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Status of hs-CRP and Vitamin D in individuals with Prehypertension

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Abstract

Hypertension is one of the most common causes of premature death under non communicable diseases. Prehypertension remains highly unnoticed and gains attention only after its manifestation as established hypertension. Prehypertension is considered as a separate category of blood pressure and early detection is need for the better management. The study includes the genders of both the sexes (n=40) of age between 35 and 50. The individuals were taken with normal blood pressure as control (Group I) and with Prehypertension as cases (Group II). Informed consent was taken from all the subjects. Data is expressed as Mean and Standard deviation and the statistical significance is determined at 5% ($p < 0.05$) level. There is a mean significant elevation of the Systolic and Diastolic blood pressure and high sensitive C-reactive protein (hs-CRP) in Group 2 in comparison to Group 1. The mean value of serum 25-hydroxy cholecalciferol is decreased significantly in Group 2. The proinflammatory state can be identified by the increased levels of hsCRP associated with vitamin D can predict the prehypertensive state. Hence, the early detection of prehypertension is necessary to prevent the development of hypertension and its associated complications.

Keywords: Prehypertension, Hypertension, hsCRP, Vitamin D

Introduction

The incidence of hypertension is on the steep rise and would reach to almost 29% by 2025 among adult population [1]. However, Prehypertension has not been looked into, many a time in general or as a matter of fact in different studies. The JNC (Joint National Committee) 7 has used the term prehypertension on the prevention, detection, evaluation and treatment of high blood pressure recommendations [2,3]. As per the JNC 7 report, the individuals with systolic blood pressure (SBP) between 120 and 139 mm Hg or diastolic blood pressure (DBP) between 80 and 89 mm Hg are considered to have prehypertension [4]. Prehypertensives are at the risk of developing hypertension twice to that of normal people [5]. Many clinical trials proved that prehypertension can be effectively prevented from progressing to hypertension [6] and further leading to cardiac ailments through the measures such as therapeutic intervention as well as life style changes [7]. However studies show that prehypertension is on the rise among Asians with almost one in every three fitting into the prehypertensive range [8]. Inflammation plays an important role in the development of hypertension [9].

The C reactive protein is identified as an inflammatory marker determining the risk of

cardiovascular morbidity and mortality [10]. Vascular inflammation is an evidential factor not only for the development of hypertension but also for its initiation [11]. C reactive protein (CRP) is a plasma protein and an inflammatory marker produced in the liver in response to interleukin-6 (IL-6) and interleukin-1β (IL-1 β) [12]. It is measured as high sensitivity CRP (hs-CRP) and is usually present in traces in healthy individuals. According to Cleveland clinic, hs-CRP less than 1 mg/L is normal, between 1 and 2.9 mg/L indicates intermediate or moderate risk and greater than 3 mg/L shows high risk for cardiovascular disease. However, greater than 10 mg/L signals for further evaluation of the cause of inflammation. hs-CRP is associated with prehypertension and recent onset of hypertension. CRP always rises before blood pressure elevation [13] Hypertension itself causes inflammation producing pro inflammatory cytokines and CRP is elevated as a defence mechanism. CRP inhibits the production of nitric oxide by endothelial cells and this causes leucocyte adhesion, platelet activation, vaso constriction and thrombosis. Angiotensin receptors are unregulated by high CRP levels. Expression of plasminogen activator inhibitor-1 by endothelial cells is enhanced [14]. These two changes could raise the blood pressure and also promote atherogenesis. Thus hs-CRP causes elevated blood pressure and can be used to predict heart attacks, strokes and other related co morbid conditions. Serum 25-OH vitamin D is the active metabolite of circulating Vitamin D**.** The serum levels <20 ng/ml is Vitamin D deficient, the vitamin D insufficiency is 21 to 29 ng/ml and the optimal concentration of 25(OH) D is at least 30 ng/ml [15].

