Crosstalk between Vitamin D and thyroid hormone with respect to patients with High Blood Pressure: A Review

Azad Kumar Singh[1*], Dr. Jaya Chandra[2], Dr Ashutosh Jain[3]

[1*]PhD Research Scholar, Department of Biochemistry, Index Medical College Hospital and Research Center, Indore.
[2]Associate professor, Department of Biochemistry, Index Medical College hospital and research centre, Indore.
[3]Assistant professor, Department of Physiology , Index Medical College hospital and research centre, Indore.

***Corresponding Author:** Azad Kumar Singh
*PhD Research Scholar, Department of Biochemistry, Index Medical College Hospital and Research Center, Indore.

ABSTRACT
By allowing the heart to pump blood to all of the body's organs, the cardiovascular system ensures that their metabolic demands are met. Systemic vascular resistance (SVR) and cardiac output (CO) are two measures that can be used to determine blood pressure and blood flow. The heart's pumping action is a good indicator of cardiac output. Blood pressure readings deviate from the normal range for a variety of reasons that affect CO or SVR. Many factors can affect the equilibrium of systemic vascular resistance and cardiac output. Both the amount of blood circulating in the body and the force of the heart's pumping action determines CO. Ensuring the body's blood volume is maintained relies heavily on the kidney's sodium regulation and fluid handling abilities. Any decrease in kidney function, no matter how slight, will have a major impact on the body's ability to regulate fluid volume because the kidneys are so important for maintaining a healthy fluid and sodium balance. Vitamin D deficiency, defined as levels below 20 ng/ml, is on the rise, even among otherwise healthy people, and is thus a major concern in global public health. Environmental factors like vitamin D play a role in numerous biological processes, including how we perceive chronic pain and how our bodies respond to infections. Patients with autoimmune thyroid disease (AITD) are at increased risk for developing vitamin D deficiency, and new evidence suggests that vitamin D may play a role in the onset of several autoimmune diseases. Pregnancy complications, abnormal thyroid function, elevated TSH levels, elevated thyroid volume, and antithyroid antibodies were all linked to low vitamin D levels in women with AITD. The article aims to understand the link between Vitamin D and the thyroid hormone in patients with hypertensive patients along with to establish a qualitative criterion within it.

Keywords: Blood Pressure, Cardiovascular system, Vitamin D, Thyroid, TSH levels

INTRODUCTION

The cardiovascular system plays a Vital role in sustaining the metabolic demands of all organs by the pumping action of heart. The blood pressure and blood flow can be determined by cardiac output (CO) and systemic vascular resistance (SVR). The cardiac output can be determined by the pumping activity of the heart. There are number of factors which results in the alteration of CO or SVR leading on to alteration from the normal blood pressure [1].

Most guidelines defines hypertension as systolic BP more than 140 mmHg or diastolic BP more than 90 mmHg, where as normal BP is 120/80 mmHg or lower. The BP level between these 2 ranges is termed as prehypertension or borderline hypertension. Now a day most of the people living in developed as well as developing countries throughout the world will develop hypertension at some point of their lifetime [2,3].

The thickness of blood vessel walls and vasomotor tone determine SVR. In addition, SVR can be influenced by environmental factors, metabolic factors, and the humeral milieu. In 5% to 10% of cases, hypertension can have underlying causes. For patients with secondary hypertension, reversing hypertension to normotension is as simple as addressing the underlying cause. There may be no known cause for primary or essential hypertension. The development of hypertension can be influenced by a multitude of factors, including changes in lifestyle, advancing age, genetic predisposition, and environmental changes. Treating hypertension lowers the risk of complications and death, regardless of its aetiology. Hypertension is often asymptomatic and goes undetected in its early stages. Therefore, in order to make the diagnosis as soon as possible, blood pressure needs to be monitored regularly. The term "silent killer" may apply to it for that reason [4].

Issues related to heart disease include Cardiovascular illness, a heart condition known as congestive cardiac failure, Brain Attack, Coronary heart attack, enlargement of the left ventricle, conditions such as peripheral artery disease and others Renal illness that persists through time, chronic kidney disease, the last stage of kidney disease, Eye Diseases [5].

