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Original Research Article

A Case Control Study to Explore the Link between Vitamin D and Cellular Senescence Measured with the Enzyme Telomerase in Pre-HTN

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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 present study was conducted in the Department of Physiology for one year. Inclusion criteria for the pre-hypertensive group (pre-HTN) (n =100) were both genders between 18 and 25 years of age with SBP between 120 and 139 mmHg and DBP between 80 and 89 mmHg in apparently healthy individuals. The controls (n = 100) population were healthy individuals with 18– 25 years of age with SBP between 100 and 119 mmHg and DBP between 60 and 79 mmHg.

Results: The study population included 200 apparently healthy individuals. 100 were pre- hypertensive with the age of 21.59±1.58 and the age of controls was 19.91±1.26.Out of 200, 55 males, 44 females in pre- HTN group and 52 males, 48 females in the control group. A significant difference was not found between-group differences in height and waist-hip ratio. However, pre- HTN group subject's BMI ($P < 0.001$) and weight ($P < 0.001$) was more compared to controls. In pre-HTN group, significantly higher HR ($P < 0.001$), SBP ($P < 0.001$), DBP ($P < 0.001$), MAP ($P < 0.001$), and RPP ($P < 0.001$) were seen when compared to controls. No significant difference was seen in PP but it was slightly high in pre-HTN group and negatively associated with Vitamin D. High telomerase levels have correlation with waist-hip ratio, SBP, DBP, MAP, and RPP but no significant correlation was seen with BMI, HR, and PP.

Conclusion: It can be concluded that reduced Vitamin D levels in pre-HTN may cause derangements of cardiovascular homeostatic mechanism, enhance the speed of cellular senescence measured by telomerase.

Keywords: Hypertension, Vitamin D, Cellular Senescence.

Introduction

Deficiency of Vitamin D (Vit-D) is undertreated and pandemic yet under-diagnosed worldwide. [1-3] Reports suggest that, in Indian subcontinent, there is 70–100% deficiency of Vit-D, playing pivotal role in a higher risk of development of bone diseases and several noncommunicable diseases like cancer, metabolic diseases, and cardiovascular pathologies, [4] playing role as a major cause for higher health-care burden on Indian health-care system. [5-8] Nowadays, this scenario leading to increased interest from research and clinical trials to examine the role in chronic diseased conditions. The CYP27B1 enzyme activation, receptor of Vit-D was recognized in several cells which are not the components of calcium and phosphorous homeostasis. [9] This increased the focus on the role of D vitamin in various physiological actions. Information is not available to demonstrate the role of D vitamin in cellular processes. [10,11]

Cellular senescence is defined as the deterioration of the cells as a result of aging. [12] It is an essentially irreversible growth arrest of the cell that occurs in response to various cellular stressors, such as telomere erosion, DNA damage, oxidative stress, and oncogenic activation. [13] Cellular senescence plays a role in the development and progression of numerous diseases, such as obesity, while on the other hand, obesity could be a risk factor for accelerating the rate of cellular senescence. [14] Atherosclerosis is a type of prolonged vessel inflammation disease that exhibits a long asymptomatic phase. The progression of this

vascular abnormality could ultimately result in more severe cardiac-related complications. [15]

Obesity is thought to affect cardiovascular events. Indeed, the concept of "metabolically healthy" obesity has been studied, and it has been shown that coronary heart disease may be increased in this obesity phenotype.[16] Low 25(OH)D_3 concentrations increase the risk of hypertension, peripheral vascular disease, diabetes mellitus, myocardial infarction, heart failure, and cardiac mortality. [17] Moreover, it is reported that low 25(OH)D levels are associated with endothelial dysfunction, inflammation, increased vascular stiffness, and high coronary artery calcium scores. [18] Moreover, it is reported that shortened telomere as an early sign and characteristic feature of cellular senescence is a prognostic biomarker for the early identification of subjects at high risk of developing CVD before symptoms appear. [19]

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.

Materials and Methods

The present study was conducted in the Department of Physiology, JNKTMCH, Madhepura, Bihar, India for one year. Inclusion criteria for the pre- hypertensive group (pre-HTN) (n =100) were both genders between 18 and 25 years of age with SBP between 120 and 139 mmHg and DBP between 80 and 89 mmHg in apparently healthy individuals. The controls (n = 100) population were healthy individuals with 18– 25 years of age with SBP between 100 and 119 mmHg and DBP between 60 and 79 mmHg.

Individuals suffering from diabetes, hypertension, endocrine disorders, kidney diseases, and hypertensive patients already receiving medication were not considered to take part in this research. The volunteers were asked to not participate in heavy exercises, not drink alcohol and coffee 1 day before the data collection. Baseline, anthropometric parameters were recorded before recording of the BP by sphygmomanometer as per standard protocol. [20] Then, 5 ml of blood was collected, allowed to clot, and subjected to centrifugation to separate the serum. Serum was stored at –80°C for processing of Vit-D and telomerase levels as per the instructions provided in the commercially available kits.

Statistical analysis was done to analyze the data. To study the between-group differences, independent t-test, to assess the correlation of vitamin D with telomerase and other parameters, Pearson's correlation coefficient analysis was applied.

Results

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

Parameters	Pre-HTN (*n*=100)	Controls (*n*=100)	*P*-value
Age	21.59±1.58	19.91±1.26	0.420
Gender (male/female)	55/44	52/48	1.390
Height (cm)	171.29±9.88	168.76±7.51	0.380
Weight (kg)	64.46±10.38	59.41±8.52	<0.001
BMI (k/m^2)	24.16±4.76	22.78±4.86	<0.001
Waist to hip ratio	0.93±0.10	0.88±0.08	0.474

The study population included 200 apparently healthy individuals. 100 were pre- hypertensive with the age of 21.59±1.58 and the age of controls was 19.91±1.26.Out of 200, 55 males, 44 females in pre- HTN group and 52 males, 48 females in the control group. A significant difference was not found between-group differences in height and waist-hip ratio.

