

## PREVALENCE OF VITAMIN D DEFICIENCY IN ADULT POPULATION WITH METABOLIC SYNDROME

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### Abstract

**Background:** The study's main aim was to evaluate the prevalence of Vitamin D deficiency in adults with metabolic syndrome. **Materials and Methods:** A cross-sectional observation study was conducted on patients aged 18-60 diagnosed with metabolic syndrome after applying inclusion and exclusion criteria. A detailed history of 80 patients, including demographic profile, anthropometric measurements, blood pressure measurement, and serum biochemical parameters, was noted as per a predesigned proforma. **Result:** The commonest age group of patients noted in the study was 51-60 years (42.5%), followed by 41-50 years (35%). The majority of enrolled patients in the study were males (62.5%). The majority of the enrolled patients (60%) in the study were noted to be between 25-29.99 kg/m<sup>2</sup>, which is the pre-obese range. 26.25% of the study participants had a smoking habit. 96.25% of the enrolled participants had hypertension, 86.25% of the enrolled participants had DM, and 81.25% of the enrolled participants had dyslipidemia. The number of enrolled patients with a Vitamin D deficiency was noted to be 67.5%. The mean age of the vitamin-d deficient group was significantly higher than the vitamin-d-normal group, with a significant negative correlation between BMI and serum vitamin D levels. Most of the patients in the vitamin-D-deficient group had smoking habits versus the vitamin-D-normal group, and this difference was statistically significant. The alcohol intake, mean serum cholesterol, mean serum triglycerides, and mean serum VLDL were all noted to be significantly higher in the vitamin-D-deficient group versus the vitamin-D-normal group. The mean parathormone levels (PTH levels) were significantly higher in the vitamin-D-deficient group versus the vitamin-D-normal group. **Conclusion:** Obesity was related to lower vitamin-d levels in the enrolled participants. A significant association was noted between the history of smoking habit and vitamin D deficiency.

## INTRODUCTION

Vitamin D is a fat-soluble vitamin known for its antirachitic activity. Vitamin D can be synthesized endogenously. About 90% of the required Vitamin D is synthesized in the skin under sun exposure. It is needed for the maintenance of normal blood levels of calcium and phosphate that are required for normal mineralization of bone, muscle contraction, nerve conduction, and general cellular function in all cells of the body. It is also important for immune function, inflammation, cell proliferation, and differentiation. The prevalence of Vitamin D deficiency is reported

worldwide, both in sunshine-deficient and sunshine-sufficient countries. Still, it is the most underdiagnosed and undertreated nutritional deficiency in the world.<sup>[1,2]</sup> The community-based Indian studies of the past decade done on apparently healthy controls reported a prevalence ranging from 50% to 94%, except for one study, which reported a prevalence of 34.5%, which can be due to the low cutoff. These studies which included various age groups reflect the magnitude of the problem. High prevalence was seen throughout the country. Several epidemiological studies have found that serum vitamin D levels are inversely associated with

metabolic syndrome in Western and Asian populations. Animal models and in vitro studies have revealed some relevant mechanisms of action of vitamin D on Metabolic syndrome. However, the results of epidemiological studies on the associations between serum vitamin D deficiency and metabolic syndrome are inconsistent. In addition, many of the studies included only people younger than 60 years, and few of them focused on elderly individuals, especially people older than 80 years, which is the group with the highest prevalence of vitamin D deficiency and metabolic syndrome. Due to the lack of studies at Indian hospitals, it is difficult for the results to be generalized to individuals from the country just by extrapolating findings from other countries. Therefore, present study was conducted to evaluate the prevalence of vitamin D deficiency in Indian adult population with metabolic syndrome, at a tertiary care hospital in India.