1. Hypertension and cardiovascular disease.

Nowadays CVD becomes the major Global health hazard worldwide. The spectrum of coronary vascular disease includes coronary artery disease, stroke heart failure and other peripheral vascular diseases. Apart from cigarette smoking, diabetes and dyslipidemia, hypertension is considered to be the major risk factor for the development of premature CVD [6].
Framingham heart study quotes that hypertension is the prime cause for heart disease among men. It has been estimated that 20 % of the first myocardial infarction can be attributed by hypertension in both men and women globally. When compared to men, women with long standing hypertension will end up in stroke rather than myocardial infarction as in men. Most of the trials proves that hypertension is the prime risk factor for predicting hemorrhagic and ischemic stroke [7].

1.2 Cardiovascular Disease And Prehypertension:

CVD risk factors are not only pertained to hypertensive patients by traditional definition. Prehypertension can be referred as range of BP between Normal (120/80mmHg) and hypertensive patients (140/90mmHg). Most of the studies conclude that prehypertension is also one of the risk factor for developing the coronary artery disease and stroke. But these studies failed to relate prehypertension with this vascular events since patients with prehypertension are also having additional risk factors such as diabetes mellitus, increased body weight, elevated serum cholesterol level. The relationship between the prehypertension and theCVD can be supported by the antihypertensive therapy. Treatment of patients with prehypertension will have reduced risk of developing the CVD as compared with patients without taking treatment for prehypertension [8].
When blood pressure rises, the body tries to adjust, but the result is cardiovascular disease. Elevated blood pressure causes structural changes in the arterial and vascular tree, known as remodelling or hypertrophy, which harms the organ systems. Arteriosclerosis develops in the larger vessels as a result of the increased sheer stress brought on by hypertension. The progression of arteriosclerosis is age-dependent, meaning that the risk is higher in older patients compared to younger ones. Atherosclerosis development is also significantly impacted by hypertension. The thickening, changes in geometry, and increased mass of the left ventricle—commonly known as left ventricular hypertrophy (LVH)—is a common complication in hypertensive patients. The onset of heart failure, myocardial infarction, and cardiac arrhythmias is preceded by LVH. The majority of patients with congestive heart failure will have chronic hypertension as their only cause [9, 10].

1.3 Epidemiology

Hypertension is one of the ‘iceberg’ disease. Rule of halves states that ‘in the early 1970s, only half of the general population in the developed countries were aware of hypertension, in that only half of them gets treated for hypertension, in that only half of them were adequately treated [11].

1.4 INCIDENCE:

Due to the variability of readings among the population and chronicity of the condition, the concept of incidence in Hypertension has limited value. It has been estimated that 1.13 billion populations have been prevailing with hypertension globally in 2015.It has been estimated that overall prevalence of hypertension is 30-40 percent. Gender wise, around 24 and 20 percent in males and females respectively. The prevalence of hypertension is irrespective of the income status globally, i.e., its prevalence can be seen in lower, middle and higher income countries. Prevalence of hypertension in more common in the elderly age groups that is age more than 60 years. This contributes around 60 percent in the total hypertensive population. Due to the sedentary life style and increased weight in the population, it was estimated that the prevalence of hypertension would be increased by 15-20 percent by the year 2025. Hypertension is the leading cause for premature deaths and Disability adjusted life years (DALY) for more than 200 million population. Although there are recent advances in the modern medicine, DALYs have been increased in the recent past due to the ineffective control of blood pressure and lack of awareness among the population [12, 13].

