Association of Vitamin-D Levels with Metabolic Syndrome in Elderly Patients with Hip Fracture

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Abstract:

In this research conducted at Mahatma Gandhi Medical College and Research Institute, Pillaiyarkuppam, Puducherry, we aimed to assess the association between vitamin-D levels and metabolic syndrome (MS) in elderly patients with hip fractures. A total of 100 participants were selected, including elderly patients with hip fractures and age-matched healthy volunteers. Metabolic syndrome was identified using NCEP ATP III criteria. Results revealed significantly decreased vitamin-D levels and an increased frequency of MS or its components in elderly patients with hip fractures compared to controls. These metabolic derangements correlated significantly with low vitamin D levels. The study highlights the role of vitamin D in increasing the risk of osteoporosis, frailty, falls, and fractures, as well as its connection to metabolic changes, insulin resistance, and cardiovascular risk. Screening for vitamin D deficiency in elderly individuals with low-impact fractures, increasing sunlight exposure, and providing supplementation can prevent fractures and improve metabolic health. While the study has limitations, such as its cross-sectional nature, it underscores the need for future randomized controlled trials to evaluate the impact of vitamin D supplementation on fracture risk and metabolic outcomes. Early screening and intervention strategies can enhance the quality of life for the geriatric population.

Keywords: Vitamin D, Metabolic Syndrome, Elderly, Hip Fractures, Geriatric Health.

Introduction:

The role of Vitamin–D in the humans is said to be very important as it forms the base for the normal bone formation, good muscle health, a good human growth. The deficiency of vitamin- D leads to a number of associated diseases like rickets, osteoporosis, an increased risk of fractures, and other tooth related disorders. About 2/3rd patients with acute hip fracture have been identified to have vitamin D insufficiency [1]. The vitamin–D deficiency is also found to be associated with various metabolic diseases like diabetes, hypertension and increased cardiovascular diseases. The deficiency of vitamin –D is also seen more commonly worldwide among patients with osteoporosis. Most commonly Vitamin-D is obtained from the sunlight, when ultraviolet (UV) rays from sunlight strikes the skin the start of synthesis of cholecalciferol activates. The body needs to go through two hydroxylation's in order to activate the biological inactive form of vitamin D that is received through sunlight, meals, and supplements.[2] Additionally in the epidermis, pre-vitamin D3 is converted to vitamin D3 via a non-enzymatic process called heat isomerization. Vitamin D3 is absorbed into the bloodstream from the skin. One of several high-capacity cytochrome P450s in the hepatic parenchyma converts vitamin D3 into 25-hydroxyvitamin D3 (25OHD3); the microsomal CYP2R1 appears to have the strongest affinity for substrate vitamin D. [3] Fat-soluble vitamin is transformed into 25- hydroxyvitamin D [25(OH) D], also known as "calcitriol," via the primary hydroxylation, which takes place in the liver. The physiologically active form of vitamin D, 1,25- dihydroxy vitamin D [1,25(OH)2D], often known as "calcitriol," is created during the second hydroxylation, which largely takes place inside the kidney.[2] The serum concentrations between 20ng/ml and 29.9ng/ml are considered insufficient, whereas concentrations below 20ng/ml are considered deficient [3] Age, gender, inadequate dietary vitamin D intake, low exposure to sunlight, and lower socioeconomic position are associated with vitamin D insufficiency and insufficiencies. [2] The aged population has a higher fracture risk due to vitamin D insufficiency.[4]Vitamin D deficiency in adults can precipitate or exacerbate osteopenia and osteoporosis, cause osteomalacia and muscle weakness, and increase the risk of fracture .[5] Vitamin-D deficiency is highly prevalent among Asian Indians and has been reported in almost all age groups even among the healthy Indian subjects.[6] Deficiency of vitamin-D causes osteopenia, osteomalacia and leads to brittle bones- Osteoporosis.[5] , leading to increased risk of bone fractures .[7] It is also observed that vitamin D plays a protective role in