Vitamin D is a fat-soluble prohormone that plays an essential role in bone mineral metabolism, being involved in calcium and phosphorus metabolism and skeletal homeostasis. The main source of vitamin D is cholecalciferol or vitamin D<sub>3</sub>, synthesized by sunlight on the skin from 7-dehydrocholesterol, for which cholesterol is a precursor.<sup>[3,4]</sup> It is also available in the diet from animal (cholecalciferol) and vegetable (ergocalciferol) foods. Regardless of the source, vitamin D requires two hydroxylations in the organism to become biologically active, the first in the liver and the second in the kidney, resulting in the form known as 1,25(OH)<sub>2</sub> vitamin D or calcitriol.

## MATERIALS AND METHODS

The study was cross-sectional, observational study in Department of General medicine, Northern Railway Central Hospital, New Delhi. Patients visiting medicine Outpatient, Inpatient of Northern Railway Central Hospital of age 18-60 years diagnosed with metabolic syndrome after applying inclusion and exclusion criteria.

Data was collected between October 2022 and September 2023.

Patients visiting medicine Outpatient, Inpatient of Northern Railway Central Hospital of age 18-60 years diagnosed with metabolic syndrome.

Sample size calculation:

$$n = \frac{Z\alpha^2 * p * q}{d^2}$$

n = sample size

Z $\alpha$  at 95% CI = 1.96

p = proportion or prevalence of interest

q = 100-p

d = precision

Based on the study conducted by Ramesh Reddy Allam et al,<sup>[5]</sup> the prevalence of Vitamin D deficiency among Metabolic syndrome patients is 77.9%, by using this parameter in the given formula sample size is calculated as follow:

P=77.9%, q=22.1%, d=10%

N= 67 rounded off to 70.

As the study recruited patients presenting with Metabolic syndrome at department of general medicine, consecutive sampling method was followed. Patients fulfilling inclusion criteria were included successively.

### Inclusion Criteria

Age criteria between 18 years and 60 years of either gender and patients diagnosed with metabolic syndrome as per IDF criteria 2006.

### Exclusion criteria

Patients having disorders that change the metabolism of vitamin D like CLD (Chronic Liver Disease), CKD (chronic kidney disease), hyperparathyroidism, receiving Vitamin D replacement therapy, use of contraceptive pills or drugs that may affect lipid profile and plasma glucose, pregnancy and lactation, thyroid disorder, malabsorption syndrome, type 1 diabetes mellitus, weight loss program at the time of screening.

A cross-sectional observation study was conducted at Northern Railway Central Hospital (tertiary care center). Ethics committee approval was taken from the Ethical Review Committee of the hospital. Patients visiting medicine Outpatient and Inpatients of Northern Railway Central Hospital aged 18-60 years diagnosed with metabolic syndrome after applying inclusion and exclusion criteria. Patients from the Indoor and Outdoor Medicine Department of NRCH, New Delhi, suspected of phenotype, were screened for metabolic syndrome.

Once having met the IDF 2006 norms through its inclusion and exclusion criteria, they were enrolled for study after explaining purpose as well as risks and benefits of the study and written consent was taken simultaneously.

A detailed history of suspected patients, including demographic profile, anthropometric measurements, blood pressure measurement, and serum biochemical parameters, were noted as per predesigned proforma. Medical History- A detailed history including present complain, relevant present and past history, family history, drug history that may affect lipid profile and plasma glucose, involvement in weight losing programme were taken.

The following anthropometric measures were taken three times, and the mean was calculated: height (centimeters [cm]), weight (kilogram [kg]), and waist circumference (cm). Based on the data obtained, the body mass index (BMI) was calculated. BMI = Weight (kg)/ square of Height (m)

A BMI in the range of 18.5–22.9 kg/m<sup>2</sup> was regarded as normal, a BMI between 23.0 kg/m<sup>2</sup> and 24.9 kg/m<sup>2</sup> denoted overweight, and a BMI >25 kg/m<sup>2</sup> indicated obesity.

Blood pressure (BP)- It was measured using a manual sphygmomanometer and in sitting position after a rest of 15 minutes.

Biochemical analysis- Venous blood for biochemical analysis was obtained from the participants in four different vacutainers.