1.5 Risk factors for hypertension:

According to WHO scientific group, risk factors for hypertension can be classified into Non modifiable and Modifiable risk factors. Non- modifiable risk factors include Age- blood pressure consistently rises as the age increases, sex- Men will be affected more common than women, but women in post menopausal age group have higher risk, genetic factors, ethnicity- Black Americans of African origin have higher blood pressure when compared to whites [14].
And the modifiable risk factors obesity- Central obesity which has been indicated by increased waist to hip ratio. Central obesity has better correlation with elevated blood pressure. Salt intake: Numerous studies states that increased salt intake per day that is more than 7 to 8g/day has been better correlated with the elevated blood pressure. Saturated fat, Dietary fibre: Studies states that consumption of decreased amount of dietary fibre will lead on to hypertension, alcohol: High intake of alcohol for the prolonged period will leads to elevated blood pressure, Heart rate: When the normotensive and untreated hypertensive population matched for age and sex are compared, hypertensive group have somewhat higher heart rate than the normotensive patient. This reflects that the untreated hypertension may have increase sympathetic activity. , Physical activity: Decrease in the physical activity will leads to elevated blood pressure. So hypertension is more common with the population with sedentary lifestyle. Environmental stress All studies reveals that patients with hypertension have increased level of catecholamine than the normotensive population [15, 16].

Oral contraception remains one of the cause for hypertension in some population because of its estrogen component. Some of the other factors such as noise, vibration, temperature and humidity may require further investigations. Vitamin D deficieny is also being investigated as causal factor for hypertension. The pathogenesis studied in correlating these two factors is involving the rennin angiotensin system [17].

1.6 Mechanisms Of Hypertension

To understand the mechanism of hypertension, we need to know the factors affecting the normal and elevated blood pressure. The two main factors are cardiac output and peripheral vascular resistance. Cardiac output in turn is a product of stroke volume and heart rate. Stroke volume depends on the myocardial contractility and the size of the vessel. Peripheral vascular resistance depends on the anatomical and functional alterations in the vessel lumen of the arteriolar and small arteries [18].

1.6.1 The Renin- Angiotensin System (Ras) : A Central Regulator Of Blood Pressure

RAS is a complex systemic endocrine regulatory cascade due to its many components. The liver is the primary site of AGT production, the cascade's predominant substrate. When Renin cleaves AGT in the bloodstream to Angiotensin (Ang) 1, the RAS cascade is limited in its rate of progression. Angiotensin converting enzyme (ACE) is primarily found in the endothelial cells of blood vessels and converts Ang 1, an inactive decapeptide, into Ang 2, an active octapeptide. Additional Ang2 cleavage by aminopeptidases A and N results in Ang3 and Ang4. This enzyme, ACE2, is essential for normal heart function because it converts Ang2 to Ang (1-7)—an analogue of ACE. As the primary biological effector of RAS, Ang2 is essential for the regulation of blood pressure. The peripheral vascular resistance is raised by Ang2 because, as a vasoconstrictor, it raises vascular tone by acting on vasculature smooth muscle cells. Aldosterone secretion from the adrenal cortex is also enhanced by it. Ang2 aids water retention by the kidneys by stimulating the posterior pituitary to secrete vasopressin, also known as antidiuretic hormone. Vasopressin activates the central nervous system, which in turn increases the sensation of thirst and, consequently, the intake of water. Consequently, systemic vascular resistance and extracellular volume are both raised when the RAS cascade is activated [19]. Hypertension develops when the RAS cascade is overactivated, which in turn increases cardiac output and peripheral vascular resistance. In addition to regulating blood pressure, Ang2 is involved in various physiological and pathological processes. Some of the activities in which Ang2 is involved include fibrogenesis, atherogenesis, inflammation, cell hypertrophy, and proliferation. In other words, harmful effects are produced when the Ras cascade is activated too much. Brain, blood vessels, kidney, heart, and reproductive system are among the many tissues where RAS have been found, in addition to systemic RAS. Paracrine activation of tissue-specific RAS can lead to tissue damage in certain cases. Several G protein coupled receptors widely present in the body mediates the actions of Ang2. There are two Angiotensin receptors – Type 1 receptor (AT1) and Type 2 receptor (AT2). AT1 activation mediates most of the actions such as vasoconstriction, sodium retention, hypertrophy. AT2 activation results in vasodilation, natriuresis and growth inhibition. Hypertension and its complications are due to over activation of the RAS mediated by AT1 [20].

2. Vitamin D

Vitamin D is essential for stimulation of absorption of calcium from the gut. It is activated first in the liver to form 25 hydroxy vitamin D and then it undergoes another hydroxylation in the proximal tubules of kidney to form 1,25 hydroxy vitamin D3 which is the final active form [21].