Vitamin D regulates immune cell activity either directly or indirectly [16]. The work of Fristche and Van Etten identified the Vitamin D receptor (VDR) in the immune cells like the neutrophils, activated lymphocytes etc [17]. It also enhances the functions of dendritic cells, monocytes and macrophages. The deficiency of vitamin D and elevation of blood pressure have found to be associated with inflammatory markers. Vitamin D is inversely related to high blood pressure levels [18]. It is also found that vitamin D is associated with prehypertension independent of the compounding risk factors for hypertension such as BMI, eGFR, serum cholesterol etc, [19]. Vitamin D supplementation in insufficiency or deficiency could at least delay the onset of Hypertension from a prehypertensive stage and its complications up to a certain degree [4]. Now, vitamin D is considered an essential adjuvant for treating patients who show active inflammation. Hence, present study is taken up to establish a relation between hs-CRP, Vitamin D and prehypertension, so that the manifestation of hypertension may be delayed with due intervention at the prehypertensive stage.

Materials And Methods

After obtaining institutional ethical committee approval, healthy attendants of the patients who attended MIMS Outpatient and Inpatient Departments were chosen for the study. Both the sexes between the age group 35 to 50 were chosen. 40 subjects with normal blood pressure were taken as controls under Group 1 and 40 with Prehypertension were taken as cases under Group 2 (SBP between 120 and 139 mm Hg or DBP between 80 and 89 mm Hg). Informed consent was taken from all the subjects.

Exclusion Criteria

Subjects with hypertension, diabetes and on treatment with anti hypertensives, statins, anti-inflammatory drugs, alcoholism, and smoking were excluded. The individuals on medication which influence the serum vitamin D levels were also excluded from the study. BP measurements were taken twice after the participants were seated for 5 min using a digital automatic BP monitor. If the measurements differed by more than 10 mmHg, reading was taken for a third time and the average of two near readings were taken. Serum levels of hs-CRP and 25 hydroxy vitamin D levels were estimated from the collected blood samples. For serum hs-CRP, 2 ml of fasting, venous, non-haemolysed blood sample was collected without the aid of a tourniquet, in a plain sterile bulb and analysed immediately. The estimation of serum hs-CRP was done on Automatic analyzer with the Erba Mannheim kit. Serum 25 OH vitamin D was estimated by CLIA.

Statistical Analysis

Data is expressed as Mean and Standard deviation (mean ± SD). Statistical significance among the subjects is observed, the Z test is performed using Microsoft Excel and SPSS software 16.0.The

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statistical significance is determined at 5% ($p < 0.05$) level.

Age and sex matched individuals were chosen under Group 1 and 2 for the present study (Table I).

Results

Table 1: Comparison of mean age in Group 1 and Group 2

Parameter	Group I (n=40) 25 Males & 15 Females	Group II (n=40) 28 Males & 12 Females
	Mean ± SD	Mean ± SD
Age	44.10±4.32	44.07±4.26

The sex distribution in group I for males is (62%), females (38%) and in group II, the males are (70%) and females (30%) respectively. The mean age in group I and II is 44 and the age is ranging in both the groups is 35 to 50 (Table I)

The present work shows that in some of the subjects who claim to be healthy and not being treated for any medical or surgical condition, the systolic (between 120 and 139 mm Hg) and the diastolic blood pressure between 80 and 89 mm Hg) were in the prehypertensive range which would have gone unnoticed until hypertension manifests in due course of time (Table 2).

Table 2: Comparison of Systolic and Diastolic blood pressures among Group 1 and Group 2

Parameter	Group 1 (n=40)	Group II (n=40)	P value
	Mean ± SD	Mean ± SD	
Systolic Blood Pressure (mm Hg)	115.45±4.27	130.1 ±4.36	<0.001
Diastolic Blood Pressure (mm Hg)	74.35±5.24	84.15±1.99	<0.001

The mean Systolic and Diastolic blood pressure increased in Group 2 when compared to Group 1 and this increase is statistically significant (p value <0.05)

In these prehypertensives, the hs-CRP levels are higher compared to the normotensives. The vitamin D levels are lower in the subjects with prehypertension compared to those with normal blood pressure. These findings are statistically significant ($p < 0.05$) (Table 3 and 4).