- One 3 ml tube with NaF for testing the fasting plasma glucose; measured using Beckman Coulter DxC 700 AU machine by hexokinase G6P-OH method.
- Plain 5 ml tube for testing serum lipid profile; was measured using Beckman Coulter DxC 700 AU machine by enzymatic method.
- Plain 5 ml tube for testing Serum PTH, was measured using C.L.I.A. (Chemiluminescence Immunoassay) method.
- Patients fulfilling the IDF 2006 criteria for Metabolic syndrome were subjected to Vitamin D (25-hydroxyvitamin D [25 (OH) D]) estimation. For this, venous blood in plain 5ml vacutainer was taken and measured using C.L.I.A (Chemiluminescence Immunoassay) method.

**Statistical Analysis:** After data collection, data entry was done in Microsoft Excel. Data analysis was done with the help of statistical software using IBM SPSS Statistics (version 22.0). Discrete categorical data was presented as n (%). Quantitative/continuous data, if any, was presented with the help of Mean and Standard deviation. The comparison between study subgroups (Vitamin D deficient and Vitamin D non-deficient) for continuous variables was done using an unpaired t-test at a time point. The normality of quantitative data was checked using the Kolmogorov-Smirnov test. Proportions were compared using a chi-square test or Fisher's exact test, wherever applicable. Correlation between Vitamin D and other relevant variables was done using Pearson's correlation test. A p-value of less than 0.05 was considered statistically significant.

## RESULTS

A total of 80 patients were enrolled in the study.

The mean age was noted to be  $46.83 \pm 9.83$  years, with a median age of 48.5 years. The range of age is 23 years to 60 years. The majority of enrolled patients in the study were males (62.5%). The commonest age group of patients noted in the study was 51-60 years (42.5%), followed by 41-50 years (35%). [Table 1] The mean weight of enrolled patients was noted to be  $76.84 \pm 6.59$  kg, with a range of weight being 64 to 90 kgs. The mean height of enrolled patients was noted to be  $161.01 \pm 5.64$  cm, with a range of height being 148 to 180 cm. The mean waist circumference of enrolled patients was noted to be  $102.66 \pm 5.87$  cm, with a range of circumference being 89 to 117 cm. The mean BMI was noted to be  $29.64 \pm 2.23$  kg/m<sup>2</sup>, with a range of BMI being 25.3 to 39.4 kg/m<sup>2</sup>. Majority of the enrolled patients (60%) in study were noted to be between 25-29.99 kg/m<sup>2</sup>, which is the pre-obese range. 35% of patients in the study were from obese category (30-34.99 kg/m<sup>2</sup>) while 4 patients (5%) were morbidly obese. [Table 2] 49 of the 80 enrolled participants (61.25%) were involved in active occupations, while 31 patients (38.75%) participants were involved in sedentary type of work. [Table 3] 26.25% of the study participants had a smoking habit, while 5% of the study participants had habit of alcohol intake. [Table 4] 96.25% of the enrolled participants had hypertension, 86.25% of the enrolled participants had DM, 81.25% of the enrolled participants had dyslipidemia, while 40% of the enrolled participants had obesity. [Table 5] The mean Vitamin D levels of the study participants was noted to be  $19.29 \pm 9.41$  ng/ml, with a range of 4.99 to 46.98 ng/ml. The number of enrolled patients with a vitamin D deficiency was noted to be 67.5%, while 32.5% of the enrolled patients had normal vitamin D levels. [Table 7]

**Table 1: Age and gender based distribution in study.**

Age group (years)	Number of cases	% cases
18-30 years	7	8.75%
31-40 years	11	13.75%
41-50 years	28	35.00%
51-60 years	34	42.50%
Mean age (years)	$46.83 \pm 9.83$	
Number of males	50	62.5%
Number of females	30	37.5%