2.1 Actions Of Vitamin D In Calcium Homeostasis

Apart from these known skeletal actions of vitamin D, it has been linked in many extra skeletal diseases such as multiple sclerosis, type 2 diabetes, role in cardiovascular diseases, role in hypertension, chronic kidney disease, Rheumatoid arthritis, Respiratory infections and obstructive airway diseases. Here we will briefly discuss about its role in hypertension [22].

2.2 VITAMIN D REGULATION OF RENIN-ANGIOTENSIN SYSTEM

2.2.1 Vitamin D: Negative Endocrine Regulator of the Renin- Angiotensin system.

Until two decades ago the relationship between 1,25 (OH)2 D (Calcitriol - active form of Vitamin D) and Plasma Renin activity was unclear. It was Li et al. who first demonstrated that calcitriol influences the regulation of Renin production and secretion through Gene expression. Calcitriol functions as the negative endocrine regulator of Renin [23]. This theory was demonstrated by Vitamin D receptor (VDR) - Null mutant mice. VDR Null mutant mice develops elevated plasma levels of Renin due to the lack of VDR - mediated Vitamin D signaling. Hyperreninemia was evidenced by mRNA and protein levels which results in dramatic elevation of Renin level. These mutant mice develops higher blood pressure and cardiac hypertrophy. These effects can be corrected by ACEI or ARB. Moreover, plasma renin levels are found to be significantly reduced in wild-type mice receiving several doses of calcitriol injection [24].

2.3 **Link between Vitamin D and Blood pressure**

Like VDR knock out mice, Cyp27b1 knock out mice also develops hyperreninemia and leads on to hypertension and cardiac hypertrophy. In this model, these adverse effects are treated by exogenous calcitriol supplementation in addition to ACEI and ARBs [25]. They produced a transgenic mouse with over expression of human VDR in the juxtaglomerular

cells. The plasma renin levels are found to be significantly depressed in these transgenic mice without changes in the serum calcium or parathormone levels. These data states that calcitriol suppresses Renin expression in vivo independent of parathormone and calcium. Based on these experiments, It was found that prolonged Vitamin D insufficiency leads to elevated blood pressure, whereas supplementation of vitamin D may be beneficial to the cardiovascular system by decreasing the blood pressure [26].

2.3 Mechanism of Renin suppression

VDR is a ligand- activated transcriptional factor. It regulates both positive and negative transcriptions. Vitamin D response element (VDRE) mediates most of the positive regulations by VDR. There are numerous mechanisms for negative regulations. Intracellular cAMP stimulates the renin expression when the sympathetic nerve activity is high or when there is low tubular sodium chloride concentration. Calcitriol targets the cAMP signaling pathway and that's how it suppresses the Renin expression. This was first demonstrated by Yuan et al. The cAMP signals through the cyclic AMP response element (CRE). CRE then interacts with some transcription factors like ATF/CREB/CREM bZIP. Intracellularly ATP is converted into cAMP and this cAMP binds with protein kinase A (PKA) which causes phosphorylation. This results in the recruitment of co-activators to promote gene transcription. CAMP response element has been shown to play a vital role in the gene expression of renin. Calcitriol suppresses the renin gene transcription by direct inhibition of CRE - mediated transcriptional activity. It has been proved that calcitriol suppresses the Renin expression by blocking the cAMP pathway and thereby preventing the deleterious effects due to hyperreninemia [28].

3. Link between Vitamin D and High Blood pressure

In a study, of randomized controlled trials (RCTs) were electronically searched databases including CNKI, VIP, WanFang Data, the Cochrane Library, PubMed, and EMbase which were about oral vitamin D3 among people with vitamin D deficiency from inception to December 2017. Two reviewers independently screened literature according to the inclusion and extracted data; meta-analysis was performed using RevMan5.3. concluded Oral vitamin D3 has no significant effect on blood pressure in people with vitamin D deficiency. It reduces systolic blood pressure in people with vitamin D deficiency that was older than 50 years old or obese. It reduces systolic blood pressure and diastolic pressure in people with both vitamin D deficiency and hypertension [29].

