ISSN- O: 2458 - 868X, ISSN–P: 2458 – 8687
Index Copernicus Value: 49. 23

International Journal of Medical Science and Innovative Research (IJMSIR)
IJMSIR : A Medical Publication Hub
Available Online at: www.ijmsir.com
Volume – 3, Issue –4, July - 2018, Page No. : 291 - 298

Evaluation of Vitamin D levels in Metabolic syndrome and its correlation with glycemic profile and cardiovascular risk factors

[1]Manoj Kumar Mathur, [2]Ajeet Kumar Chaurasia, [3]Poonam Gupta, [4]Saurabh Nandwani

[1]Associate Professor, Department of Medicine, MLN medical College Allahabad, Uttar Pradesh

[2]Associate Professor, Department of Medicine, MLN medical College Allahabad, Uttar Pradesh

[3]Associate Professor, Department of Medicine, MLN medical College Allahabad, Uttar Pradesh

[4]Junior Resident, Department of Medicine, MLN medical College Allahabad, Uttar Pradesh

Correspondence Author: Dr Ajeet Kumar Chaurasia, Associate Professor ,Department of Medicine , MLN Medical College Allahabad ,Uttar Pradesh, India.

Type of Publication: Original Research Paper

Conflicts of Interest: Nil

Abstract

Aims: Evaluation of Vitamin D levels in people with metabolic syndrome and to evaluate the relationship between Vitamin D and traditional Cardiovascular disease risk factors [blood pressure, FBS/PPBS, obesity, dyslipidemia, hsCRP.

Settings and Design: Observational cross-sectional study.

Methods and Material: Study was conducted in the Department of Medicine, MLN Medical College and SRN Hospital, Allahabad. Individuals aged ≥18 years and ≤65 years of either sex with metabolic syndrome were taken as cases and healthy individuals were taken as controls. Plasma 25(OH)D, Fasting plasma glucose, post prandial glucose, lipid profile, A1C, and inflammatory markers (hsCRP) were measured. Anthropometric data were also obtained .

Results: In our study out of 62 cases the mean age was 47.61±8.83 years and in 50 control the mean age was 47.54±9.49 years. The mean of plasma 25(OH)D was 18.90 ng/ml and percentages of vitamin-D deficiency and insufficiency were 64.51 % and 24.19 % respectively in metabolic syndrome patients group. The mean of plasma 25(OH)D was 23.91 ng/ml and percentages of vitamin D deficiency and insufficiency were 38% and 34% respectively in control group. Vitamin-D status was inversely associated with the serum TG, Waist Circumference, body mass index (BMI) ,elevated glucose levels ,hsCRP. And was positively correlated with HDL levels.

Conclusion: Vitamin D levels were significantly decreased in metabolic syndrome patients as compared to control . Most metabolic syndrome components and glycemic profile were significantly correlated to serum 25(OH)D levels. The findings of this study revealed that vitamin D deficiency may have an important role in metabolic syndrome and its components.

Keywords: Metabolic syndrome, glycemic profile ,Vitamin D, hsCRP.

Introduction

Coronary heart disease (CHD) remains the leading cause of mortality in men and women[1,2]. Primary risk factors for CHD in both sexes include older age, smoking, diabetes mellitus, dyslipidemia, hypertension, physical inactivity, obesity, the metabolic syndrome, a family history of

premature CHD (males <55 and females <65 years old), and a personal history of peripheral arterial disease[2–5]. Vitamin D has garnered recent attention for its potential cardio-protective properties and has become a topic of considerable interest in the clinical researches . An increased incidence of CHD and hyperlipidemia in higher latitudes has been ecologically correlated with less sunlight[6]. Other studies report that those with a lower exposure to ultraviolet light had lower vitamin D concentrations and a higher risk of CHD , myocardial infarction, and hypertension[7–9]. Lower serum concentrations of vitamin D have also been associated with increased risk of sudden cardiac death[10], peripheral arterial disease[11], and greater carotid intima-medial thickness[12] .

