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Establishing a Connection between Vitamin D and Telomerase-Measured Cellular Senescence in Pre-HTN: An Observational Study

[1]Dr. Deivanayagame B, [2]Dr. Bharathi U, [3]Dr. Priyadharisini J, [4]Dr. Ramkumar Boopathirajan

[1]Associate Professor, Department of Physiology, Sri Lakshmi Narayana Institute of Medical Sciences, Puducherry, India

[2,3]Associate Professor, Department of Pathology, Sri Lakshmi Narayana Institute of Medical Sciences, Puducherry, India

[4]Professor, Department of Community Medicine, P K Das Institute of Medical Sciences, Ottapalam, Kerala, India

Corresponding author: Dr. Deivanayagame B

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KEYWORDS

Hypertension, Vitamin D, cellular senescence

ABSTRACT:

Aim: The aim of the present study was to explore the link between Vitamin D and cellular senescence measured with the enzyme telomerase in pre-HTN.

Methods: The current observational research was carried out by the Physiology Department in association with Pathology. Participants were required to be of either sex and have a systolic blood pressure (SBP) of 120-139 mm Hg and a diastolic blood pressure (DBP) of 80–89 mm Hg in order to be included in the pre-hypertensive group (n = 75). People in the control group (n = 75) were all healthy adults (i.e., 18-25 years old) whose systolic blood pressure (SBP) was 100–119 mm Hg and diastolic blood pressure (DBP) was 60-79 mm Hg.

Results: About 150 healthy people were studied. 75 patients were pre-hypertensive, aged 22.58±1.56, whereas controls were 18.82±1.24. Out of 150, 45 males, 30 females were pre-HTN and 40 men, 35 females were control. Height and waist-hip ratio did not vary significantly across groups. Compared to controls, pre-HTN group subjects had higher BMI ($P < 0.001$) and weight ($P < 0.001$). The pre-HTN group had substantially higher HR, SBP, DBP, MAP, and RPP compared to controls ($P < 0.001$). PP was somewhat higher in pre-HTN group and adversely linked with Vitamin D. Waist-hip ratio, SBP, DBP, MAP, and RPP are correlated with high telomerase levels, whereas BMI, HR, and PP are not.

Conclusion: Reduced Vitamin D levels in pre-HTN may disrupt cardiovascular homeostatic mechanism and accelerate telomerase-measured cellular senescence.

INTRODUCTION

Untreated high blood pressure (hypertension) poses a significant risk for cardiovascular illnesses, including coronary artery disease, myocardial infarction, and stroke [1]. The study findings indicate that a lack of vitamin D improves the progression of hypertension (HT) [2]. Vitamin D deficiency, defined as having a 25-OH-D level below 30 ng/mL, is a separate risk factor for hypertension and contributes to increased cardiovascular mortality [3]. Vitamin D plays a crucial role in maintaining calcium balance and regulating bone health. It is well recognised that supplementing vitamin D in older individuals may effectively decrease the likelihood of fractures [4].

Arterial hypertension (AH) is a prevalent illness characterized by elevated arterial blood pressure (BP). This indicates that the arterial blood pressure remains consistently raised due to the force exerted by the blood on the artery walls. This alteration impacts the cardiovascular system, including the heart, which must exert significant effort to adequately circulate blood throughout the body [5]. HT is often described as a sustained blood pressure reading of ≥140/90 mmHg [6]. The maintenance of a normal blood pressure relies on the equilibrium between the cardiac output and the vascular resistance over the whole body. Moreover, the cardiac output relies on the stroke volume and heart rate (HR) [7].