**Table 2: Weight, height, waist circumference details of enrolled cases**

Parameters assessed	Calculated values
Weight details	
Mean weight (kg)	$76.84 \pm 6.59$
Median weight (kg)	76
Minimum weight (kg)	64
Maximum weight (kg)	90
Height details	
Mean height (cm)	$161.01 \pm 5.64$
Median height (cm)	160
Minimum height (cm)	148
Maximum height (cm)	180
Waist circumference (cm)	
Mean abdominal girth (cm)	$102.66 \pm 5.87$
Median abdominal girth (cm)	102
Minimum abdominal girth (cm)	89

Maximum abdominal girth (cm)	117
BMI	
Mean BMI (kg/m <sup>2</sup> )	29.64 ± 2.23
Median BMI (kg/m <sup>2</sup> )	29.50
Minimum BMI (kg/m <sup>2</sup> )	25.3
Maximum BMI (kg/m <sup>2</sup> )	39.4

**Table 3: BMI based distribution in study**

BMI (kg/m <sup>2</sup> )	Number of cases	% cases
18.5-24.99 kg/m <sup>2</sup>	0	0.00%
25-29.99 kg/m <sup>2</sup>	48	60.00%
30-34.99 kg/m <sup>2</sup>	28	35.00%
>35 kg/m <sup>2</sup>	4	5.00%

**Table 4: Smoking and alcohol habit noted in study**

Status	Smoking	Alcohol
Yes	21 (26.25%)	4 (5%)
No	59 (73.75%)	76 (95%)

**Table 5: Comorbidities noted in study**

Comorbidities	Number of patients	% of patients
Hypertension	77	96.25%
Diabetes mellitus (DM)	69	86.25%
Dyslipidemia	65	81.25%
Obesity	32	40.00%
Coronary artery disease (CAD)	4	5.00%
Chronic obstructive pulmonary disease (COPD)	4	5.00%
Cerebrovascular accident (CVA)	1	1.25%

**Table 6: Investigations of enrolled cases**

Parameters assessed	Calculated values
Mean serum cholesterol (mg/dl)	182.93 ± 51.97
Mean serum triglycerides (mg/dl)	159.78 ± 70.80
Mean serum HDL (mg/dl)	39.83 ± 12.03
Mean serum LDL (mg/dl)	113.59 ± 33.67
Mean serum VLDL (mg/dl)	33.78 ± 10.27
Mean FPG (mg/dl)	122.21 ± 30.78
Mean systolic blood pressure (mm Hg)	136.75 ± 14.97
Mean diastolic blood pressure (mm Hg)	86.93 ± 13.05

**Table 7: Vitamin D levels of enrolled cases**

Parameters assessed	Calculated values
Mean Vitamin D levels (ng/ml)	19.29 ± 9.41
Median Vitamin D levels (ng/ml)	18.29
Minimum Vitamin D levels (ng/ml)	4.99
Maximum Vitamin D levels (ng/ml)	46.98
Number of patients with Vitamin-D deficiency	54 (67.5%)
Number of patients with normal Vitamin-D	26 (32.5%)

**Table 8: Comparison of baseline patient characteristics between Vitamin-D-deficient and Normal Vitamin D subgroups**

Parameter assessed	Vitamin-D-deficient group (n=54)	Normal Vitamin D group (n=26)	P value
Mean Vitamin D (ng/ml)	14.15 ± 4.70	29.99 ± 7.53	0.001*
Mean age (years)	49.63 ± 10.56	43.31 ± 7.71	0.03*
Mean weight (kg)	76.24 ± 6.68	77.08 ± 6.36	0.68
Mean height (cm)	160.56 ± 5.95	161.96 ± 4.89	0.71
Mean waist circumference (cm)	102.72 ± 6.06	102.54 ± 5.57	0.82
Mean BMI (kg/m <sup>2</sup> )	29.48 ± 2.32	29.96 ± 2.05	0.76
Gender distribution			
Number of males	32 (59.26%)	18 (69.23%)	0.21
Number of females	22 (40.74%)	8 (30.77%)	
Occupation			
Active	28 (51.85%)	21 (80.77%)	0.001^
Sedentary	26 (48.15%)	5 (19.23%)	
Smoking			
Yes	17 (31.48%)	4 (15.38%)	0.02^
No	37 (68.52%)	22 (84.62%)	
Alcohol intake			
Yes	3 (5.56%)	1 (3.85%)	0.47
No	51 (94.44%)	25 (96.15%)	

