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Research Article

RELATIONSHIP BETWEEN VITAMIN D DEFICIENCY AND RISK OF METABOLIC SYNDROME IN POSTMENOPAUSAL WOMEN

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ABSTRACT

The purpose of this study is to find out the relationship between vitamin D deficiency and risk of metabolic syndrome in postmenopausal women. The present cross-sectional study was conducted in 200 postmenopausal women who were attended executive health checkup OPD at Medanta-The Medicity, Gurgaon. Serum Vitamin D levels were estimated by chemiluminescent microparticle immunoassay method. Data were analyzed by using SPSS software, version 22.0. The results revealed that the prevalence of vitamin D deficiency and metabolic syndrome were 70.5% and 58% in postmenopausal women. A significant and negative correlation ($p<0.001$) was found between vitamin D deficiency and metabolic syndrome components. Vitamin D status was significantly related to the risk of developing metabolic syndrome (OR 4.16, 95% CI 2.18-7.92, p-value <0.001). Postmenopausal women who had vitamin D deficiency are at increased risk of metabolic syndrome that predisposes cardiovascular diseases and Type2 diabetes mellitus.

INTRODUCTION

Vitamin D deficiency has become a public health problem amongst all age-groups especially in older women with a prevalence of 50-90%[(1-3)]. Vitamin D seems to have an anti-inflammatory and immune modulating properties. The active molecule of vitamin D downregulates the proinflammatory cytokines and control the inflammatory response which draws more attention toward its role in metabolic syndrome[(4)]. Metabolic syndrome (MS) is a cluster of various metabolic abnormalities like abdominal obesity, hyperglycemia, dyslipidemia, and hypertension[(5)]. The leading causes of vitamin D deficiency and increased risk of MS are aging, sedentary lifestyle, unhealthy nutrition and weight gainin postmenopausal women[(6)].

In recent years, the possible relationship between Vitamin D and hyperglycemia with insulin resistance, obesity, dyslipidemia and increased blood pressure for the emergence of MS has gained interest. A meta-analysis of 28 studies demonstrated that higher serum vitamin D levels were associated with a 55% reduction in diabetes, a 51% decreased risk of the MS and a 33% lower risk of cardiovascular disease (CVD)[(7)].Till date, there are lots of controversies related to the association between Vitamin D deficiency and high risk of metabolic syndrome[(8-14)].Therefore, the present study aimed to find out whether the levels of Vitamin D has an effect on metabolic syndrome and its components in postmenopausal women.

MATERIALS AND METHODS

The present cross-sectional study was designed and conducted in the Department of Biochemistry at G.R. Medical College, Gwalior (M.P.) and Medanta-The Medicity, Gurgaon.

Inclusion and Exclusion criteria: Total 200 postmenopausal women who were visited for executive health checkup with age group of >45 years and amenorrhea or whose last menstruation occurred at least 12 months prior were included. Women who were either suffering from or had a prior history of CVD, bone disorder, malignancy, and chronic renal & liver disease were excluded from the study. Hormone replacement therapy used by women were also excluded. The study was approved by institutional ethical committee board. The information pertaining to the study was filled in proforma and informed consent were taken voluntarily from all the participants.

Anthropometric Measurement: Height (cms) and weight (Kg) were measured with a digital scale and a stadiometer with head held in straight position with bare feet and wearing light indoor clothes. Body mass index (BMI) was calculated by using formula i.e. weight (kg)/ height squared (m^2). Waist

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circumference (WC) was measured at the midpoint between the lowest rib and the top of the iliac crest by using a measuring tape (cms). Blood pressure (BP) was measured with the digital instrument on the right arm after a 5-minute rest in sitting position.

Laboratory Assessment: After initial enrolment, 5ml of fasting venous blood samples were drawn from all the studied women. Blood was allowed to clot at room temperature 37°C for 30 minutes, and serum was obtained immediately by centrifugation at 3000 rpm for 10 to 20 minutes. The serum sample was analyzed for a set of biochemical parameters included fasting blood sugar (FBS), total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), very low-density lipoprotein cholesterol (VLDL-C), were measured by using dry slide chemistry method in an automated VITROS 5600 analyzer (Johnson-Johnson ®, Rochester, NY, USA). Serum vitamin D levels were measured by chemiluminescent microparticle immunoassay (CMIA) with an automated Architect® i2000 SR analyzer (Abbott Diagnostic Division, Barcelona, Spain). Internal and external quality control was run routinely before performing the assay analysis. Serum concentration of vitamin D less than equal to 30 ng/ml were classified as deficient and more than 30 ng/mL as sufficient based on the latest recommendation of international endocrine society clinical guideline[15]. Metabolic syndrome was defined on the basis of NCEP ATP III criteria for Asian Indian[16]. The patients were considered as suffering from metabolic syndrome if they fulfill at least 3 or 5 criteria of the following:

- Abdominal Obesity: Waist circumference (WC) ≥ 80 cm (Women)
- High Fasting Blood Sugar (FBS)level: ≥100mg/dL
- High Triglyceride (TG) level: ≥150mg/dL
- Low High-Density Lipoprotein-Cholesterol (HDL-C) level: ≤50 mg/dL (Women)
- High Blood Pressure (BP): > 130 mmHg systolic or >85 mmHg diastolic

Statistical Analysis: Data was entered in Microsoft Excel 2013 and statistical analysis was done by using Statistical package for social science (SPSS) software Version 22.0. Results of the study were expressed in mean±SD and percentage. Student's t-test was used to compare between two groups. Pearson's correlation was used to find out the correlation between vitamin D deficiency and biochemical parameters. Odds ratio (OR)was used to study the relationship between the risk of metabolic syndrome and vitamin-D deficiency. A two-tailed p-value less than 0.05 was considered as statistically significant.

RESULTS

A total 200 postmenopausal women participated in the study of which 70.5% had vitamin D deficiency and 58% had metabolic syndrome. In our study, we observed a significant decrease in serum vitamin D levels and HDL-C while significant increase in BMI, WC, SBP, FBS, TG, TC, LDL-C, and VLDL-C ($p<0.001$) in postmenopausal women with deficient vitamin D levels as compared with sufficient vitamin D levels group (Table 1). Serum vitamin D levels were also significantly decreased ($p<0.001$) in postmenopausal women with metabolic syndrome as compared to without metabolic syndrome group (Table 2). We also observed a significant negative correlation between vitamin D deficiency and all the components of metabolic syndrome except HDL-C which was significantly and positively correlated in postmenopausal women (Table 3).The odds ratio for metabolic syndrome components including abdominal obesity (OR 5.77, 95% CI 2.94-11.34, p-value <0.001), impaired fasting sugar (OR 5.70, 95% CI 2.94-11.04, p-value <0.001), hypertension (OR 5.90, 95% CI 3.05-11.43, p-value <0.001), and hypertriglyceridemia (OR 3.09, 1.65-5.81, p-value <0.05) had significantly higher odds for having vitamin D deficiency (Table 4).

Table 1 Comparative aspects of anthropometric and biochemical parameters in postmenopausal women with sufficient and deficient vitamin D levels.

Parameters	Postmenopausal Women(n=200)	
	Sufficient Vitamin D levels (n=59)	Deficient Vitamin D levels (n=141)
Serum Vitamin D levels (ng/mL)	40.32 ±10.86	11.83±15.86**
Height (cms)	1.66±0.10	1.68±0.07^{NS}
Weight (kg)	64±10.23	68.41±8.47*
BMI (Kg/m^2)	23.63±4.09	24.25±3.97*
WC (cms)	81.49±9.38	92.05±11.16**
SBP (mmHg)	123.29±5.57	133.46±9.45**
DBP(mmHg)	82.08±3.32	82.95±4.18^{NS}
FBS(mg/dL)	86.42±11.46	102.33±13.12**
TC(mg/dL)	183.36±21.56	211.11±15.41**
TG(mg/dL)	135.55±25.22	156.77±25.62**
HDL-C(mg/dL)	37.44±7.16	31.58±6.3**
LDL-C(mg/dL)	116.46±22.42	144.51±20.56**
VLDL-C(mg/dL)	30.11±5.04	31.35±5.12*

**Highly statistically significant ($p<0.001$), * Statistically significant ($p<0.05$), ^{NS}Non significant ($p>0.05$)

Table 2 Comparative aspects of serum vitamin D levels in postmenopausal women with and without metabolic syndrome.

Parameters	Postmenopausal Women(n=200)	
	Without MS (n=84)	With MS (n=116)
Serum Vitamin D levels (ng/mL)	32.26±16.28	14.86±10.77**

**Highly statistically significant ($p<0.001$)

Table 3 Pearson's correlation between vitamin D deficiency and metabolic syndrome components in postmenopausal women

Parameters	Vitamin D Deficiency	
	Correlation Coefficient (r)	p-value
BMI	-0.211	0.012*
WC	-0.754	0.000**
SBP	-0.884	0.000**
DBP	-0.915	0.000**
FBS	-0.643	0.007**
TC	-0.236	0.005**
TG	-0.693	0.000**
HDL-C	0.301	0.000**
LDL-C	-0.207	0.014*
VLDL-C	-0.198	0.02*

**Highly statistically significant ($p<0.001$), * Statistically significant ($p<0.05$)

Table 4 Odds ratio (OR) for various components of metabolic syndrome and vitamin-D status