While identifying a definitive root cause for most

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instances of hypertension (HT) is sometimes challenging, there are many risk factors that may contribute to its development. Several established risk factors, such as age, family history, obesity, sedentary lifestyle, smoking, excessive salt intake, heavy alcohol consumption, and even pregnancy, contribute to the development of hypertension [5]. In addition to lifestyle risk factors, some prescription medications, such as oral contraceptives, non-steroidal anti-inflammatory medicines, cyclosporin, erythropoietin (EPO), and glucocorticoids (steroid hormones), may also elevate blood pressure and cause hypertension [8]. The regulation of a normal blood pressure relies on the equilibrium between the heart's pumping capacity and the resistance of the blood vessels in the body. The regulation of blood pressure involves the interaction of electrical, biological, and mechanical factors. The sympathetic nervous system serves as the electrical component, while the renin-angiotensin-aldosterone system (RAAS), neurotransmitters such as norepinephrine (noradrenaline) and cytokines make up the biochemical component. The mechanical component consists of the heart rate (HR) and the widening or narrowing of the arterioles through vasodilation or vasoconstriction. Hence, hypertension (HT) arises when the body's arterial blood pressure control systems fail, leading to impaired vascular regulation [7].

The objective of this research was to investigate the association between Vitamin D and cellular senescence, as evaluated by the enzyme telomerase, in individuals with pre-HTN.

MATERIALS AND METHODS

The present observational study was conducted by the Department of Physiology.

The inclusion criteria for the pre-hypertensive group (pre-HTN) (n = 75) consisted of people of both genders, aged between 18 and 25 years, with systolic blood pressure (SBP) ranging from 120 to 139 mmHg and diastolic blood pressure (DBP) ranging from 80 to 89 mmHg. These participants were required to be seemingly healthy. The control group consisted of 75 persons who were in good health and aged between 18 and 25 years. Their systolic blood pressure (SBP) ranged from 100 to 119 mmHg, while their diastolic blood pressure (DBP) ranged from 60 to 79 mmHg.

Individuals afflicted with diabetes, hypertension, endocrine disorders, renal ailments, and hypertensive patients already undergoing medication were excluded from participating in this study.

METHODOLOGY

The subjects were instructed to abstain from engaging in strenuous physical activity, consuming alcohol, and consuming coffee within 24 hours before to the data collection. Prior to measuring blood pressure using a sphygmomanometer according to established guidelines, baseline anthropometric measurements were taken [9]. Subsequently, a 5 ml blood sample was obtained, allowed to coagulate, and then exposed to centrifugation in order to isolate the serum. The serum was held at a temperature of -80 °C in order to process the levels of Vit-D and telomerase, following the instructions specified in the commercially available kits.

Data was subjected to statistical analysis. In order to examine the differences between groups, an independent t-test was used. To evaluate the relationship between vitamin D and telomerase, as well as other parameters, Pearson's correlation coefficient analysis was used.

RESULTS

Parameters	Pre-HTN (*n*=75)	Controls (*n*=75)	*P*-value
Age	22.58±1.56	18.82±1.24	0.460
Gender (male/female)	45/30	40/35	1.390
Height (cm)	172.28±8.72	169.71±8.52	0.316
Weight (kg)	65.45±10.40	58.42±8.72	<0.001
BMI (k/m^2)	23.17±4.66	23.67±4.72	<0.001
Waist to hip ratio	0.90±0.12	0.87±0.07	0.474

Table 1: Comparison of anthropometric characteristics between pre-HTN and controls

The sample consisted of 150 people who seemed to be in good health. Out of the total, 75 individuals had pre-

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hypertension at an average age of 22.58±1.56, whereas the control group had an average age of 18.82±1.24. Among the total of 150 participants, there were 45 men and 30 females in the pre- HTN group, whereas the control group consisted of 40 males and 35 females. No significant disparities were seen in height and waist-hip ratio across the groups.