Vitamin D receptors (VDRs) have been identified in many tissues including vascular smooth muscle cells[13],cardiomyocytes, and coronary arteries[14,15]. Given the presence of VDRs in the vascular system, including the coronary arteries, there are several biologically plausible pathways through which vitamin D could lead to improved cardiovascular health. Activation of the VDR, for instance, has been shown to inhibit vascular smooth muscle cell proliferation, which is believed to be cardioprotective[16].

Vitamin D deficiency may be linked with metabolic syndrome by the virtue of some of these observations: (1) vitamin D may blunt the effect of advanced glycation end products on endothelial cells, which contribute to the increased arterial stiffness and endothelial dysfunction observed in individuals deficient in vitamin D; (2) vitamin D may exert protective effects on the vessel walls by inhibition of macrophage to foam cell formation and via its anti-inflammatory effects; (3) vitamin D sufficiency has been associated with downregulation of the renin-angiotensin-aldosterone system [17].

C-reactive protein (CRP) is a member of the pentraxin family of proteins. It is an acute phase reactant synthesized mainly by the liver. Serum CRP levels are elevated in response to acute infections, inflammatory conditions and trauma. The hsCRP assays have been standardized across several commercial platforms and can be accurately measured from fresh or frozen plasma[18]. The hsCRP is the most widely evaluated biomarker in the quest for an ideal biomarker for global cardiovascular disease (CVD) risk prediction.

Aim of the study

The aim of the study was evaluation of Vitamin D levels in people with metabolic syndrome and to evaluate the relationship between Vitamin D and traditional Cardiovascular disease risk factors [blood pressure, FBS/PPBS, obesity, dyslipidemia, hsCRP] . This study could help determine Vitamin D as a risk factor in population with metabolic syndrome and its significance and therapeutic role.

Material and Methods

This study was an observational cross-sectional study. Ethical Committee approval was taken from Institutional Ethics Committee.

All individuals aged ≥18 years and ≤65 years of either sex with metabolic syndrome diagnosed as per NCEP ATPIII criteria who visited to medicine OPD or admitted in medicine department Swaroop Rani Nehru Hospital, Allahabad, were included as case. Age matched healthy individuals were taken as controls in this study .

Patients with history of coronary heart disease and/or carotid or peripheral vascular disease, known case of metabolic bone disease, On Vitamin D or calcium therapy, Chronic kidney disease patients, Liver disease, lipid-lowering therapy (statins, ezetimibe, fibrates, nicotinic acid, and omega3), chronic intake of anti-inflammatory medicines (steroidal and non steroidal), acute and/or chronic inflammatory diseases were excluded from study .

After obtaining written informed consent, patient qualifying inclusion criteria were assessed and demographic data was recorded and subjects were interviewed about medical history, education, family medical history, and intake of medications. Anthropometric measurements (Weight, height, body mass index (BMI), and waist circumferences) were taken. Blood pressure was measured as per recommendations of the Seventh Joint National Committee, with the subject sitting and after 5 minutes of rest. Venous blood samples were taken after 12-hour fasting for determining the following biochemical parameters: Complete blood count (CBC), Liver function test (LFT) ,Lipid Profile : Total cholesterol (total-C) ,HDL-C, Triglycerides, LDL cholesterol (LDL-C) , Blood glucose : fasting , post prandial , HBA_1C , Serum Creatinine and Serum urea , Vitamin D :25 (OH) Vitamin D , hsCRP

Other investigations like ECG, 2 D Echocardiography were also done

Statistical analysis: Categorical variables were presented in number and percentage (%) and continuous variables were presented as mean ± SD.

Statistical tests were applied as follows-

1. Quantitative variables were compared using Unpaired t-test

2. Pearson correlation coefficient/Spearman rank correlation coefficient was used to assess the association of various quantitative parameters.

A p value of <0.05 was considered statistically significant. The data was entered in MS EXCEL spreadsheet and analysis was done using Statistical Package for Social Sciences (SPSS) version 19.