Another study on; Does Vitamin D Deficiency Lead to Hypertension and concluded Hypertension (HTN) or high blood pressure is one of the most chronic and deadliest disorders in the world. There are many risk factors responsible for HTN which include age, race, using tobacco, high salt intake, etc. One of the risk factors we would like to highlight is low vitamin D levels. While there is strong evidence that Vitamin D plays an important role in maintaining bone and muscle health, there has been recent debate regarding its role in hypertension. However, there are many studies that have shown an indirect relation between 25-hydroxyvitamin D serum level and blood pressure. However, we suggest that more studies, especially randomised trials, should be conducted [30].

Vitamin D, as a natural medicine, is known to regulate calcium and phosphate homeostasis. But abundant research has shown that vitamin D also plays a regulatory role in autoimmunity, inflammation, angiogenesis and vascular cell activity. Since the vitamin D receptor (VDR) is widely distributed in vascular endothelial cells, vascular smooth muscle cells and cardiomyocytes, the role of vitamin D and VDR in hypertension has received extensive attention. Hypertension is a disease with high incidence and high cardiovascular risk. In recent years, both clinical trials and animal experiments have shown that vitamin D plays a regulatory role in decreasing blood pressure (BP) through inhibiting renin-angiotensin-aldosterone system activity, modulating function of vascular wall and reducing vascular oxidative stress. A growing body of data suggest that vitamin D deficiency is associated with increased cardiovascular disease risk in hypertension, even short-term vitamin D deficiency may directly raise BP and promote target organ damage. Due to the high correlation between vitamin D and hypertension, vitamin D supplementation therapy may be a new insight in the treatment of hypertension. The aim of this review will explore the mechanisms of the vitamin D and VDR in regulating the BP and protecting against the target organ damage [31].

Christian Legarth et al. (2018) studied on The Impact of Vitamin D in the Treatment of Essential Hypertension; investigated, whether there is a possible link between vitamin D supplementation and the reduction of blood pressure in hypertensive patients. The renin-angiotensin-aldosterone system is known for being deeply involved in cardiovascular tonus and blood pressure regulation. Hence, many of the pharmaceutical antihypertensive drugs inhibit this system. Interestingly, experimental studies in mice have indicated that vitamin D supplementation significantly lowers renin synthesis and blood pressure. It is conceivable that similar mechanisms may be found in the human organism. Regarding this, large-scale cross-sectional studies suggest the serum 25(OH)D-level to be inversely correlated to the prevalence of hypertension. However, randomized controlled trials (RCTs) have not found a clear association between vitamin D supplementation and improvements in hypertension. Nevertheless, the missing association of vitamin D and hypertension in clinical trials can be due to suboptimal study designs. There are hints that restoration of serum 25(OH)D levels during vitamin D therapy is essential to achieve possible beneficial cardiovascular effects. It is important to perform long-term trials with a short dose interval and a high bioavailability of supplementation. Taken together, more RCTs are required to further investigate if vitamin D can be beneficial for the reduction of blood pressure [32].

Waled Mohamed Alsalmi et al. (2018)[17] studied on Correlation Between Hypothyroidism, Hyperthyroidism, and Lipid Profile in Thyroid Dysfunction Patients; concluded that there is an increase in the most lipid profile in both hypothyroid and hyperthyroid patients and finally dyslipidemia which is one of the major risk factors for atherosclerosis and coronary

disease. There is an increase in total cholesterol, VLDL-C, and levels and decreased in HDL-C in hypothyroidism patients. And there is also increase in total and LDL cholesterol, and decreased in HDL-C level in hyperthyroidism patients [33].