Parameters	Pre-HTN (*n*=75)	Controls (*n*=75)	*P*-value
HR (BPM)	87.43±4.76	82.48±4.82	<0.001
SBP (mmHg)	122.18±4.82	114.6±5.55	<0.001
DBP (mmHg)	81.69±4.07	74.36±4.90	<0.001
PP (mmHg)	41.69±4.96	39.01±5.65	0.172
MAP (mmHg)	93.57±2.84	87.73±3.75	<0.001
RPP	10960.82±702.78	9082.78±488.82	<0.001

Table 2: Comparison of cardiovascular parameters between pre-HTN and controls

Nevertheless, the BMI ($P < 0.001$) and weight ($P < 0.001$) of the pre-hypertension group subjects were higher in comparison to the control group. In the pre-hypertension group, there were substantially higher values of heart rate ($P < 0.001$), systolic blood pressure ($P < 0.001$), diastolic blood pressure ($P < 0.001$), mean arterial pressure ($P < 0.001$), and rate-pressure product ($P < 0.001$) compared to the control group. There was no notable disparity seen in PP. However, it was slightly elevated in the pre-HTN group and exhibited a negative correlation with Vitamin D.

Parameters	Pre-HTN (*n*=100)	Controls (*n*=100)	*P*-value
Vitamin D (ng/ml)	19.21±4.36	21.03±6.34	0.048
Telomerase (IU/ml)	35.85±16.84	7.05±4.96	<0.001

Table 3: Comparison of Vitamin D and telomerase levels between pre-HTN and controls

Elevated telomerase levels exhibit a positive link with waist-hip ratio, systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), and rate-pressure product (RPP). However, no significant correlation was seen with body mass index (BMI), heart rate (HR), and pulse pressure (PP).

DISCUSSION

Hypertension is a prevalent health issue that imposes substantial financial burden on the healthcare system and is a major contributor to both mortality and morbidity on a global scale.10 Hypertension is a prevalent and significant risk factor for several cardiovascular diseases, such as myocardial infarction, cerebral stroke, congestive heart failure, peripheral vascular disorders, and renal disease [11]. Eliminating excessive blood pressure is projected to result in a 35% decrease in stroke incidence and an 18% decrease in heart attack occurrence [12, 13]. In order to alleviate the impact of hypertension, it is necessary to implement a comprehensive lifestyle intervention that encompasses various components. These include shedding excess weight, engaging in more physical activity, limiting the intake of sodium and alcohol, and adhering to a dietary regimen similar to the Dietary Approach to Stop Hypertension. This diet should consist of ample amounts of fruits, vegetables, and low-fat dairy products, while minimizing the consumption of saturated fats [14]. Furthermore, it has been suggested that enhancing vitamin D levels might serve as a readily adjustable risk factor [15].

The research sample consisted of 150 people who were deemed to be in good health. Out of the whole sample, 75 individuals had pre-hypertension and their average age was 22.58±1.56. The average age of the control group was 18.82±1.24. Among the total of 150 participants, there were 45 men and 30 females in the pre-HTN group, whereas the control group consisted of 40 males and 35 females. No significant between-group variations were observed in height and waist-hip ratio. The prevalence of Vitamin D insufficiency has become a significant concern in public health, impacting about half of the global population [16]. Furthermore, apart from decreased sunshine

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exposure [17], genetic and environmental variables have been proposed as potential contributors to this widespread occurrence, including pollution, dietary habits, a sedentary lifestyle and stress [18]. Furthermore, vitamin D is now recognized not only as a crucial regulator of calcium metabolism and bone health, but also as a controller of several cellular processes, such as differentiation and metabolism. This component may elucidate the rationale for the association between hypovitaminosis D and increased overall mortality shown in many cohort analyses [19], while also highlighting the considerable reduction in mortality achieved with vitamin D therapy [20]. In an ongoing investigation, Zhao *et al.* [21] provided a comprehensive account of a favourable correlation between Vitamin D and hypertension as well as pre-hypertension. Forman *et al.* [22] found a direct correlation between Vitamin D levels and the occurrence of hypertension in a study involving 38,388 men from the Health Professionals' follow-up study and 77,531 females from the Nurses' Health Study. They also observed a positive association between Vitamin D and hypertension in a subset of participants. In addition, research conducted as part of the second Nurses' Health research revealed a direct correlation between blood Vitamin D levels and hypertension in a sample of 1484 young females. The NHANES study found a negative correlation between systolic blood pressure (SBP) and vitamin D levels in 12,644 people [23].