metabolic syndrome and cardiovascular diseases [8,9] and hence its deficiency has been linked to increased incidence of these diseases. Though deficiency of Vitamin -D among the elderly is known, only a little is known on the long-term effects of hypovitaminosis D on the fractures. [10] Reduced serum Vitamin-D levels lead to an increased (PTH) parathyroid hormone levels in the body leading to bone loss, and increased risk of hip fractures.[11] The subclinical insufficiency of 25- OHD is contemplated to increase the risk of osteoporotic hip fracture in the elderly people.[12] Association of vitamin D with the components of metabolic syndrome has been recently observed.[13] Metabolic syndrome is defined as a combination of different conditions such as hypertension, central obesity, hyperglycemia, elevated triglycerides levels, cholesterol, reduced high-density lipoprotein levels and the insulin resistance [14,15,16] Metabolic syndrome has become a major concern of health sector in recent times. So far, the mechanisms adjuvant to the role of vitamin D in metabolic syndrome remains insufficient, it is viewed that the 25(OH)D3 could be linked to decreased insulin secretion and sensitivity [17,18] obesity [19,20], and hypertension [21], diabetes [22,23]. The various components of metabolic syndrome like abdominal obesity, hypertension, dyslipidemia and abnormal glucose metabolism have been associated with osteoporosis. These components might affect bone differently. Obesity has been shown to increase bone mineral density owing to its association with higher 17 β-estradiol levels and higher mechanical load, which may protect bone [24, 25]. But visceral fat accumulation is also associated with higher levels of pro-inflammatory cytokines, which may up-regulate receptor activators of nuclear kappa B ligand, leading to increased bone resorption and therefore decreased Bone Mass Density [26, 27]. Similarly, association between dyslipidemia and hypertension with bone metabolism is also inconclusive. Recent meta-analysis on association of metabolic syndrome with Bone Mass Density and fractures were inconclusive if, metabolic syndrome is associated with bone health beyond the contribution of its individual components. [28] Hence in this study, we aim to evaluate the association of metabolic syndrome with Vitamin D levels in elderly patients diagnosed with hip fracture.

Aim:

A study to evaluate the association between vitamin–D levels and metabolic syndrome among elderly patients diagnosed with hip fracture at Mahatma Gandhi Medical College & Research Institute (MGMCRI).

Objectives:

- To assess the levels of vitamin-D among elderly patients having metabolic syndrome diagnosed with hip fracture.
- To evaluate the presence of metabolic syndrome among elderly patients having metabolic syndrome diagnosed with hip fracture.
- To associate between the levels of vitamin-D and metabolic syndrome among elderly patients diagnosed with hip fracture.

Methodology:

Study Design:

It is a cross-sectional study. The study included elderly patients (>60 years) with hip fracture and metabolic syndrome admitted to the Orthopedics ward as cases. Age- and gender-matched healthy volunteers attending master health check-up in the same hospital were recruited as controls.

Study Setting and Period

The study was carried out in the Department of Biochemistry in collaboration with the Department of Orthopaedics at Mahatma Gandhi Medical College & Research Institute, Pillaiyarkuppam, Puducherry, over a period of six months after obtaining approval from the Institutional Human Ethics Committee.

Inclusion and Exclusion Criteria

All consenting elderly patients (>60 years) admitted with hip fracture were included as cases, while those with high-impact fractures were excluded from the study.

Sampling Technique and Sample Size

Participants were selected using a purposive sampling technique. A total of two groups

were studied, with 50 subjects in each group. The sample size was calculated with 80% power and a 5% level of significance, based on a previous study on vitamin D levels in hip fracture patients. Considering a mean difference of 5.7 nmol/L and a standard deviation of 10.1 nmol/L, the sample size was estimated at 50 per group.

Study Variables

The study variables included:

- Socio-demographic characteristics: age, gender, fracture details
- Anthropometric measures: height, weight, waist circumference, hip circumference, body mass index (BMI), and waist-hip ratio
- Biochemical parameters: fasting glucose, total cholesterol, triglycerides, high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), very-low-density lipoprotein cholesterol (VLDL-C), and vitamin D
- Outcome variables: vitamin D and metabolic syndrome
- Confounding variables: none identified

Data Collection Procedure

Ethical clearance was obtained from the Institutional Research Council and Ethics Committee prior to the study. Written informed consent was obtained from all participants. Detailed demographic and medical history, treatment regimen, vital signs, and anthropometric measurements were documented. Blood samples (2 mL) were collected for biochemical analyses, which included fasting blood glucose, lipid profile, and vitamin D. Fasting glucose was estimated by the glucose oxidase method, serum total cholesterol by the cholesterol oxidase method, HDL-C by a direct homogeneous enzymatic method, triglycerides by the glycerol oxidase method, and LDL-C was calculated using Friedewald's equation. Vitamin D was measured by electrochemiluminescence immunoassay (ECLIA). Metabolic syndrome was identified according to the NCEP ATP III criteria. Data were coded systematically for further statistical analysis.

Statistical Analysis

The data were analysed using descriptive and inferential statistics. Categorical variables were expressed as percentages, and continuous variables were presented as mean ± standard deviation. Group comparisons were performed using the Chi-square test and the independent Student's t-test. The association between study parameters was assessed using the Pearson correlation test or the Spearman rank correlation test, wherever applicable. A p-value < 0.05 was considered statistically significant.

