

VITAMIN D STATUS IN PATIENTS WITH CARDIOMETABOLIC SYNDROME

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ABSTRACT

Objective: To compare the vitamin D status in patients of cardiometabolic syndrome (CMS) with that of normal individuals in our local population of Khyber Pakhtunkhwa (KPK), Pakistan.

Material and Methods: Fifty adult patients of CMS and fifty controls were selected in Endocrinology Unit, Hayatabad Medical Complex (HMC), Peshawar by convenient consecutive sampling. Duration of study was from January 2012 to April 2012. Age, sex, height, weight, waist circumference, B.P (blood pressure) were measured. Fasting blood sugar (FBS) and lipid profile were assessed by using venous blood. Vitamin D status (25-hydroxyvitamin D) of patients and controls was analyzed by ELISA (Enzyme Linked Immunosorbent Assay). Data was analyzed using independent t-test, chi-square test and Levene's test for equality of variance. P value was calculated by Fischer exact test.

Results: 42% had low vitamin D levels in the cases whereas 4% of controls had hypovitaminosis D. The odds ratio (OR) was 0.139 with confidence interval of .037 - .530 and P value < 0.01 which showed that vitamin D was a protective factor for the development of CMS.

Conclusion: It is concluded that in our local population, there is significant prevalence of vitamin D deficiency in patients suffering from CMS.

Key Words: Cardiometabolic, syndrome, 25-hydroxy, vitamin D, waist, circumference.

INTRODUCTION

Vitamin D has a pivotal role not only in maintaining bone health¹ and calcium homeostasis but its deficiency has been found to be associated with many other disorders, one of these is CMS.^{2,3,4} CMS is a group of metabolic derangements that include increased waist circumference, insulin resistance, hypertension, raised serum triglyceride levels and reduce serum high density lipoproteins.⁵ Central abdominal obesity is a main feature which reveals that CMS has a strong relationship between waist circumference and increasing adiposity.⁶ Visceral fat is strongly linked with the condition.⁷

Pathophysiology include components of renin-angiotensin-system (RAS), adipocytokines, dysfunction of the hypothalamic-pituitary-adrenal (HPA) axis and insulin resistance.⁵ According to Zittermann et al, vitamin D may affect cell proliferation, inflammation,

vascular calcification, and BP through the RAS.⁸ High concentrations of tumor necrosis factor alpha (TNF- α) and interleukin (IL-6) will result in formation of C-reactive protein (CRP) in the liver.⁹ Lack of Vitamin D is common throughout the world. Approximately, about 1 billion global population is suffering from vitamin D insufficiency or deficiency.¹⁰ Vitamin D insufficiency is mostly defined as 25(OH)D level of 21-29ng/milliliter and vitamin D deficiency as <20ng/milliliter. The optimal concentration of 25(OH)D is taken at least 30ng/milliliter, >150ng/milliliter is toxicity.¹¹ Recommended dosage of vitamin D for adults more than 19 years of age is 1500-2000 IU/day.^{12,13,14}

The best indicator of vitamin D in people without kidney disease is serum 25(OH)D as it has a longer half-life.¹³ Function of vitamin D in regulating pancreatic β -cells is revealed by vitamin D receptors (VDRs) in pancreatic β -cells nuclei where binding of vitamin D takes place. VDR discovered in 1969¹⁴ is a ligand triggered transcription factor expressed in most tissues like vascular smooth muscle, endothelium, osteoblasts, pancreatic β -cells, skeletal muscle, cardiomyocytes, brain, breast and prostate gland.^{1,10} Vitamin D modifies gene expression at the cellular level.¹ Due to these features, vitamin D can also affect tissues that are not involved in bone metabolism.^{15,16}

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MATERIAL AND METHODS

Fifty adult patients both males and females were selected through convenient consecutive sampling from the admitted patients in Endocrinology Unit, HMC, Peshawar, Pakistan. According to inclusion criteria of our study, patients with CMS were selected as per definition of International Diabetes Federation (IDF) which also included ethnic specific waist circumference.

Patients suffering from conditions as rheumatoid arthritis, thyroid or parathyroid disorders, adrenal insufficiency, renal failure, heart failure, bone metabolic disorders, diabetes mellitus type I, malignancies etc. were excluded as these affect the metabolic functions of the body. Subjects with the history of using drugs such as steroids, calcium and vitamin D were also excluded from the study. Fifty normal apparently healthy males and females, mostly age and sex matched relatives of the patients were included as controls.

Body weight was recorded on a digital scale (Seca 840; Seca GmbH, Hamburg, Germany). Height was measured with a scale in centimeters. Waist circumference was measured in cm. Measuring tape was put around the waist in the horizontal plane halfway between the costal margin and the iliac crest at the end of normal expiration. Blood pressure was recorded by using mercury sphygmomanometer.

5 ml of blood was obtained in fasting condition and allowed to clot. Serum was separated by centrifugation within 30-45 minutes. The serum samples were then properly labeled and stored at -18 to -20°C (frozen) for further investigation in batches in HMC pathology laboratory.

Fasting blood sugar estimation was done on fresh blood samples 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.