Nevertheless, the pre-hypertension group had significantly higher body mass index (BMI) ($P < 0.001$) and weight ($P < 0.001$) compared to the control group. Compared to the control group, the pre-HTN group exhibited substantially elevated heart rate ($P < 0.001$), systolic blood pressure ($P < 0.001$), diastolic blood pressure ($P < 0.001$), mean arterial pressure ($P < 0.001$), and rate-pressure product ($P < 0.001$). There was no notable disparity seen in PP. However, it was slightly elevated in the pre-HTN group and exhibited a negative correlation with Vitamin D. Elevated telomerase levels are positively associated with waist-hip ratio, systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), and rate-pressure product (RPP). However, there is no significant link seen between telomerase levels and body mass index (BMI), heart rate (HR), and pulse pressure (PP). Prior studies have shown a correlation between increased levels of Vitamin D and extended telomere length. This highlights the potential beneficial effects of this hormone on cellular ageing and age-related ailments.[24] evaluation of cellular senescence in this work was conducted by using telomerase. This enzyme aims to impede the process of telomere shortening [25]. Cell telomere loss is believed to be primarily caused by cell division, although to a small extent. However, other factors, including as oxidative stress, have also been identified as playing a role in accelerating the rate of telomere shortening [26]. The precise method via which decreased levels of Vitamin D are linked to cellular senescence is believed to rely on the notion that telomerase levels may be influenced by oxidative stress, with greater levels of oxidative stress leading to increased telomerase activity. Cells in most sophisticated organisms may lack the capacity for division. Hayflick illustrated this phenomenon in 1961 [27].

CONCLUSION

Therefore, it is possible to draw the conclusion that decreased levels of vitamin D in pre-HTN may lead to disruptions in the homeostatic mechanism of the cardiovascular system, as well as an increase in the rate of cellular senescence as assessed by telomerase.

References

[1] Legarth C, Grimm D, Krueger M, Infanger M, Wehland M. Potential beneficial effects of vitamin d in coronary artery disease. Nutrients. 2019 Dec;12(1):99.

[2] Wimalawansa SJ. Vitamin D and cardiovascular diseases: Causality. The Journal of steroid biochemistry and molecular biology. 2018 Jan;175:29-43.

[3] Rai V, Agrawal DK. Role of vitamin D in cardiovascular diseases. Endocrinology and Metabolism Clinics. 2017 Dec;46(4):1039-59.

[4] Delmi M, Rapin CH, Bengoa JM, Bonjour JP, Vasey H, Delmas PD. Dietary supplementation in elderly patients with fractured neck of the femur. The Lancet. 1990 Apr;335(8696):1013-6.

[5] High Blood Pressure (Hypertension).

[6] Elliott WJ. Systemic hypertension. Current problems in cardiology. 2007 Apr;32(4):201-59.

[7] O'Shea PM, Griffin TP, Fitzgibbon M. Hypertension: The role of biochemistry in the diagnosis and management. Clinica Chimica Acta.

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www.jchr.org

JCHR (2024) 14(1), 1838-1842 | ISSN:2251-6727

2017 Feb;465:131-43.

[8] Williams B. Resistant hypertension: an unmet treatment need. The Lancet. 2009 Oct;374(9699):1396-8.

[9] Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo Jr JL, *et al*. Seventh report of the joint national committee on prevention, detection, evaluation and treatment of high blood pressure. hypertension. 2003 Dec;42(6):1206-52.

[10] Mittal BV, Singh AK. Hypertension in the developing world: challenges and opportunities. American Journal of Kidney Diseases. 2010 Mar;55(3):590-8.