**Table 9: Comparison of laboratory investigations and blood pressure between Vitamin-D-deficient and Normal Vitamin D subgroups**

Parameter assessed	Vitamin-D-deficient group (n=54)	Normal Vitamin D group (n=26)	P value
Mean Vitamin D levels (ng/ml)	14.15 ± 4.70	29.99 ± 7.53	0.001*
Mean serum cholesterol (mg/dl)	185 ± 43.51	173.62 ± 48.37	0.001*
Mean serum triglycerides (mg/dl)	163.11 ± 37.94	151.85 ± 77.34	0.01*
Mean serum HDL (mg/dl)	39.85 ± 12.21	39.77 ± 11.89	0.89
Mean serum LDL (mg/dl)	113.35 ± 22.76	114.08 ± 26.15	0.76
Mean serum VLDL (mg/dl)	34.85 ± 10.59	30.54 ± 19.78	0.04*
Mean FPG (mg/dl)	122.06 ± 23.02	123.54 ± 24.10	0.47
Mean systolic blood pressure (mm Hg)	136.48 ± 15.75	137.31 ± 13.31	0.54
Mean diastolic blood pressure (mm Hg)	86.00 ± 12.19	86.85 ± 14.73	0.65
Mean serum PTH (pg/ml)	38.60 ± 31.35	31.84 ± 9.55	0.03*

**Table 10: Correlation of Vitamin D levels with various laboratory parameters**

Parameter assessed	Correlation coefficient (r)	Confidence interval	Interpretation of correlation	P value
Age (years)	-0.31	-0.17 to -0.44	Moderate negative	0.001*
BMI (kg/m <sup>2</sup> )	-0.34	-0.13 to -0.52	Moderate negative	0.001*
Serum cholesterol (mg/dl)	-0.03	-0.24 to 0.19	Negligible	0.79
Serum triglycerides (mg/dl)	0.01	-0.20 to 0.23	Negligible	0.91
Serum HDL (mg/dl)	-0.05	-0.26 to 0.17	Negligible	0.69
Serum LDL (mg/dl)	0.03	-0.18 to 0.25	Negligible	0.76
Serum VLDL (mg/dl)	-0.08	-0.29 to 0.14	Negligible	0.48
Serum FPG (mg/dl)	0.03	-0.15 to 0.27	Negligible	0.98
Serum PTH (pg/ml)	-0.28	-0.39 to -0.17	Mild negative	0.02*

The mean vitamin D levels in the deficient group (n=54) was 14.15 ± 4.70 ng/ml, while it was 29.99 ± 7.53 ng/ml in the normal vitamin-d group (n=26). The mean age of the vitamin-D-deficient group was significantly higher than that of the vitamin-D-normal group (p<0.05). The mean weight, height, waist circumference and BMI were comparable between the two groups of patients (p>0.05). The gender distribution was also comparable statistically (p>0.05); however, the proportion of female patients was higher in the vitamin-D deficient group versus the vitamin-D-normal group numerically (40.74% vs 30.77%).

Most proportion of patients in the vitamin-D-deficient group had a sedentary lifestyle versus vitamin-D-normal group (48.15% vs 19.23%) and this difference was statistically significant (p<0.05). Most of the patients in the vitamin-D-deficient group were smoker (31.48%) versus vitamin-D-normal group (15.38%) and this difference was statistically significant (p<0.05).

The alcohol intake was statistically comparable between both the study groups (p>0.05).

The mean serum cholesterol, mean serum triglycerides, and mean serum VLDL, mean parathormone levels (PTH levels) were all noted to be significantly higher in the in the vitamin-D-deficient group versus vitamin-D-normal group (p<0.05).