Table 3 Comparative study of serum 25-hydroxy cholecalciferol in Group 1 and Group 2

Parameter	Group I (n=40)	Group II (n=40)	P value
	Mean ± SD	Mean ± SD	
25-hydroxy cholecalciferol (ng/mL)	31.25 ± 2.44	17.85± 4.59	<0.001

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The mean serum 25-hydroxy cholecalciferol is decreased in Group2 when compared to Group 1 and this decrease is statistically significant (p value <0.05).

Table 4: Comparative study of serum hs-CRP in Group1 and Group 2

Parameter	Group I (n=40)	Group II (n=40)	P value
	Mean ± SD	Mean ± SD	
hS-CRP	0.77± 0.30	2.49±0.84	<0.001

The mean serum hs-CRP is increased in Group2 when compared to Group 1 and this increase is statistically significant (p value <0.05).

Discussion

In the third National Health and Nutrition Examination survey (NHANES III) in the United States, there was a clear association of elevated CRP levels with blood pressure [20]. The same findings were established among both men and women by ATTICA study in Europe [21]. The women's health study in United States gave a similar report that CRP levels are higher in prehypertensives and there is a risk of developing Hypertension [22]. Various mechanisms establishing the link between the CRP and Hypertension have been put forth. Elevated CRP stimulates endothelial dysfunction which down regulates NO synthesis causing vasoconstriction. Angiotensin II type 1 receptor is expressed by vascular smooth muscle cells. This leads to the development of hypertension [23]. Circulatory Inflammatory markers are an inevitable finding in arterial stiffening measured by pulse wave velocity and augmentation index. Increase in the large artery stiffness is associated with increased blood pressure [24]. The study of Ki Chul Sung and other workers found that in Korean population, hs-CRP was an independent risk factor for the development of hypertension. Even the CRP levels have come down along with the blood pressures when the patients were treated with Angiotensin converting enzyme inhibitor in few clinical trials [25]. Positive association between hs-CRP and BP is attributed also to oxidative stress and interaction with adhesion molecules, Plasminogen activator inhibitor and LDL cholesterol uptake. Moreover, hs-CRP levels vary with the duration of hypertension and are significantly elevated with a history of shorter duration that is less than 1 year compared to the history of longer duration of more than five years [26]. Vitamin D too has profound influence on blood pressures. It improves endothelial function and alters the production of proinflammatory cytokines. Vitamin D also reduces the activity of Renin angiotensin aldosterone system. It also reduces the Parathyroid hormone levels [27]. A meta analysis of observational studies and genetic studies reported that there is 16% higher risk of hypertension with every 16ng/ml decrement in Vitamin D [28] and also the polymorphisms related to lower vitamin D status are associated with elevated blood pressure. The guidelines for prehypertension have an unequivocal role in preventing the occurrence of high blood pressures. However identifying the subjects with prehypertension when primary prevention is effective requires still more awareness among the general public. Prevention or reduction of hypertension by vitamin D through its immunomodulatory and anti inflammatory effects is clearly evident in many studies. It acts on rennin angiotensin system as an endogenous inhibitor causing a decrease in blood pressure [29]. The present study reflects the need to identify the rising sign of inflammation measuring as hs-CRP and Vitamin D levels in subjects who may be on the threshold of prehypertension and consequently prevent the continuum to hypertension and cardiovascular diseases.

Summary

In the present study, otherwise normal individuals were diagnosed as prehypertensives as per JNC 7 classification of prehypertension. These individuals showed a higher range of hs-CRP compared to

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normotensives. Vitamin D levels have also showed a fall in prehypertensives. The deficiency of vitamin D and the elevation of blood pressure are associated with inflammatory marker production measured as hs-CRP in the present study.