Results and Discussion

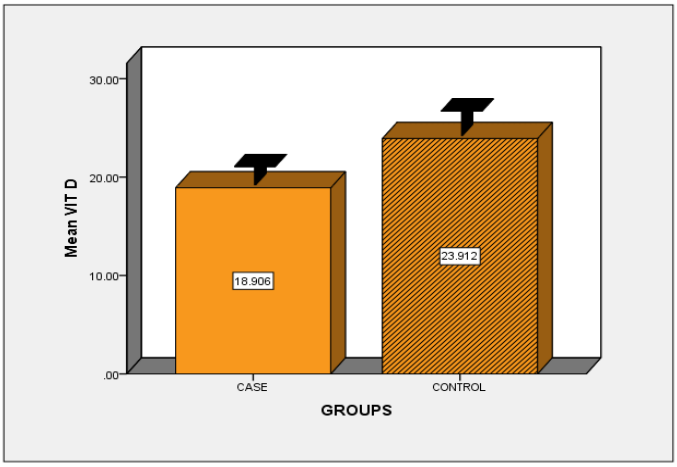
The present observational case control study included 112 subjects out of which 62 were cases and 50 were controls.

The mean age of cases was 47.61±8.83 year and in controls the mean age was 47.54±9.49 year. Both groups were perfectly matched regarding age distribution. Maximum study subjects were in between 41-50 years of age. In the cases there were 30 males and 32 females. In the control there were 32 male and 18 female. In the cases male: female ratio was 1: 1.06 and in control male: female ratio was 1.7: 1.

Table 1 : Mean values of components of metabolic syndrome , BMI , A1C and vitamin D in cases and controls

Variabes	GROUPS	N	Mean	SD	p
AGE (years)	CASE	62	47.612	8.837	.967
	CONTROL	50	47.540	9.435	
SBP (mmHg)	CASE	62	147.540	9.495	.000
	CONTROL	50	128.320	9.322	
DBP (mmHg)	CASE	62	87.580	9.297	.000006
	CONTROL	50	78.260	8.263	
BMI (Kg/m^2)	CASE	62	30.551	4.052	.000
	CONTROL	50	26.478	3.005	
WC (cm)	CASE	62	102.741	11.980	.000
	CONTROL	50	92.000	11.785	
FBG (mg/dl)	CASE	62	128.693	22.472	.000002
	CONTROL	50	98.500	14.934	
PPG (mg/dl)	CASE	62	181.967	31.176	.000001
	CONTROL	50	137.240	16.338	
A1C (%)	CASE	62	7.83	1.273	.000
	CONTROL	50	5.852	.558	
TG (mg/dl)	CASE	62	170.338	24.158	.
	CONTROL	50	131.780	10.515	.000
HDL (mg/dl)	CASE	62	46.774	13.358	.000002
	CONTROL	50	57.760	8.411	
VIT D (ng/ml)	CASE	62	18.906	7.745	.003

Figure 1 : Comparison of mean vitamin D in between cases and controls



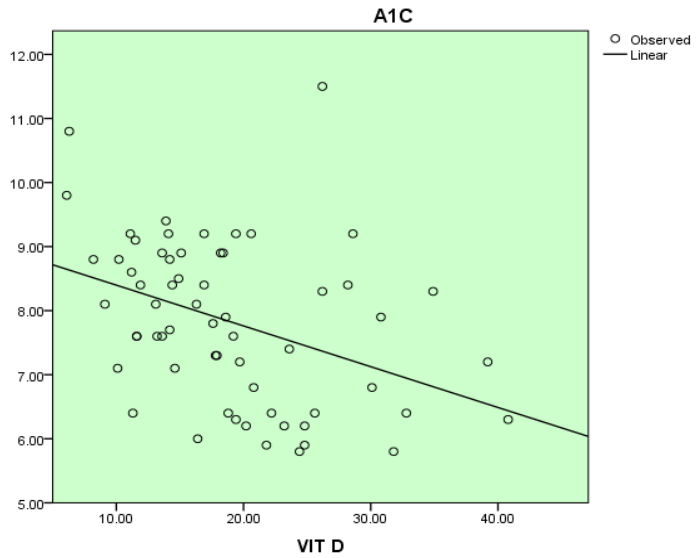
The mean Vitamin D in case group was 18.90 ±7.74 mmHg and in control group was 23.91 ± 9.13 mmHg which was statistically significant (p <0.05). Both groups had mean vitamin D level that was well below normal vitamin D level (≥30 ng/ ml) ,but mean vitamin D level was significantly lower in cases as compared to controls .