P<0.05 considered significant by Pearson's correlation coefficient test. (±) 0.01 to 0.1 = Negligible; (±) 0.11 to 0.30 = Mild correlation; (±) 0.31 to 0.50 = Moderate correlation; (±) >0.50 = Strong correlation.

There was a statistically significant negative correlation between age and serum vitamin D levels, as well as BMI and serum vitamin D levels (p<0.05). In addition, a statistically significant negative

correlation was also noted between serum PTH levels and serum vitamin D levels (p<0.05).

## DISCUSSION

Study was conducted to address this debatable topic, wherein we wanted to understand the vitamin D deficiency in the metabolic syndrome group, and understand the patient characteristics of the vitamin-D deficient patients in comparison to those with normal vitamin D, in Indian population.

A total of 80 patients were enrolled in the study. The mean age was noted to be 46.83 ± 9.83 years, with a median age of 48.5 years. The range of age is 23 years to 60 years. Majority of patients in the study were in the age group 51-60 years (42.5%), followed by 41-50 years (35%). Male patients (62.5%) outnumbered the female (37.5%) in the present study. In the study by Pathania et al,<sup>[6]</sup> the mean age of the subjects was 43.81±10.45 years. 51.1% were males, while 48.9% were females. In the study by AlDabhani et al,<sup>[7]</sup> 58% of the study population were females; mean age was similar between males and females. The mean age of the enrolled patients was 39.9 years. In the study by Liu et al,<sup>[8]</sup> the average age of patients was 85 years as elderly patients from China were enrolled. The study population comprised of 56% females and 44% males.

The mean Vitamin D levels of the study participants was noted to be 19.29 ± 9.41 ng/ml, with a range of 4.99 to 46.98 ng/ml. The prevalence of vitamin-D deficiency in the metabolic syndrome population was noted to be 67.5% in study. The mean vitamin D levels in the deficient group (n=54) was 14.15 ± 4.70 ng/ml, while it was 29.99 ± 7.53 ng/ml in the normal vitamin D group (n=26). In a similar study by Pathania et al,<sup>[6]</sup> prevalence of vitamin D deficiency (<20 ng/ml) in the Metabolic syndrome patients was

76%. In the study by AlDabhani et al,<sup>[7]</sup> the prevalence of vitamin D deficiency in the Metabolic syndrome patients was 64%, which was a finding very close to our study. In the study by Liu et al,<sup>[8]</sup> the Metabolic syndrome patients with vitamin-D deficiency formed 41.3% of the study population.

The mean age of the vitamin-D-deficient group was significantly higher than the vitamin-D-normal group ( $p < 0.05$ ). There was a statistically significant negative correlation between age and serum vitamin D levels ( $p < 0.05$ ). This shows that elderly population with metabolic syndrome were more prone to be having vitamin D deficiency. The elderly population is highly prone to develop alterations in the mechanisms of 25(OH)D synthesis, mainly due to physiological changes related to the ageing process.<sup>[9]</sup> The high prevalence of hypovitaminosis D in the elderly could be associated with changes in mineral bone density, decreased sun exposure, and secondary hyperparathyroidism.<sup>[10]</sup> The study by Quaggiotto et al,<sup>[12]</sup> corroborated with the present study, showing from a laboratory databank analysis that high levels of 25(OH)D were detected in young individuals, while aged individuals presented the lowest values of 25(OH)D. Other studies also suggest that vitamin D deficiency among older people and could be a risk factor for the development of osteoporosis and osteomalacia.