Conclusion

The hs-CRP detects the pro-inflammatory state and along with vitamin D deficiency can act as a warning signal for the development of prehypertension. Therefore, the early detection of elevated hs-CRP or decreased vitamin D or detection of prehypertension should be a wakeup call to prevent the development of hypertension and the consequent risk associated with it such as Coronary artery disease and stroke . Our study emphasizes the seriousness of prehypertension progressing to hypertension and insists on the promotion of appropriate life style modification or therapeutic approach to prevent as well as control elevated blood pressure.

References

1. Kearney PM, Whelton M, Reynolds K, Muntner P, Whelton PK, He J. Global burden of hypertension: analysis of worldwide data. The lancet. 2005; 365 (9455):217-23.
2. Singh RB. Indian Consensus for Prevention of Hyertension and Coronary Artery Disease: Indian Consensus Group: Report of a Consensus Development Workshop Conducted by the Indian Society of Hypertension and the International College of Nutrition, New Delhi, 1995. Journal of Nutritional & Environmental Medicine. 1996; 6(3):309-18.
3. Singh RB, Suh IL, Singh VP, Chaithiraphan S, Laothavorn P, Sy RG, Babilonia NA, Rahman AR, Sheikh S, Tomlinson B, Sarraf-Zadigan N. Hypertension and stroke in Asia: prevalence, control and strategies in developing countries for prevention. Journal of human hypertension. 2000; 14(10-11):749.
4. Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo Jr JL, Jones DW, Materson BJ, Oparil S, Wright Jr JT, Roccella EJ. The seventh report of the joint national committee on prevention, detection, evaluation, and treatment of high blood pressure: the JNC 7 report. *JAMA*. 2003; 289 (19):2560-71.
5. Vasan RS, Larson MG, Leip EP, Kannel WB, Levy D. Assessment of frequency of progression to hypertension in non-hypertensive participants in the Framingham Heart Study: a cohort study. The Lancet. 2001; 358 (9294):1682-6.
6. Julius S, Nesbitt SD, Egan BM, Weber MA, Michelson EL, Kaciroti N, Black HR, Grimm Jr RH, Messerli FH, Oparil S, Schork MA. Feasibility of treating prehypertension with an angiotensin-receptor blocker. New England Journal of Medicine. 2006. 20; 354 (16):1685-97.
7. Trials of Hypertension Prevention Collaborative Research Group. Effects of weight loss and sodium reduction intervention on blood pressure and hypertension incidence in over-weight people with high normal blood pressure: the Trials of Hypertension Prevention, Phase II. Arch. Intern. Med.. 1997; 157:657-67.
8. Choi KM, Park HS, Han JH, Lee JS, Lee J, Ryu OH, Lee KW, Cho KH, Yoon D, Baik SH, Choi DS. Prevalence of prehypertension and hypertension in a Korean population: Korean National Health and Nutrition Survey 2001. Journal of hypertension. 2006; 24 (8):1515-21.
9. Bataillard A, Renaudin C, Sassard J. Silica attenuates hypertension in Lyon hypertensive rats. Journal of hypertension. 1995; 13(12 Pt 2):1581-4.
10. Retterstol L, Eikvar L, Bohn M, Bakken A, Erikssen J, Berg K. C-reactive protein predicts death in patients with previous premature myocardial infarction—a 10 year follow-up study. Atherosclerosis. 2002; 160 (2):433-40.
11. LI Jian-jun. Inflammation in hypertension: primary evidence. Chin Med J. 2006;119:1215-21.
12. Hirschfield GM, Pepys MB. C-reactive protein and cardiovascular disease: new insights from an old molecule. Qjm. 2003; 96 (11):793-807.
13. Coban E, Ozdogan M, Yazicioglu G, Sari R. The effect of fenofibrate on the levels of high sensitivity C-reactive protein in dyslipidaemic hypertensive patients. International journal of clinical practice. 2005;59 (4):415-8.