We found that patients with metabolic syndrome were having lower Vitamin D levels than those without. The mean of plasma 25(OH) D was 18.90 ng/ml and percentages of vitamin D deficiency [vit D <20ng/ml] and insufficiency [vit D: 21-29 ng/ml] were 64.51 % and 24.19 % respectively in metabolic patients group. The mean of plasma 25(OH) D was 23.91 ng/ml and percentages of vitamin D deficiency [vit D <20ng/ml] and insufficiency [vit D: 21-29 ng/ml] were 38% and 34% respectively in control group.

62% of the controls (Without Metabolic syndrome) were having Vitamin D levels more than 20 ng/ml while this percentage was only 35.48% in the case group i.e. the metabolic syndrome. There was significant difference (p=0.003 i.e. < 0.05) in the mean serum Vitamin D levels between cases (Metabolic syndrome) and the control (without Metabolic syndrome) group. This suggested that the Vitamin D levels were significantly lower in the case group (metabolic syndrome group) with more of the patients with hypovitaminosis.

Thus it was found that low vitamin D status was inversely associated with metabolic syndrome. Most metabolic syndrome components and glycemic profile (fasting plasma glucose, post prandial glucose and HbA_1c) were significantly correlated to serum 25(OH) D levels in both metabolic syndrome patients and normal healthy controls.

Figure 2 : Scatter diagram showing correlation between A1C and vitamin D in case group



There is weak negative correlation between A1C and Vitamin D which is statistically significant (p < 0.5)

We found that vitamin D status was inversely associated with the serum TG, Waist Circumference, BMI and elevated glucose levels, which are also considered to be cardiovascular risk factors. Vitamin D was positively correlated with HDL levels. Vitamin D is also inversely related hsCRP (which is also considered to be a cardiovascular risk factor). No significant association was found between serum 25(OH) D and blood pressure.

Discussion

In this study , it was found that despite being a country with high levels of sun exposure, the prevalence of vitamin D deficiency is very high , both in patients with metabolic syndrome (64.51%) and in controls i.e healthy individuals (38%). This is consistent with previous observations in India which have shown high prevalence of vitamin D deficiency

In this study it was found that patients with Metabolic syndrome were having lower Vitamin D levels than those without. The mean of plasma 25(OH)D was 18.90 ng/ml and percentages of vitamin D deficiency [vit D <20ng/ml] and insufficiency [vit D: 21-29 ng/ml] were 64.51 % and 24.19 % respectively in metabolic syndrome patients group. The mean of plasma 25(OH)D was 23.91 ng/ml

and percentages of vitamin D deficiency [vit D <20ng/ml] and insufficiency [vit D: 21-29 ng/ml] were 38% and 34% respectively in control group.

Thus study shows that vitamin D status was inversely associated with Metabolic syndrome. Most metabolic syndrome components and glycemic profile (fasting plasma glucose, post prandial glucose and HbA1c) were significantly correlated to serum 25(OH)D levels in both metabolic syndrome patients and normal healthy controls . We found that vitamin D status was inversely associated with the serum TG, Waist Circumference, body mass index (BMI) and elevated glucose levels, which are also considered to be cardiovascular risk factors. Vitamin D was positively correlated with HDL levels. Vitamin D is also inversely related to hsCRP (which is also considered to be a cardiovascular risk factor) in metabolic syndrome patients. No significant association was found between serum 25(OH)D and blood pressure.