The mean BMI was noted to be  $29.64 \pm 2.23$  kg/m<sup>2</sup>, with a range of BMI being 25.3 to 39.4 kg/m<sup>2</sup>. Majority of the enrolled patients (60%) in study were noted to be between 25-29.99 kg/m<sup>2</sup>, which is the pre-obese range. 35% of patients in the study were from obese category (30-34.99 kg/m<sup>2</sup>) while 4 patients (5%) were morbidly obese. Additionally, there was a statistically significant negative correlation between BMI and serum vitamin D levels ( $p < 0.05$ ). This indicated that greater degree of obesity was related with lower levels of vitamin-d in the enrolled participants. A meta-analysis of 23 cross-sectional and cohort studies in the West showed that the prevalence of vitamin D deficiency was 35% higher in obese subjects compared to the eutrophic group (PR: 1.35; 95% CI: 1.21-1.50) and 24% higher than in the overweight group (PR: 1.24; 95% CI: 1.14-1.34).<sup>[12]</sup> The principle mechanism agreed upon for the higher prevalence of vitamin D insufficiency and deficiency in obese individuals has been termed as volumetric dilution of vitamin D, which explains the higher distribution of vitamin D in obese individuals, lowering the serum concentrations of vitamin D. Another study highlights the decreased expression of cytochrome P450 2J2 gene coding for the enzyme 25-hydroxylase and cytochrome P450 27B1 coding for the enzyme 1 $\alpha$ -hydroxylase in obese individuals.<sup>[13]</sup>

The gender distribution was also comparable statistically ( $p > 0.05$ ); however, the proportion of female patients was higher in the vitamin-d deficient group versus the vitamin-D-normal group numerically (40.74% vs 30.77%). Thus, females did show a trend of having greater vitamin-d deficiency

chance in study. This may be linked to the fact that many of the females in India are housewives, who are at home and hence, having a sedentary lifestyle. This leads to lower exposure of these individuals to the sunlight as they are mostly indoors, leading to lower pre-vitamin-D3 production.

A high prevalence of vitamin D insufficiency in a sunlight-rich tropical country of India might appear counter-intuitive at first, but changing lifestyle and food habits, sedentary nature, reduced sunlight exposure with clothing and sunscreens, and increasing UVB absorbing pollutants can explain this conundrum.

Most of the patients in the vitamin-D-deficient group had smoking habit versus vitamin-D-normal group (31.48% vs 15.38%) and this difference was statistically significant ( $p < 0.05$ ). This showed that there may be a link between the smoking habit and vitamin-D deficiency. A study from the U.K. Biobank indicated that tobacco smoking increased the risk of vitamin-d deficiency in adults. Similarly, a study in Finland among 5714 adults aged 30-79 years showed lower serum 25(OH)D concentrations in former and current smokers than never- or less than 1-year smokers. Evidence from a study in Sweden in young men showed that smokers consistently had lower serum vitamin D concentrations than non-smokers. In addition, significantly low serum 25(OH)D3 levels were observed in both active and passive smoking groups, according to the report from Soldin et al,<sup>[14]</sup> who evaluated steroid hormone concentrations of 293 women age 18-45 years in the United States. The mechanisms for lowering vitamin D with smoking exposure remain unclear. Some molecular pathways have been reported. Smoking exposure causes a disruption of vitamin D metabolism, related to the dysfunction of vitamin and D-parathyroid hormone (PTH) axis. The simultaneous decrease in PTH and calcitriol has been observed in a population with smoking exposure. The reduction in 1 $\alpha$ -hydroxylase with exposure to cigarette smoking extract also has been reported. In addition, the dysregulation of genes that encode for the enzymes involving vitamin D metabolism may explain the deleterious effect of smoking exposure on serum vitamin D. The decreased concentration of serum vitamin D with smoking exposure may also be related to disturbances in food intake. A study evaluating smoking exposure, dietary calcium, and vitamin D concentrations in women showed that tobacco smoking can change the taste of dietary intake, and thereby result in lower intake of vitamin D from food; moreover, this change can be reversed by smoking cessation.