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14. Sinha S, Kar K, Soren M, Dasgupta A. hsCRP in pre-hypertension and hypertension: a prospective study in Southern Asian region. International Journal of Research in Medical Sciences. 2017; 2 (4):1402-7.

15. JUN JG, Hahn TJ. Natural and synthetic sources of circulating 25-hydroxyvitamin D in man. Nature. 1973; 244 (5417):515.

16. Institute of Medicine (US) Standing Committee on the Scientific Evaluation of Dietary Reference Intakes. Dietary reference intakes for calcium, phosphorus, magnesium, vitamin D, and fluoride. National Academies Press (US); 1997.

17. Fritsche J, Mondal K, Ehrnsperger A, Andreesen R, Kreutz M. Regulation of 25- hydroxyvitamin D3-1α-hydroxylase and production of 1α, 25-dihydroxyvitamin D3 by human dendritic cells. Blood. 2003; 102 (9):3314-6.

18. Patel S, Farragher T, Berry J, Bunn D, Silman A, Symmons D. Association between serum vitamin D metabolite levels and disease activity in patients with early inflammatory polyarthritis. Arthritis & Rheumatism: Official Journal of the American College of Rheumatology. 2007;56 (7):2143-9.

19. Sabanayagam C, Shankar A, Somasundaram S. Serum vitamin D level and prehypertension among subjects free of hypertension. Kidney and Blood Pressure Research. 2012; 35(2):106-13.

20. King DE, Egan BM, Mainous III AG, Geesey ME. Elevation of C-reactive protein in people with prehypertension. The Journal of Clinical Hypertension. 2004 ; 6 (10):562-8.

21. Chrysohoou C, Pitsavos C, Panagiotakos DB, Skoumas J, Stefanadis C. Association between prehypertension status and inflammatory markers related to atherosclerotic disease: The ATTICA Study. American journal of hypertension. 2004; 17 (7):568-73.

22. Sesso HD, Buring JE, Rifai N, Blake GJ, Gaziano JM, Ridker PM. C-reactive protein and the risk of developing hypertension. JAMA. 2003 ; 290 (22) :2945-51.

23. Montero I, Orbe J, Varo N, Beloqui O, Monreal JI, Rodríguez JA, Díez J, Libby P, Páramo JA. C-reactive protein induces matrix metalloproteinase-1 and-10 in human endothelial cells: implications for clinical and subclinical atherosclerosis. Journal of the American College of Cardiology. 2006; 47 (7):1369-78.

24. Boos CJ, Lip GY. Elevated high-sensitive C-reactive protein, large arterial stiffness and atherosclerosis: a relationship between inflammation and hypertension?. Journal of human hypertension. 2005; 19 (7):511.

25. Santi RG, Valeff EC, Duymovich CR, Mazziotta D, Mijailovsky NE, Filippa GC, Maltez R, Hernandez VA, Monroy AG, Borzi JG, Acheme RA. Effects of an angiotensin-converting enzyme inhibitor (ramipril) on inflammatory markers in secondary prevention patients: RAICES Study. Coronary artery disease. 2005;16 (7): 423-9.

26. King DE, Egan BM, Mainous III AG, Geesey ME. Elevation of C-reactive protein in people with prehypertension. The Journal of Clinical Hypertension. 2004; 6 (10): 562-8.

27. Brickman A, Nyby M, von Hungen K, Eggena P, Tuck M. Parathyroid hormone, platelet calcium, and blood pressure in normotensive subjects. Hypertension. 1991; 18 (2):176-82.

28. Burgaz A, Orsini N, Larsson SC, Wolk A. Blood 25-hydroxyvitamin D concentration and hypertension: a meta-analysis. Journal of hypertension. 2011; 29 (4):636-45.

29. Ullah MI, Uwaifo GI, Nicholas WC, Koch CA. Does vitamin d deficiency cause hypertension? Current evidence from clinical studies and potential mechanisms. International journal of endocrinology. 2010; 2010

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