The results are consistent with those of previous studies in the Unites States and Canada.[19,20,21] . Data from NHANES III using a representative sample of 8421 US adults 20 years and older also found that those with Metabolic Syndrome had significantly lower mean serum 25(OH)D levels (28.0 ng/mL) compared to those without Metabolic Syndrome (31.6 ng/mL; $P < 0.001$).[20] In addition, a study in 1818 adults 20 years and older from the Canadian Health Measures Survey found that participants with at least three components of Metabolic Syndrome had significant lower mean serum 25(OH)D levels (25.1 ng/mL) compared with participants with two components or less (29.5 ng/mL; $P < 0.0001$).[19]

Among the Metabolic Syndrome components, the highest correlation found with serum 25(OH)D levels was with waist circumference followed by HDL and TG . These findings are consistent with NHANES data, in which an inverse correlation was found between 25(OH)D levels and TG and WC.[20] In addition, similar results were observed in a cross-sectional study of 343 overweight or obese Caucasian individuals,[22] suggesting that this association is independent of the degree of obesity.

Knekt P et al 2008 [23] found significant correlations between 25(OH)D levels and FBG. Mitri et al 2014 [24] found significant correlations between 25(OH)D levels and FBG, waist circumference, and HDL-C . However, a small study conducted in Greece among 52 individuals with Metabolic Syndrome and 58 health controls only found an inverse correlation between 25(OH)D levels and TG , but not with the other component criteria of Metabolic Syndrome (WC, BP, HDL-C, and FBG).[25] In this study they didn't find any correlation between vitamin D and WC, HDL ,FBG which is against our study.

In AusDiab study, Gagnon et al[26] used baseline (1999–2000) and 5-yr follow-up data of the Australian Diabetes, Obesity, and Lifestyle Study (AusDiab). They studied those without MetS at baseline and with complete data .They had shown that serum 25(OH)D concentrations of 23ng/ml or lower were associated with up to a significant 74% increased risk of developing MetS compared with those with concentrations of 34 ng/ml or higher. Low concentrations of serum 25(OH)D were also associated with higher WC, FPG, serum triglyceride levels, and insulin resistance (HOMA2-IR) at 5 yr, which are likely the basis of this increased MetS risk. These findings matched our study.

Shifa K et al[27] 2017 conducted a cross-sectional study in a tertiary care teaching hospital in India. They found that levels of hsCRP were significantly high ($p<0.01$) whereas vitamin D levels were significantly low ($p<0.01$) in subjects with dyslipidemia compared to the control subjects. The Pearson Correlation between hsCRP and Vitamin D showed statistically significant negative correlation suggesting that a decrease in vitamin D increase the inflammatory process. This study matched

our study where vitamin D levels were negatively correlated with hsCRP .

Prasad et al[28] 2012 conducted a case control study on 101 healthy populations residing in Nandyal urban area, India aged between 30-50 years who had no history of diabetes. They found in the total population the prevalence of vitamin D deficiency was 76.23 %. The prevalence of MS in vitamin D deficient group was higher than in normal vitamin D group. In the study significant inverse association were present for vitamin D with central obesity, hyperglycemia, hypertriglyceridimia and hypertension which matched our study except correlation with hypertension .

In a similar observational cross-sectional Indian study conducted in the Department of Obstetrics and Gynecology, Bharati Hospital, Pune, Ashok et al[29] found that waist circumference (WC), systolic blood pressure (BP), and triglyceride concentrations were inversely associated with vitamin D concentrations. 84% are with deficient levels of vitamin D. This Indian study also matched our study except that no significant correlation was seen in our study between blood pressure and vitamin D.