Concluding Remark

One of the most common endocrine disorders seen in clinical practice is hypothyroidism. Because of its pleiotropic properties and ubiquitous receptor expression, vitamin D has demonstrated beneficial effects in a multitude of systems beyond its conventional function in bone health. The complex molecular relationship between vitamin D and the thyroid has long captivated scientists. There have been efforts to prove that vitamin D plays a role in thyroid disorders. Vitamin D's function in hypothyroidism has been surveyed in this article.There has been a recent focus on vitamin D's function as an immune modulator, and vitamin D deficiency is a worldwide health concern. Vitamin D may play a key role in lowering the prevalence of autoimmune diseases, according to mounting evidence. However, there is currently inconclusive evidence regarding its involvement in autoimmune and thyroid diseases.Vitamin D has pleiotropic effects on many different bodily systems, and some research has linked vitamin D insufficiency to hypertension. The effects of vitamin D supplementation on patients with hypertension have been the subject of conflicting findings in various interventional studies. Previous observational and interventional studies have demonstrated the association between vitamin D and hypertension among different populations, and this article reviews the literature that has suggested a mechanism involving vitamin D in the regulation of blood pressure.Hypertension and diabetes may be more common in people with insufficient vitamin D levels. All of these things put you at higher risk of developing heart disease. It is not yet known whether taking a vitamin D supplement every day reduces the risk of cardiovascular disease. It could only benefit people whose vitamin D levels are extremely low.

References

1. Gordan, R., Gwathmey, J. K., & Xie, L. H. (2015). Autonomic and endocrine control of cardiovascular function. World journal of cardiology, 7(4), 204.
2. Furst, B., & González-Alonso, J. (2023). The heart, a secondary organ in the control of blood circulation. Experimental Physiology.
3. Gamperl, A. K., & Driedzic, W. R. (2009). Cardiovascular function and cardiac metabolism. In Fish physiology (Vol. 27, pp. 301-360). Academic Press.
4. Kalehoff, J. P., & Oparil, S. (2020). The story of the silent killer: a history of hypertension: its discovery, diagnosis, treatment, and debates. Current Hypertension Reports, 22(9), 72.
5. Fuchs, F. D., & Whelton, P. K. (2020). High blood pressure and cardiovascular disease. Hypertension, 75(2), 285-292.
6. Lawes, C. M., Vander Hoorn, S., & Rodgers, A. (2008). Global burden of blood-pressure-related disease, 2001. The Lancet, 371(9623), 1513-1518.
7. Yano, Y., & Kario, K. (2012). Nocturnal blood pressure and cardiovascular disease: a review of recent advances. Hypertension Research, 35(7), 695-701.
8. Brunström, M., & Carlberg, B. (2018). Association of blood pressure lowering with mortality and cardiovascular disease across blood pressure levels: a systematic review and meta-analysis. JAMA internal medicine, 178(1), 28-36.
9. Schultz, M. G., La Gerche, A., & Sharman, J. E. (2017). Blood pressure response to exercise and cardiovascular disease. Current hypertension reports, 19, 1-7.
10. Gu, D., Kelly, T. N., Wu, X., Chen, J., Duan, X., Huang, J. F., ... & He, J. (2008). Blood pressure and risk of cardiovascular disease in Chinese men and women. American journal of hypertension, 21(3), 265-272.
11. Rahimi, K., Emdin, C. A., & MacMahon, S. (2015). The epidemiology of blood pressure and its worldwide management. Circulation research, 116(6), 925-936.
12. Zhou, B., Perel, P., Mensah, G. A., & Ezzati, M. (2021). Global epidemiology, health burden and effective interventions for elevated blood pressure and hypertension. Nature Reviews Cardiology, 18(11), 785-802.
13. Lawes, C. M., Vander Hoorn, S., Law, M. R., Elliott, P., MacMahon, S., & Rodgers, A. (2006). Blood pressure and the global burden of disease 2000. Part II: estimates of attributable burden. Journal of hypertension, 24(3), 423-430.
14. Mohammed Nawi, A., Mohammad, Z., Jetly, K., Abd Razak, M. A., Ramli, N. S., Wan Ibadullah, W. A. H., & Ahmad, N. (2021). The prevalence and risk factors of hypertension among the urban population in Southeast Asian countries: a systematic review and meta-analysis. International journal of hypertension, 2021(1), 6657003.
15. Singh, S., Shankar, R., & Singh, G. P. (2017). Prevalence and associated risk factors of hypertension: A cross-sectional study in urban Varanasi. International journal of hypertension, 2017(1), 5491838.
16. Floras, J. S. (2013). Blood pressure variability: a novel and important risk factor. Canadian Journal of Cardiology, 29(5), 557-563.
17. Singh, S., Shankar, R., & Singh, G. P. (2017). Prevalence and associated risk factors of hypertension: A cross-sectional study in urban Varanasi. International journal of hypertension, 2017(1), 5491838.