The mean serum cholesterol, mean serum triglycerides, and mean serum VLDL were all noted to be significantly higher in the in the vitamin-D-deficient group versus vitamin-D-normal group ( $p < 0.05$ ). This indicates that greater increase in lipid parameters were related with vitamin-d deficiency in study. A similar trend was noted by the study conducted by Pathania et al,<sup>[6]</sup> who noted a weak

negative correlation was also seen between vitamin D levels and lipid profile parameters like total cholesterol, triglycerides, and LDL, but not HDL; a finding very similar to our study. A similar result was seen in a cross-sectional study by Jiang et al,<sup>[15]</sup> of 3788 adults in China, showing a significant inverse correlation between 25(OH) vitamin D and triglycerides ( $\beta$  coefficient=-0.077,  $p<0.05$ ) and LDL cholesterol ( $\beta$  coefficient=-0.245,  $p<0.05$ ). A meta-analysis of 17 cross-sectional studies, including 25,394 subjects, found an inverse association between 25(OH) vitamin D and triglycerides, total cholesterol, and LDL cholesterol and a direct association with HDL cholesterol in children and adolescents. The mechanisms by which vitamin D could affect lipid profiles are not well defined. Vitamin D can affect lipoprotein metabolism and reduce triglyceride synthesis and secretion in the liver, increasing very low-density lipoprotein (VLDL) receptor expression. Hence its deficiency can lead to increased TG and VLDL levels.<sup>[16]</sup>

The mean parathormone levels (PTH levels) were noted to be significantly higher in the in the vitamin-D-deficient group versus vitamin-D-normal group ( $p<0.05$ ). Individuals with low vitamin D levels were those who had higher values of PTH, while individuals with high values of vitamin D showed low values of PTH. Low 25(OH)D status leads to reduced efficiency in intestinal calcium absorption, and the body reacts by increasing the secretion of parathyroid hormone (PTH). Especially in elderly people, increased serum PTH concentration can cause bone turnover and bone loss, defects in mineralization, and increased risk of fractures. Furthermore, vitamin D supplementation with calcidiol, in addition to improving serum 25-OH-D, also significantly lowers PTH levels, reducing secondary hyperparathyroidism.<sup>110</sup>The association between parathyroid hormone (PTH) and vitamin D may be an important determinant of bone remodelling, mainly in the elderly.

Vitamin D induces the activation of calpain and caspase-12, the enzymes involved in the apoptosis of fat tissue. Blumberg et al,<sup>[17]</sup> found that liganded vitamin D receptors of 3T3-L1 cells in the adipose tissue repressed both CCAAT/enhancer binding protein (C/EBP)- $\alpha$  and peroxisome proliferator-activated receptors (PPAR)- $\gamma$  expression via inhibition of C/EBP- $\beta$  expression and action and was a potent inhibitor of adipogenesis. The link between this vitamin and adipokines and inflammatory factors, especially in metabolic syndrome patients, received less attention. Pott-Junior et al,<sup>[18]</sup> found that when comparing Metabolic syndrome subjects, serum levels of interleukin 10 (IL-10), IL-1 $\alpha$ , and tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ) showed a trend towards higher levels in subjects with vitamin D deficiency. In intervention studies, vitamin D supplementation can increase adipokine concentrations in obese or overweight adults.<sup>[19]</sup> All these findings strengthen the hypothesis of the presence of vitamin D deficiency in metabolic

syndrome patients, but how much vitamin D supplementation effective in metabolic syndrome cases is still to be studied. The acceleration of peripheral vascular disease, hypertension, and cardiac-associated mortality, in general, are all highly prevalent in vitamin D-deficient individuals, thus compounding the ill effects of obesity.<sup>[20]</sup>

#### Limitations of study

The sample size was limited, and the study was done at only one hospital. Hence, the over-generalization of the results for whole Indian population should be done with caution. Since this study is cross-sectional, the directionality of the relationship between adiposity, vitamin D, Metabolic syndrome, and diabetes could not be elucidated.

## CONCLUSION

A substantial proportion of metabolic syndrome Indian patients were noted to have vitamin-D deficiency. Elderly population, predominantly females, with metabolic syndrome were more prone to be having vitamin-D deficiency. Greater degree of obesity was related with lower levels of vitamin-d in the enrolled participants. A significant association was noted between the history of smoking habit and vitamin-D deficiency. A greater increase in lipid parameters were significantly related with vitamin-D deficiency in study. Future studies with a larger sample size and multicentre study design can help in validating our study findings.

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