[11] Holick MF. Vitamin D: important for prevention of osteoporosis, cardiovascular heart disease, type 1 diabetes, autoimmune diseases, and some cancers. Southern medical journal. 2005 Oct;98(10):1024-8.

[12] Colley RC, Garriguet D, Janssen I, Craig CL, Clarke J, Tremblay MS. Physical activity of Canadian adults: accelerometer results from the 2007 to 2009 Canadian Health Measures Survey. Health reports. 2011 Mar;22(1):7.

[13] Warburton DE, Charlesworth S, Ivey A, Nettlefold L, Bredin SS. A systematic review of the evidence for Canada's Physical Activity Guidelines for Adults. International journal of behavioral nutrition and physical activity. 2010 Dec;7(1):1-220.

[14] Elmer PJ, Obarzanek E, Vollmer WM, Simons-Morton D, Stevens VJ, Young DR, *et al*. Effects of comprehensive lifestyle modification on diet, weight, physical fitness and blood pressure control: 18-month results of a randomized trial. Annals of internal medicine. 2006 Apr;144(7):485-95.

[15] Hosseinpanah F, Yarjanli M, Sheikholeslami F, Heibatollahi M, Eskandary PS, Azizi F. Associations between vitamin D and cardiovascular outcomes; Tehran Lipid and Glucose Study. Atherosclerosis. 2011 Sep;218(1):238-42.

[16] Vitamin D. deficiency. Holick MF. N Engl J Med. 2007;357:266-81.

[17] Lucas RM, Ponsonby AL, Dear K, Valery PC, Taylor B, Van Der Mei I, *et al*. Vitamin D status: multifactorial contribution of environment, genes and other factors in healthy Australian adults across a latitude gradient. The Journal of steroid biochemistry and molecular biology. 2013 Jul;136:300-8.

[18] Holick MF. Environmental factors that influence the cutaneous production of vitamin D. The American journal of clinical nutrition. 1995 Mar;61(3):S638-45.

[19] Pludowski P, Holick MF, Pilz S, Wagner CL, Hollis BW, Grant WB, *et al*. Vitamin D effects on musculoskeletal health, immunity, autoimmunity, cardiovascular disease, cancer, fertility, pregnancy, dementia and mortality-a review of recent evidence. Autoimmunity reviews. 2013 Aug;12(10):976-89.

[20] Amer M, Qayyum R. Relationship between 25-hydroxyvitamin D and all-cause and cardiovascular disease mortality. The American journal of medicine. 2013 Jun;126(6):509-14.

[21] Zhao G. Forde S, Li C, Kris-etherton PM, Etherton TD, Balluz LS. Independent associations of serum concentrations of 25-hydroxyvitamin d and parathyroid hormone with blood pressure among us adults. J hypertens. 2010;28:1821-8.

[22] Forman JP, Giovannucci E, Holmes MD, Bischoff-Ferrari HA, Tworoger SS, Willett WC, *et al*. Plasma 25-hydroxyvitamin D levels and risk of incident hypertension. Hypertension. 2007 May;49(5):1063-9.

[23] Scragg R, Sowers M, Bell C. Serum 25-hydroxyvitamin D, ethnicity and blood pressure in the Third National Health and Nutrition Examination Survey. American journal of hypertension. 2007 Jul;20(7):713-9.

[24] Richards JB, Valdes AM, Gardner JP, Paximadas D, Kimura M, Nessa A, *et al*. Higher serum vitamin D concentrations are associated with longer leukocyte telomere length in women. The American journal of clinical nutrition. 2007 Nov;86(5):1420-5.

[25] Von Zglinicki T. Telomeres and replicative senescence: is it only length that counts? Cancer letters. 2001 Jul;168(2):111-6.

[26] Von Zglinicki T. Oxidative stress shortens telomeres. Trends in biochemical sciences. 2002 Jul;27(7):339-44.

[27] Hayflick L. The limited in vitro lifetime of human diploid cell strains. Experimental cell research. 1965 Mar;37(3):614-36.