18. Baksi, A. J., Treibel, T. A., Davies, J. E., Hadjiloizou, N., Foale, R. A., Parker, K. H., ... & Hughes, A. D. (2009). A meta-analysis of the mechanism of blood pressure change with aging. Journal of the American College of Cardiology, 54(22), 2087-2092.
19. de Morais, S. D., Shanks, J., & Zucker, I. H. (2018). Integrative physiological aspects of brain RAS in hypertension. Current hypertension reports, 20, 1-12.
20. Huang, Z., Cao, J., Yao, Y., Jin, X., Luo, Z., Xue, Y., ... & Ge, J. (2020). The effect of RAS blockers on the clinical characteristics of COVID-19 patients with hypertension. Annals of translational medicine, 8(7).
21. Holick, M. F., & Slominski, A. T. (2024). Photobiology of vitamin D. In Feldman and Pike's Vitamin D (pp. 27-45). Academic Press.
22. Han, Y. P., Kong, M., Zheng, S., Ren, Y., Zhu, L., Shi, H., & Duan, Z. (2013). Vitamin D in liver diseases: from mechanisms to clinical trials. Journal of gastroenterology and hepatology, 28, 49-55.
23. Li, Y. C. (2010). Vitamin D, renin, and blood pressure. In Vitamin D: Physiology, Molecular Biology, and Clinical Applications (pp. 937-953). Totowa, NJ: Humana Press.
24. Zhang, Z., Zhang, Y., Ning, G., Deb, D. K., Kong, J., & Li, Y. C. (2008). Combination therapy with AT1 blocker and vitamin D analog markedly ameliorates diabetic nephropathy: blockade of compensatory renin increase. Proceedings of the National Academy of Sciences, 105(41), 15896-15901.
25. Zhang, Z., Zhang, Y., Ning, G., Deb, D. K., Kong, J., & Li, Y. C. (2008). Combination therapy with AT1 blocker and vitamin D analog markedly ameliorates diabetic nephropathy: blockade of compensatory renin increase. Proceedings of the National Academy of Sciences, 105(41), 15896-15901.
26. Cheung, K. S., Chan, E. W., Seto, W. K., Wong, I. C., & Leung, W. K. (2020). ACE (angiotensin-converting enzyme) inhibitors/angiotensin receptor blockers are associated with lower colorectal cancer risk: a territory-wide study with propensity score analysis. Hypertension, 76(3), 968-975.
27. Condoleo, V., Pelaia, C., Armentaro, G., Severini, G., Clausi, E., Cassano, V., ... & Sciacqua, A. (2021). Role of vitamin D in cardiovascular diseases. Endocrines, 2(4), 417-426.
28. Wimalawansa, S. J. (2018). Vitamin D and cardiovascular diseases: Causality. The Journal of steroid biochemistry and molecular biology, 175, 29-43.
29. He S, Hao X. The effect of vitamin D3 on blood pressure in people with vitamin D deficiency: A system review and meta-analysis. Medicine. 2019 May;98(19):e15284.
30. Varshil M, Shivika A. Does Vitamin D Deficiency Lead to Hypertension?. Cureus. 2017;9(2):e1038.
31. Lin L, Zhang L, Li C, Gai Z, Li Y. Vitamin D and vitamin D receptor: New insights in the treatment of hypertension. Current Protein and Peptide Science. 2019 Oct 1;20(10):984-95.
32. Legarth C, Grimm D, Wehland M, Bauer J, Krüger M. The impact of vitamin D in the treatment of essential hypertension. International journal of molecular sciences. 2018 Feb 3;19(2):455.
33. Alsalmi WM, Shaglouf LH, Azab AE. Correlation between hypothyroidism, hyperthyroidism, and lipid profile in thyroid dysfunction patients. Clin Med J. 2018;4(2):6-14.