CORRELATION OF VITAMIN D WITH HYPERTENSION IN PATIENTS WITH CARDIOMETABOLIC SYNDROME

Robina Usman[1], Farzana Khan[2], Munaza Khattak[3], Zain ul Abideen[4]

[1-3] Department of Physiology, Peshawar Medical College, Peshawar - Pakistan
[4] Department of Physiology, KIMS, Kohat - Pakistan.
Address for Correspondence:
Dr. Robina Usman
Assistant Professor, Department of Physiology, Peshawar Medical College, Riphah International University, Islamabad - Pakistan.
Email: robinariaz999@gmail.com
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ABSTRACT

Objective: To find out correlation between vitamin D and hypertension in patients with cardiometabolic syndrome (CMS).

Methodology: It was a case control study carried out from January to April 2012. Fifty adult patients of CMS and fifty controls were selected in Endocrinology Unit of Hayatabad Medical complex (HMC) by purposive sampling. Controls were age and gender matched relatives of patients. CMS patients were selected by IDF criteria. Waist circumference and blood pressure was recorded. Fasting blood sugar and lipid profile were assessed. 25-hydroxy vitamin D concentrations in serum were estimated by ELISA in HMC pathology laboratory. Analysis was done by using SPSS 17. Chi-square test was applied among individuals with different blood pressure and vitamin D2 levels.

Results: Mean systolic BP was 141.82 ±15.16 and 119.84 ±7.20 mmHg in patients and controls respectively, whereas mean diastolic BP was 88.70 ±6.211 and 75.70 ±5.15mmHg respectively. Vitamin D2 in cases and controls came out to be 15.03 ±18.11 and 24.11 ±17.05 ng/ml respectively. A significant p value of <0.05 was obtained suggesting a likely correlation between hypertension and hypovitaminosis D. Pearson's correlation for systolic BP was r =-0.175, p value =0.18. For diastolic BP, r =0.194, p = 0.05 (correlation was significant at level 0.05). OR was 5.053 revealing hypovitaminosis D to be a likely risk factor.

Conclusion: Our results suggest that hypertension is likely to be correlated with hypovitaminosis D.

Key Words: Cardiometabolic syndrome, 25-hydroxy vitamin D, hypertension

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INTRODUCTION

Cardiometabolic syndrome (CMS) or metabolic syndrome is a group of interrelated metabolic derangements that include increased waist circumference, decreased serum high density lipoproteins, increased serum triglyceride levels, hypertension and insulin resistance[1].

Definitions by the World Health Organization (WHO), National Cholesterol Education Program Adult Treatment Panel III and International Diabetes Federation (IDF) agree that the core criteria of metabolic syndrome include: i) blood glucose impairment (hyperglycemia and/or insulin resistance), ii) excess abdominal/body fat (increased waist and/or obesity), iii) dyslipidemia (low HDL-cholesterol and/or high triglycerides), and iv) elevated blood pressure. However, criteria and cut-off values differ between these definitions, implying that different definitions may identify different people[2].IDF in 2005, improved the definition of the CMS which is shown in table 1.

For clinical diagnosis, a higher cut point is used for different ethnic groups in the USA but, ideally for epidemiological studies, ethnic group specific cut points should be used for people of the same ethnic group[4].

Hypovitaminosis D has been associated with various components of CMS. An inverse correlation has been observed between the prevalence of CMS and vitamin D status in various studies[5,6]. Maki et al[7] carried out a study on 257 men and women and found low serum vitamin D independently associated with CMS and with one of the markers of metabolic syndrome, HDL-C. Alexander et al[8] reported an inverse association between vitamin D and CMS by analyzing data collected by National Health and Nutrition Examination (NHANES) III survey. Hypovitaminosis D causes increased renin-angiotensin II expression[9]. Vitamin D regulates BP by inhibiting gene expression of renin. Renin, an enzyme is an important component of RAS (renin angiotensin system) and regulates BP[10]. In obesity, RAS is up-regulated leading to sodium retention. Adipose tissue produces all components of RAS and adipocytes express angio-

Table 1: International Diabetes Federation metabolic syndrome criteria

Components	Definitions
Central Obesity	Waist circumference (see below) ethnicity specific plus any two of the following:
Raised Triglycerides	≥1.7mmol/l (150 mg/dl) or specific treatment for this lipid abnormality
Reduced HDL-Cholesterol	<1.03 mmol/l (40 mg/dl) in males <1.29 mmol/l (50 mg/dl) in females Or specific treatment for this lipid abnormality
Raised Fasting Plasma Glucose	Fasting plasma glucose ≥5.6 mmol/l (100 mg/dl) or previously diagnosed type 2 diabetes
	If >5.6 mmol/l or 100 mg/dl, oral glucose tolerance test is strongly recommended but is not necessary to define presence of the syndrome
Raised Blood Pressure	Systolic: ≥130 mmHg or Diastolic: ≥85 mmHg or treatment of previously diagnosed hypertension