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

Parameters	Pre-HTN (*n*=100)	Controls (*n*=100)	*P*-value
HR (BPM)	86.44±5.70	81.49±4.86	<0.001
SBP (mmHg)	124.16±4.88	112.4±4.56	<0.001
DBP (mmHg)	83.67±4.06	75.35±3.95	<0.001
PP (mmHg)	40.72±5.92	38.02±5.58	0.172
MAP (mmHg)	95.55±2.85	88.72±3.77	<0.001
RPP	10953.86±706.74	9088.72±492.85	<0.001

However, pre- HTN group subject's BMI ($P < 0.001$) and weight ($P < 0.001$) was more compared to controls. In pre-HTN group, significantly higher HR ($P < 0.001$), SBP ($P < 0.001$), DBP ($P < 0.001$), MAP ($P < 0.001$), and RPP ($P < 0.001$) were seen when compared to controls. No significant difference was seen in PP but it was slightly high in pre-HTN group and negatively associated with Vitamin D.

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

Parameters	Pre-HTN (*n*=100)	Controls (*n*=100)	*P*-value
Vitamin D (ng/ml)	18.22±4.32	22.02±6.24	0.044
Telomerase (IU/ml)	34.86±17.83	7.03±5.95	<0.001

High telomerase levels have correlation with waist-hip ratio, SBP, DBP, MAP, and RPP but no significant correlation was seen with BMI, HR, and PP.

Discussion

Hypertension is a common health problem, one of the leading costs to the health care system, and a significant cause of mortality and morbidity worldwide. [21] Hypertension is also one of the most common and influential risk factors of cardiovascular disease including myocardial infarction, cerebral stroke, congestive heart failure, peripheral vascular disorders and kidney disease. [22] It has been estimated that eliminating high blood pressure would reduce the occurrence of stroke by 35% and heart attacks by 18%. [23,24] To reduce the burden of hypertension, a multicomponent lifestyle intervention that includes weight loss, increased physical activity, restricted sodium and alcohol consumption, and adherence to a Dietary Approach to Stop Hypertension like diet with plenty of fruits, vegetables, and low-fat dairy items and little saturated fat is needed. [25] Moreover, improved vitamin D status has been proposed as an easily modifiable risk factor. [26]

The study population included 200 apparently healthy individuals. 100 were pre- hypertensive with the age of 21.59±1.58 and the age of controls was 19.91±1.26.Out of 200, 55 males, 44 females in pre- HTN group and 52 males, 48 females in the control group. A significant difference was not found between-group differences in height and waist-hip ratio. Vitamin D deficiency has recently emerged as a public health problem, affecting almost 50% of the population worldwide. [27] In addition to the reduced exposition to sunlight [28], also genetic and environmental factors have been suggested as a cause of this pandemic, such as pollution, diet, sedentary life style and stress. [29] Moreover, vitamin D is no longer considered as only a pivotal mediator of calcium metabolism and skeletal health, but it also regulates several cell functions, including differentiation and metabolism. This aspect may explain the reason why hypovitaminosis D has been proved to be an independent risk factor for overall mortality in various cohort analyses [30], whereas vitamin D supplementation significantly reduced mortality. [31] Zhao et al [32] in an ongoing report detailed a positive relationship between Vit-D and hypertension and pre-HTN. Forman et al [33] reported a positive relationship between Vit-D and self-revealed occurrence hypertension among 38,388 men from the Health Professionals' follow-up study and 77,531 females from the Nurses' Health Study; a positive affiliation was likewise detailed between Vit-D and hypertension in a subsample of members. Further, a study concentrate from the second Nurses' health study detailed a positive relationship between serum Vit-D and hypertension among 1484 young females. In the NHANES, SBP was demonstrated to be conversely connected with Vit-D among 12,644 participants. [34]

However, pre- HTN group subject's BMI ($P < 0.001$) and weight ($P < 0.001$) was more compared to controls. In pre-HTN group, significantly higher HR ($P < 0.001$), SBP ($P < 0.001$), DBP ($P < 0.001$), MAP ($P < 0.001$), and RPP ($P < 0.001$) were seen when compared to controls. No significant difference was seen in PP but it was slightly high in pre-HTN group and negatively associated with Vitamin D. High telomerase levels have correlation with waist-hip ratio, SBP, DBP, MAP, and RPP but no significant correlation was seen with BMI, HR, and PP. Earlier reports have shown that higher Vitamin D is related to longer telomere length, which underscores the conceivably advantageous impacts of this hormone on cell senescence and age-related conditions. [35] In this study, cellular senescence was assessed using telomerase. This enzyme attempts to inhibit the process of telomere shortening. [36] Since the cell telomere loss appears to result from cell division just to a fractional degree, different components, particularly oxidative stress, were attested to assume a job in the expanded rate for shortening of telomeres. [37] The exact mechanism by which lower Vit-D levels are associated with this cellular senesce is hypothesized dependent on the perceptions recommends that the degrees of the telomerase may really be related to oxidative stress, with higher oxidative stress prompting higher telomerase levels. Cells of nearly complex organism may not have an ability to divide. This marvel was depicted by Hayflick in 1961. [38]

Conclusion

It can be concluded that reduced Vitamin D levels in pre-HTN may cause derangements of cardiovascular homeostatic mechanism, enhance the speed of cellular senescence measured by telomerase.

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