Conclusion

In conclusion, Vitamin D values were significantly decreased in metabolic syndrome patients as compared to controls in this hospital-based study . Vitamin D status was inversely associated with the serum TG, Waist Circumference, and elevated glucose levels, which are also considered to be cardiovascular risk factors. Vitamin D was positively correlated with HDL levels. Vitamin D is also inversely related to hsCRP (which is also considered to be a cardiovascular risk factor) .These results have important public health implications for developing recommendations directed to increase vitamin D levels in the population, such as increasing sun exposure or promoting the use of vitamin D supplements. Improving vitamin D levels may reduce the risk of Metabolic Syndrome and its components, which may help prevent its progression to type 2 diabetes mellitus and cardiovascular conditions

Limitations of the study

This was a cross-sectional study; thus, it cannot establish the temporal relationship between vitamin D status and Metabolic Syndrome. In addition, study is hospital based and may not be representative of the population in general . Known and suspected risk factors for Metabolic Syndrome such as physical activity, smoking, alcohol drinking, family history of CVD were not included when tabulating the data for study protocol. This precludes our ability to comment on other confounding factors. Longitudinal studies with large population are needed to confirm these results.

References

1. Roger VL, Go AS, Lloyd-Jones DM, Adams RJ, Berry JD, Brown TM, et al. AHA statistical update: heart disease and stroke statistics—2011 update; a report from the American Heart Association. Circulation. 2011 Feb 1;123(4):e18-e209

2. Mosca L, Barrett-Connor E, Kass Wenger N. Sex/gender differences in cardiovascular disease prevention: what a difference a decade makes. Circulation. 2011 Nov 8;124(19):2145-54

3. Lloyd-Jones DM, Larson MG, Beiser A, Levey D. Lifetime risk of developing coronary heart disease. Lancet. 1999 Jan 9;353(9147):89-92.

4. Mosca L, Banka CL, Benjamin EJ, Berra K, Bezanson JL, Dolor RJ, et al. Evidence-based guidelines for cardiovascular disease prevention in women: 2007 update. Circulation. 2007 Mar 20;115(11):1481-501.

5. Mosca L, Grundy SM, Judelson D, King K, Limacher M, Oparil S, et al. AHA/ACC scientific statement: consensus panel statement. Guide to preventative cardiology for women. American Heart

Association/American College of Cardiology. J Am Coll Cardiol. 1999 May;33(6):1751-5

6. Grimes DS, Hindle E, Dyer T. Sunlight, cholesterol and coronary heart disease. Q J Med. 1996 Aug;89(8):579-89

7. Rostand SG. Ultraviolet light may contribute to geographic and racial blood pressure differences. Hypertension. 1997 Aug;30(2 Pt 1):150-6.

8. Giovannucci E, Liu Y, Hollis BW, Rimm EB. 25-hydroxyvitamin D and risk of myocardial infarction in men. Arch Intern Med. 2008 Jun 9;168(11):1174-80

9. Forman JP, Giovannucci E, Homes MD, Bischoff-Ferrari HA, Tworoger SS, Willett WC, Curhan GC. Plasma 25-hydroxyvitamin D levels and risk of incident hypertension. Hypertension. 2007 May;49(5):1063-9.

10. Pilz S, Marz W, Wellnitz B, Seelhorst U, Fahrleitner-Pammer A, Dimai HP, Boehm BO, Dobnig H. Association of vitamin D deficiency with heart failure and sudden cardiac death in a large cross-sectional study of patients referred for coronary angiography. J Clin Endocrinol Metab. 2008 Oct;93(10):3927-35

11. Melamed ML, Munter P, Michos ED, Uribarri J, Weber C, Sharma J, Raggi P. Serum 25- hydroxyvitamin D levels and the prevalence of peripheral arterial disease. Atheroscler Thromb VascBiol. 2008; 28:1179–1185.

12. Targher G, Bertolini L, Padvoani R, Targher G, Bertolini L, Padovani R, et al. Serum 25- hydroxyvitamin D3 concentrations and carotid artery intima-media thickness among type 2 diabetic patients. Clin Endocrinol. 2006; 65:593–597.