*Waist circumference for asian men is ≥90 cm and women is ≥80 cm according to IDF consensus[3].

tensin receptors[11]. Higher circulating C-Reactive proteins (CRP) concentration indicate low-grade systemic inflammation and along with elevated pro-inflammatory cytokines, CRP contributes to the development of atherosclerotic plaques[12]. Deranged lipid metabolism, activation of the RAS, and hyperleptinemia lead to the development of hypertension[10].

Since hypovitaminosis D is a treatable cause and if it can be implicated in causing hypertension in patients with CMS, we can very well correct it thus preventing occurance of hypertension in such patients. This will be of huge benefit and this was the reason that lead us to find out a correlation between hypertension and hypovitaminosis D in patients with CMS.

METHODOLOGY

Fifty adult patients both males and females were selected through purposive sampling from the admitted patients in Endocrinology Unit, of HMC. Fifty normal apparently healthy males and females, mostly age and sex matched relatives of the patients were included as controls. Patients with cardiometabolic syndrome were selected according to IDF criteria which included ethnic specific waist circumference for asians (waist circumference ≥90cm for men, ≥80cm for women).

The following subset of patients were excluded from the study because these conditions affect the metabolic functions of the body. Based on history, self-reporting of or receiving treatment for conditions as renal failure, rheumatoid arthritis, thyroid or parathyroid disorders, heart failure, bone metabolic disorders, adrenal insufficiency and malignancies were excluded. Patients with the history of using drugs such as steroids, calcium, vitamin D and other substances that can affect bone metabolism were also excluded from the study.

Body weight was recorded using a digital scale. Height was measured using a measuring tape with patient standing straight against the wall. Waist circumference was measured by using a measuring tape in cm. The measuring tape was put around the waist in the horizontal plane in the center between the lower border of ribs and the iliac crest at the end of normal expiration[14].

Blood pressure was recorded by using mercury sphygmomanometer. 5ml of blood was obtained in fasting condition and allowed to clot. Serum was separated by centrifugation within 30-45 minutes. Fasting glucose level was determined. Rest of the serum samples, properly labeled were stored at -18 to -20°C (frozen) for further investigation in batches in HMC pathology laboratory. Fasting blood sugar estimation was done by using the kit Glucose Liquicolor GOD-PAP (Glucose oxidase-phenol and 4 aminophenazone) catalogue number 10121 by Human (Germany) on Roche/Hitachi 902 Automatic Analyzer through enzymatic colorimetric test. GOD-PAP Method was used for glucose estimation[14]. Total serum cholesterol, serum triglycerides (TG) and high density lipoproteins-cholesterol (HDL-C) were estimated by enzymatic colorimetric method on Roche/Hitachi 902 Automatic Analyzer[15]. 25-hydroxy vitamin D concentrations in serum were estimated by ELISA technique using commercially available kit Euroimmun 25-hydroxy vitamin D ELISA (Germany) on ELISA Instrument Euroimmun Analyzer 1, fully automated ELISA processor (Germany) according to manufacturer's

instructions[16]. It was also carried out in HMC Pathology laboratory. Vitamin D levels were assessed as follows according to criteria in an article by Michael F. Holick[17]: (<20ng/ml=deficiency; 21-29 ng/ml=insufficiency; >30 ng/ml=normal and >150 ng/ml=intoxication).

Data analysis was performed using statistical package for the social sciences (SPSS) 17. Data of the whole study population was expressed as mean ±SD. Chi-square test was applied among individuals with different blood pressure status and vitamin D2 levels. This study was ethically approved by the IRB (instituitional review board) of Peshawar Medical College and Hayatabad medical Complex .Written informed consent was taken from the study participants.

RESULTS

The number of study participants was 100. As it was a matched study the relative percentages of males and females in both the groups was almost the same that is 48% and 50% males in cases and controls group versus 52% and 50% females for the respective groups (table 2). The number of study participants who had hypertension were 22 and 19 having low and normal vitamin D2 level respectively (table 3). There were 11 individuals who were normotensive with low vitamin D2. P value was significant (0.01) (table 4). The risk of developing hypertension was 5 times (odds ratio 5.053) greater for people with low vitamin D2 compared to people having normal D2 level. Individuals with normal vitamin D2 levels had very little risk (0.197) to develop hypertension.