Parameters	Vitamin D Sufficient (>30ng/mL) n(%)	Vitamin D Deficient (≤30ng/mL) n(%)	OR (95%)	p-value
Metabolic Syndrome	20 (33.8%)	96 (68.0%)	4.16 (2.18-7.92)	<0.0001**
Abdominal obesity (WC ≥80cms)	27 (45.7%)	117 (82.9%)	5.77 (2.94-11.34)	<0.0001**
Impaired fasting sugar (FBS ≥100 mg/dL)	19 (32.2%)	103 (73.0%)	5.70 (2.94-11.04)	<0.0001**
Hypertriglyceridemia (TG≥150 mg/dL)	25 (42.3%)	98(69.5%)	3.09 (1.65-5.81)	<0.05*
Low HDL-C levels (HDL-C<50 mg/dL)	45 (76.2%)	109(77.3%)	1.05(0.51-2.17)	0.874^{NS}
Hypertension (BP ≥130/85mmHg)	20 (33.8%)	106(75.2%)	5.90 (3.05-11.43)	<0.0001**

**Highly statistically significant (p<0.001), * Statistically significant (p<0.05), ^{NS}Non significant (p>0.05)

DISCUSSION

Vitamin D deficiency and metabolic syndrome (MS) has become one of the major health problems in postmenopausal women. In our study, the overall prevalence of vitamin D deficiency and metabolic syndrome were 70.5% and 58% in postmenopausal women. Previous studies reported the similar findings in postmenopausal women[10,13,17-18].

In the present study, the metabolic syndrome components were significantly increased in the deficient group when compared to sufficient group in postmenopausal women. A significant negative correlation (p<0.001) was observed between vitamin D deficiency and MS components in postmenopausal women, in agreement with few other studies[7,12,14,19]. Evidence from an increasing number of studies suggested that vitamin D levels were inversely associated with abdominal adiposity, impaired fasting sugar, hypertriglyceridemia, and arterial hypertension[12,19-20]. We also observed a significant relationship between vitamin D deficiency and metabolic syndrome (OR 4.16) and its components including hypertension (OR 5.90), abdominal obesity (OR 5.77), impaired fasting sugar (OR 5.70), and hypertriglyceridemia (OR 3.09). The possible mechanism for the causal association between vitamin D and risk of MS in postmenopausal women has been proposed. Vitamin D is a fat-soluble vitamin and stored in adipose tissue. It inhibits inflammatory response via down-regulate the production and expression of proinflammatory cytokines[4]. Some invitro and invivo studies suggest that 1, 25-dihydroxycholecalciferol may control blood pressure through the renin-angiotensin system by suppressing renin expression at a juxtaglomerular cell[22-23]. Vitamin D also influences insulin secretion in pancreatic β-cell through vitamin D receptor and insulin sensitivity, which have a main role in MS. Related to the insulin sensitivity, vitamin D deficiency is the risk of insulin resistance, and this might cause an elevation of the levels of VLDL and TG[21]. Hypovitaminosis D has been reported to be associated with a more atherogenic lipid profile, which is a major risk factor for progression toward MS, and CVD.

Menopause marks an important health transition in woman's life. Due to decline in estrogen hormone and aging, the synthesis of vitamin D is reduced in the skin[11]. Estrogen hormone also stimulates the activity of 1α hydroxylase enzyme that is responsible for the production of 1, 25-dihydroxycholecalciferol. With an advancing age, a fall in estrogen hormone will affect the activity of vitamin D[24]. Low levels of estrogen cause the accumulation of visceral fat that could lead to abdominal obesity and associated with increased insulin resistance, free fatty acid, and decreased adiponectin. These factors contribute to increased secretion of apolipoprotein-B containing particles, leading to hypertriglyceridemia and increased hepatic lipase activity, which lead to a predominance of small dense LDL particles and a reduction in the large anti-atherogenic HDL_2 particles[25]. These results imply that the decrease of serum estrogen amplifies the negative effects of a low vitamin D and increased cardio-metabolic risk in post-menopausal women. Therefore, postmenopausal women had higher tendency to develop obesity, hyperglycemia, and hypertension due to the decline in estrogen and vitamin D hormone, visceral fat accumulation, insulin sensitivity and activation of the renin-angiotensin-aldosterone system (RAAS) that could lead to metabolic syndrome. The limitations of the study include- we are unable to analyze various risk factors like sun-exposure, daily exercise, dietary intake and other factors that could affect vitamin D levels.

CONCLUSION

Vitamin D deficiency is an alarming issue in postmenopausal women in India. Our finding has given rise to concerns about the status of vitamin D and risk of metabolic syndrome in postmenopausal women. Our study suggests that there is an inverse relationship between vitamin D deficiency and MS. Postmenopausal women with vitamin D deficiency had a higher risk of obesity, hyperglycemia, increased blood pressure and hypertriglyceridemia that could lead to MS which predisposes CVD and T2DM.

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