey, L., Sun, C., Layek, B. and Singh, J. (2023). Neurogenic hypertension, the blood–brain barrier, and the potential role of targeted nanotherapeutics. *International Journal of Molecular Sciences* **24**: 2213.
41. Pan, A., Teng, G.G., Yuan, J.M. and Koh, W.P. (2015). Bidirectional association between self-reported hypertension and gout: The Singapore Chinese Health Study. *PLOS ONE* **10**: e0141749.
42. Parati, G., Goncalves, A., Soergel, D., Bruno, R.M., Caiani, E.G., Gerdts, E., Mahfoud, F., Mantovani, L., McManus, R.J., Santalucia, P. and Kahan, T. (2023). New perspectives for hypertension management: Progress in methodological and technological developments. *European Journal of Preventive Cardiology* **30**: 48-60.
43. Sabanayagam, C., Wang, J.J., Mitchell, P., Tan, A.G., Tai, E.S., Aung, T., Saw, S.M. and Wong, T.Y. (2011). Metabolic syndrome components and age-related cataract: The Singapore Malay eye study. *Investigative Ophthalmology and Visual Science* **52**: 2397-2404.
44. Santana, L.M., Perin, L., Lunelli, R., Inácio, J.F.S., Rodrigues, C.G., Eibel, B. and Goldmeier, S. (2019). Sexual dysfunction in women with hypertension: A Systematic Review and Meta-analysis. *Current Hypertension Reports* **21**: 1-10.
45. Santisteban, M.M., Iadecola, C. and Carnevale, D. (2023). Hypertension, neurovascular dysfunction, and cognitive impairment. *Hypertension* **80:** 22-34.
46. Sayin, N., Kara, N. and Pekel, G. (2015). Ocular complications of diabetes mellitus. *World Journal of Diabetes* **6**: 92.
47. Sharp, S.I., Aarsland, D., Day, S., Sønnesyn, H. and Ballard, C. (2011). Hypertension is a potential risk factor for vascular dementia: systematic review. *International Journal of Geriatric Psychiatry* **26**: 661-669.
48. Shinohara, K. (2023). Emerging topics on basic research in hypertension: Interorgan communication and the need for interresearcher collaboration. *Hypertension Research **2023*** **:**1-8.
49. Skoog, I. and Gustafson, D. (2013). Update on hypertension and Alzheimer's disease. *Neurological Research* **28**: 605-611.
50. Tedla, F.M., Brar, A., Browne, R. and Brown, C. (2011). Hypertension in chronic kidney disease: Navigating the evidence. *International Journal of Hypertension* **2011**: 1-9.
51. Tzourio, C. (2022). Hypertension, cognitive decline, and dementia: An epidemiological perspective. *Dialogues in Clinical Neuroscience* **9**: 61-70.
52. Veeramani, P.V.A. and Bhaskaran, B. (2023). Prevalence of hypertensive retinopathy in hypertensive patients evaluated in Saveetha Hospitals, Chennai. *Journal of Pharmaceutical Negative Results* **13**: 7025-7031.
53. Viigimaa, M., Doumas, M., Vlachopoulos, C., Anyfanti, P., Wolf, J., Narkiewicz, K. and Mancia, G. (2011). Hypertension and sexual dysfunction: Time to act. *Journal of Hypertension* **29**: 403-407.

54. Wang, S., Chen, Y., Wang, L., Liu, H. and Han, P. (2020). Are COVID-19 patients with hypertension at higher risk in China? *Journal of Hypertension* **38**: 1384-1385.
55. WHO (2021). Hypertension. Hypertension https://www.who.int/news-room/fact-sheets/detail/hypertension (accessed Jan 30, 2023).
56. WHO (2022). India Hypertension Control Initiative, a high impact and low-cost solution. India Hypertension Control Initiative, a high impact and low-cost solution https://www.who.int/india/news/detail/02-06-2022-india-hypertension-control-initiative--a-high-impact-and-low-cost-solution (accessed Jan 30, 2023).
57. Yang, G., Tan, Z., Zhou, L., Yang, M., Peng, L., Liu, J., Cai, J., Yang, R., Han, J., Huang, Y. and He, S. (2020). Effects of angiotensin II receptor blockers and ACE (angiotensin-converting enzyme) inhibitors on virus infection, inflammatory status, and clinical outcomes in patients with COVID-19 and hypertension: A single-center retrospective study. *Hypertension* **76**: 51-58.
58. Yu, X., Lyu, D., Dong, X., He, J. and Yao, K. (2014). Hypertension and risk of cataract: A Meta-Analysis. *PLOS ONE* **9**: 1-17.

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