A low level of association was observed between systolic, diastolic BP and vitamin D2. Pearson's coefficient(r) was (-.175), p value =0.18 and (-.194), p value =0.05 for systolic and diastolic BP (mmHg) respectively. However, this correlation remained statistically significant for diastolic blood pressure only.

Table 2: Characteristics of study population

Characteristics	Cases (n=50) Mean (±SD)	Controls (n=50) Mean(±SD)	P value
Demographics			
Age (years)	51.30±5.25	50.40±4.84	0.53
Height (cm)	158.2±6.71	161.42±7.17	0.74
Weight (kg)	75.40±10.74	59.72±5.99	0.04*
Clinical Variables			
Systolic BP (mmHg)	141.82±15.16	119.84±7.20	0.04*
Diastolic BP (mmHg)	88.70±6.211	75.70±5.15	0.04*

*(significant) S.D. = standard deviation

Table 3: Mean blood pressure among cases and controls

Blood pressure	Cases n=50	Controls n=50	Total n=100	P value
Normal	9 (18%)	50 (100%)	59 (59%)	0.03*
High	41 (82%)	0 (0%)	41 (41%)	

*(significant) Key: Blood Pressure (B.P) interpretation3 Normal: less than 130/85 mmHg
High: greater than or equal to 130/85 mmHg

Table 2: Cross tabulation of vitamin D2 and blood pressure

Vitamin D2 Status	Blood Pressure		Total	P value
	Hypertension	Normal		
Low	22	11	33	0.01
Normal	19	48	67	
Total	41	59	100	
	41.0 %	59.0 %	100%	

DISCUSSION

Our study revealed a likely correlation between hypovitaminosis D and hypertension. Compared to people having normal vitamin D2 level, those with hypovitaminosis D were 5.05 times at a greater risk of developing hypertension in patients with CMS. Similarly, Forman et al[18] observed an association between hypovitaminosis D and hypertension. Individuals with hypovitaminosis D had 3.2 times higher risk of hypertension compared to individuals with optimal vitamin D levels. Also, a study in Netherlands by Snijder et al[19] found that blood pressure and vitamin D levels were inversely related. However, in contrast to this study, Griffin et al[20] did not find any association between vitamin D status and current blood pressure. This may be due to geographical differences, dress, complexion etc.

Our study showed that those individuals with a high diastolic BP were found to have low vitamin D levels depicted by a significant p value and proven by Pearson's correlation. Vitamin D was found to be inversely related to diastolic BP in our study but had no correlation with the systolic BP. This finding was supported by some studies while in others, results were different. Judd et al[21] found an inverse relationship between vitamin D and systolic BP by the data of NHANES III.

Several studies have demonstrated that relatively higher serum 25(OH)D levels result in lower average blood pressure, reducing prevalence of hypertension[22]. Furthermore, Scragg et al[22] observed the data from NHANES III and found that diastolic blood pressure was 1.6 mmHg lower ($p < 0.05$) and systolic blood pressure was 3.0 mmHg lower ($p < 0.001$) in individuals in the highest quintile of vitamin D status compared to participants in the lowest quintile of vitamin D status after adjusting for ethnicity, age, gender and physical activity. Hypovitaminosis D in overweight or obese individuals may be the cause of increased BP as observed by Morse et al[23] in their study. The possible explanation is that adipose tissue stores vitamin D decreasing its bioavailability[24]. Furthermore, obese individuals have fewer outdoor activities, have less sun exposure, which is the major source of vitamin D[25]. Reduced vitamin D in subjects of this study can be due to the sample collection in winter, covered dress or indoor living where there is lack of exposure to sun. The other cause may be obesity in which adipose tissue acts as a "metabolic well"[26]. The patients in our study were around fifty years of age when they are more prone to develop osteoarthritis, leading to lesser physical activity and putting on extra pounds as a result.

LIMITATIONS

Our study had some limitations like physical activity was not considered and average sun exposure index was not calculated. Some of the female participants covered their faces with veils along with the fully covered dress. Darker complexion was also not taken into account. Air pollution was also not considered which may hinder penetration of UVB rays in the skin. Lastly, it was a case control study with a small sample size. In future, studies should be carried out with a larger sample and a better study design to yield a better result.

CONCLUSION

This study suggests a likely correlation between hypovitaminosis D and hypertension in patients with CMS.

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CONTRIBUTORS

RU Conceived the idea, collected data, drafted the manuscript and final revision of the manuscript. FK helped compilation and interpretation of data and statistical analysis. MK did references collection and critical revision of manuscript. ZUA did data collection and lab work. All authors contributed significantly to the submitted manuscript.