Total serum cholesterol: High density lipoproteins-cholesterol (HDL-C) and serum triglycerides (TG) were estimated by enzymatic colorimetric method on Roche/Hitachi 902 Automatic Analyzer. 25-OH vitamin D estimation: 25-hydroxy vitamin D concentration in serum was 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 in the HMC Pathology laboratory. According to the interpretation criteria of the ELISA kit for vitamin D used, normal level of vitamin D was 8.2 ng/ml to 37.4 ng/ml. Patients having levels below 8.2 ng/ml were included in low vitamin D level group while those having more than or equal to 8.2 ng/ml were placed in normal to high vitamin D group.

Data collected in current study was evaluated using Statistical Package for the Social Sciences (SPSS) version 17. Data of the whole study population was expressed as mean \pm SD. Independent sample t-test was applied for the calculation of statistically significant mean values. P-value was obtained by Fischer's Exact Test.

RESULTS

The demographic variables of CMS patients and controls are shown in Table 1. Absolute Vit-D levels among the cases and the controls were calculated. The SPSS window was directed to calculate significant mean value for the vitamin D levels in subjects with CMS

Table 1: Demographics and vitamin D level in cases and control

	Cases (n=50) mean (\pm SD)	Controls (n=50) mean (\pm SD)	P-value
Age (years)	51.30 \pm 5.25	50.40 \pm 4.84	0.53
Height (cm)	158.2 \pm 6.71	161.42 \pm 7.17	0.74
Weight (kg)	75.40 \pm 10.74	59.72 \pm 5.99	0.04*
Vitamin D3 (ng/ml)	15.03 \pm 08.11	24.11 \pm 07.0	< 0.01*

*(significant) S.D. = standard deviation

Table 2: The relative incidence of subcategories of vitamin D levels based on gender among cases and controls

Vitamin D	Cases n=50		Controls n=50		P-value	
	Males	Females	Males	Females	0.84	NS
Low	9 (18%)	12 (24%)	1 (2%)	1 (2%)		
Normal= High	15 (30%)	14 (28%)	24 (48%)	24 (48%)		

NS (not significant)

Normal range: 8.2 to 37.4 ng/ml

Normal-High: more than or equal to 8.2 ng/ml

Key: vitamin D level interpretation

Low: less than 8.2 ng/ml

against the Vit-D levels in individuals not having CMS. Interestingly, P-value of 0.01 was obtained by Fischer's Exact Test. The OR for the P-value was 0.139 with 95% confidence interval of 0.037 - 0.530. This proposes that Vit-D is a protective element in the development of CMS.

A further sub categorization of this finding of reduced Vit-D levels in 42% cases on the basis of gender revealed that 18% among them were males and 24% were females. These values when plotted against the 2% males and females in controls yielded an insignificant P-value of 0.84 implying that it is CMS rather than the gender which is a determining factor and that both the genders are susceptible to hypovitaminosis D Table 2.

DISCUSSION

Examination Survey NHANES 2003-2006 showed that low Vit- D status is inversely associated with metabolic syndrome as observed by Maki et al.¹⁸ They reported an OR of 0.40 (95% CI 0.27-0.59; P <0.001). In a study, by Minambres et al carried out in Spain in 2012, the proportion of patients with CMS was higher in patients with hypovitaminosis D than in patients with normal vitamin D levels (19.8% versus 6.2%, P <0.001).¹⁹ Likewise, in our study, 21 patients of CMS (about 42%) had hypovitaminosis D as compared to 2 normal individuals in controls (about 4%). In our study OR of 0.13 (95% CI 0.03-0.53; P<0.01) was obtained. Similar results were observed by Miñambres I et al¹⁹ that an association between vitamin D concentration and cardio-metabolic risk factors in the young and middle aged and urban Chinese population. About 66% of the obese or over weight patients were deficient of vitamin D as compared to healthy individuals not having CMS.²⁰ Lu et al also observed that decreased level of vitamin D increased the risk of CMS.²⁰ Recently, it has been observed that low level of vitamin D in obese individuals activates the Calpain and Caspase-12, enzymes involved in the apoptosis of fat tissue.²¹

Sergeev IN in their study reported an odds ratio of 0.46 (95% CI 0.32-0.67, P <0.001) for CMS in the highest quintile of vitamin D versus the lowest quintile using NHANES III (1988-1994) data²¹. Association did not differ between men and women (P-value = 0.726). Similarly, our study showed hypovitaminosis D in CMS patients with OR of 0.13 (95% CI 0.03- 0.53; P=0.01)³ but both the genders were equally susceptible to CMS and hypovitaminosis D, revealed by an insignificant P value of 0.84.

Results of studies carried out by Moy FM et al highlighted the high prevalence of vitamin D insufficiency among Malay adults in Kuala Lumpur. Vitamin D insufficiency was independently associated with younger age, female gender, greater abdominal obesity and CMS.²² The finding was similar to our study as far as the association of vitamin D with CMS was concerned but female gender in this study was more prone to

hypovitaminosis D. This is in contrast with our study where no difference was found on the basis of gender. This might be due to our small sample size.

CONCLUSION

Vitamin D is a protective factor for the development of CMS. Adults with poor vitamin D status are at increased risk for CMS. Early diagnosis and treatment of this condition is of great importance because vitamin D deficient state can be corrected by diet, exposure to sunshine and oral vitamin D supplements which are easy and cost effective measures.

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AUTHOR'S CONTRIBUTION

Following authors have made substantial contributions to the manuscript as under:

- Usamn R:** Concept and idea.
Khan F: Data collection.
Wadud S: Laboratory work.
Zafar S: Compilation of data and statistics.
Abideen ZU: Reference collection.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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