13. Merke J, Milde P, Lewicka S, Hugel U, Klaus G, Mangelsdorf DJ, et al. Identification and regulation of 1,25-dihydroxyvitamin D3 receptor activity and biosynthesis of 1,25- dihydroxyvitamin D3. Studies in cultured bovine aortic endothelial cells and human dermal capillaries. J Clin Invest. 1989; 83:1903–1915.

14. Schnatz PF, Nudy M, O'Sullivan DM, Jiang X, Cline JM, Kaplan JR, et al. The quantification of vitamin D receptors in coronary arteries and their association with atherosclerosis. Maturitas. 2012; 73:143–147.

15. Schnatz PF, Nudy M, O'Sullivan DM, Jiang X, Cline JM, Kaplan JR, et al. Coronary artery vitamin D receptor expression and plasma concentrations of vitamin D: their association with atherosclerosis. Menopause. 2012 Sep; 19(9):967–973.

16. Wu-Wong JR, Nakane M, Ma J, Ruan X, Kroeger PE. Effects of vitamin D analogs on gene expression profiling in human coronary artery smooth muscle cells. Atherosclerosis. 2006 May;186(1):20-8

17. G. N. Thomas, B. ´o Hartaigh, J. A. Bosch et al., "Vitamin D levels predict all-cause and cardiovascular disease mortality in subjects with the metabolic syndrome: the Ludwigshafen Risk and Cardiovascular Health (LURIC) Study. Diabetes Care. 2012 May;35(5):1158-64.

18. Ridker PM. Clinical application of C-reactive protein for cardiovascular disease detection and prevention. Circulation. 2003;107:363–9.

19. Brenner DR, Arora P, Garcia-Bailo B, et al. Plasma vitamin D levels and risk of metabolic syndrome in Canadians. J Investig Med 2011;34:E377–E384

20. Ford ES, Ajani UA, McGuire LC, Liu S. Concentrations of serum vitamin D and the metabolic syndrome among U.S. adults. Diabetes Care 2005; 28: 1228-1230

21. Maki KC, Fulgoni VL, Keast DR, et al. Vitamin D intake and status are associated with lower prevalence of metabolic syndrome in US Adults: National Health and Nutrition Examination Surveys 2003–2006. Metab Syndr Relat Disord 2012;10:363–372

22. Miñambres I, Sánchez-Hernández J, Sánchez-Quesada J, et al. The association of hypovitaminosis d with the metabolic syndrome is independent of the degree of obesity. ISRN Endocrinol 2012;2012:691803.

23. Knekt P, Laaksonen M, Mattila C, et al. Serum vitamin D and subsequent occurrence of type 2 diabetes. Am J Epidemiol 2008;19:666–671

24. Mitri J, Nelson J, Ruthazer R, et al. Plasma 25-hydroxyvitamin D and risk of metabolic syndrome: An ancillary analysis in the Diabetes Prevention Program. Eur J Clin Nutr 2014;68:376–383

25. Makariou S, Liberopoulos E, Florentin M, et al. The relationship of vitamin D with non-traditional risk factors for cardiovascular disease in subjects with metabolic syndrome. Arch Med Sci 2011;8:437–443.

26. Ridker PM, Wilson PW, Grundy SM. Should C-reactive protein be added to metabolic syndrome and to assessment of global cardiovascular risk? Circulation 2004;109:2818–2825.

27. Shifa K.1, Jithesh T. K.1, Mirshad P. et al. Vitamin D Deficiency and Inflammatory Marker in Subjects with Dyslipidemia. American Journal of Biochemistry 2017; 7(1):6-9.

28. Kedam.Durga Prasad et.al A study of vitamin D and metabolic syndrome in urban population Int J Biol Med Res. 2012; 3(2):1731-1734

29. Ashok P, Balsubramanian B, Joshi S,Kharche JS, Vaidya SM. Associations of vitamin D with metabolic syndrome components in Indian urban middle-aged women. Natl J Physiol Pharm Pharmacol 2017;7(5):497