Results and Outcome:

TABLE 1: BASELINE CHARACTERISTICS OF THE STUDY SUBJECTS

SL.No.	Parameters	Cases n=50	Controls n=50	p value≠
1.	Age	70.92 ± 8.60	69.48 ± 4.97	0.308
2.	Gender (M:F)	26:24	26:24	-
3.	Hypertension	15 (30%)	13 (26%)	0.824*
4.	Diabetes	18 (36%)	15 (30%)	0.671*
5.	Weekly sunlight exposure (hrs)	14.59 ± 12.07	14.57 ± 9.45	0.993

≠ Student t test, * Chi-square test

In this study, 50 elderly patients with hip fracture and age & gender matched healthy volunteers were recruited. Table 1 depicts that among 50 patients with hip fracture, 34 (68%) of them had inter-trochanteric fracture of femur, 15 (30%) had neck of femur fracture and 1 (2%) had sub-trochanteric fracture of femur. There was no significant difference in the sunlight exposure among the cases and controls. Both cases and controls were collected during the same time period to avoid seasonal bias in vitamin D levels. (Table 1)

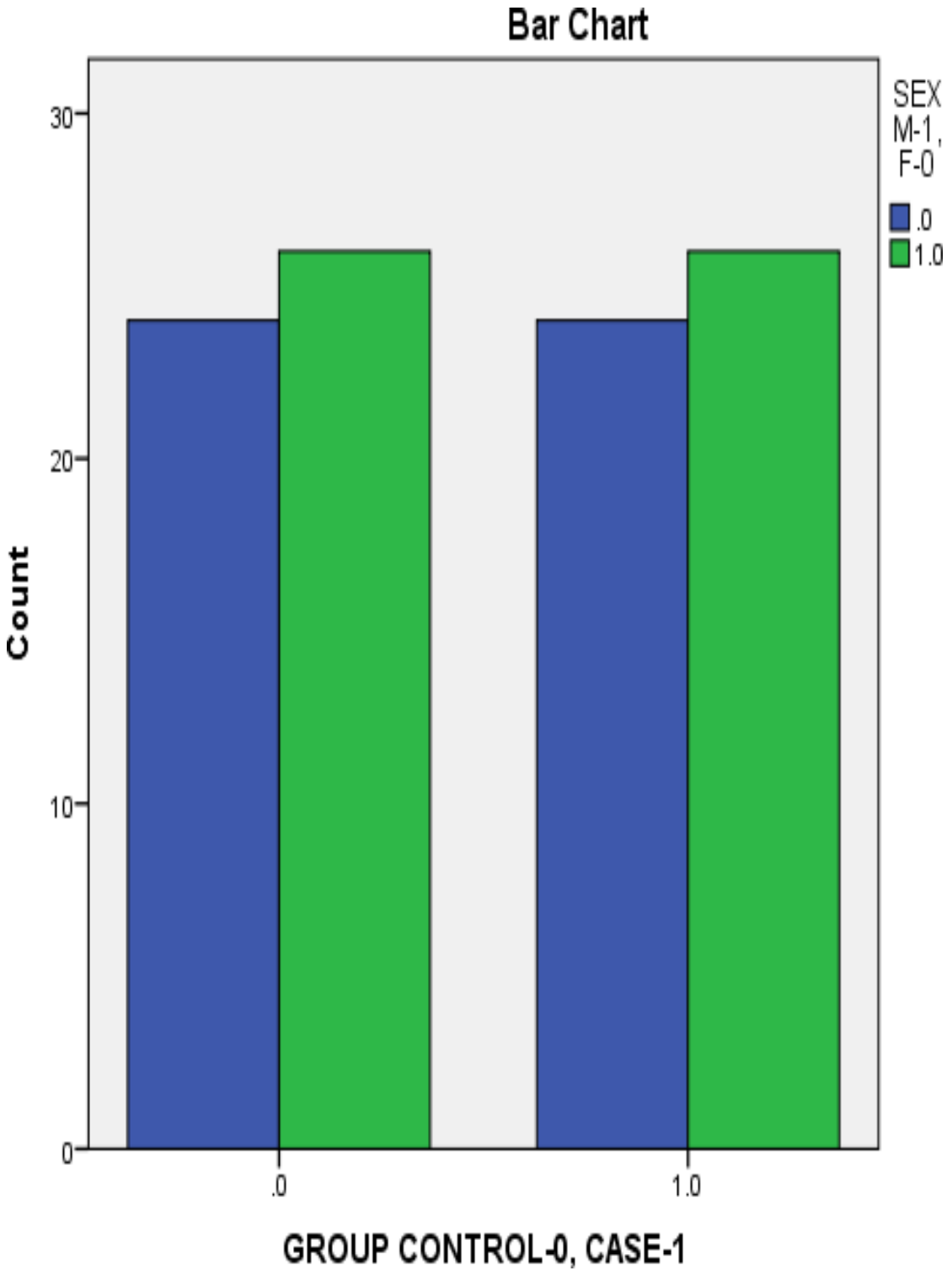

Figure 1: Gender distribution among cases & controls

Figure 1 depicts the gender distribution among the cases and controls. In each group of 50 subjects, there were 26 males & 24 females.

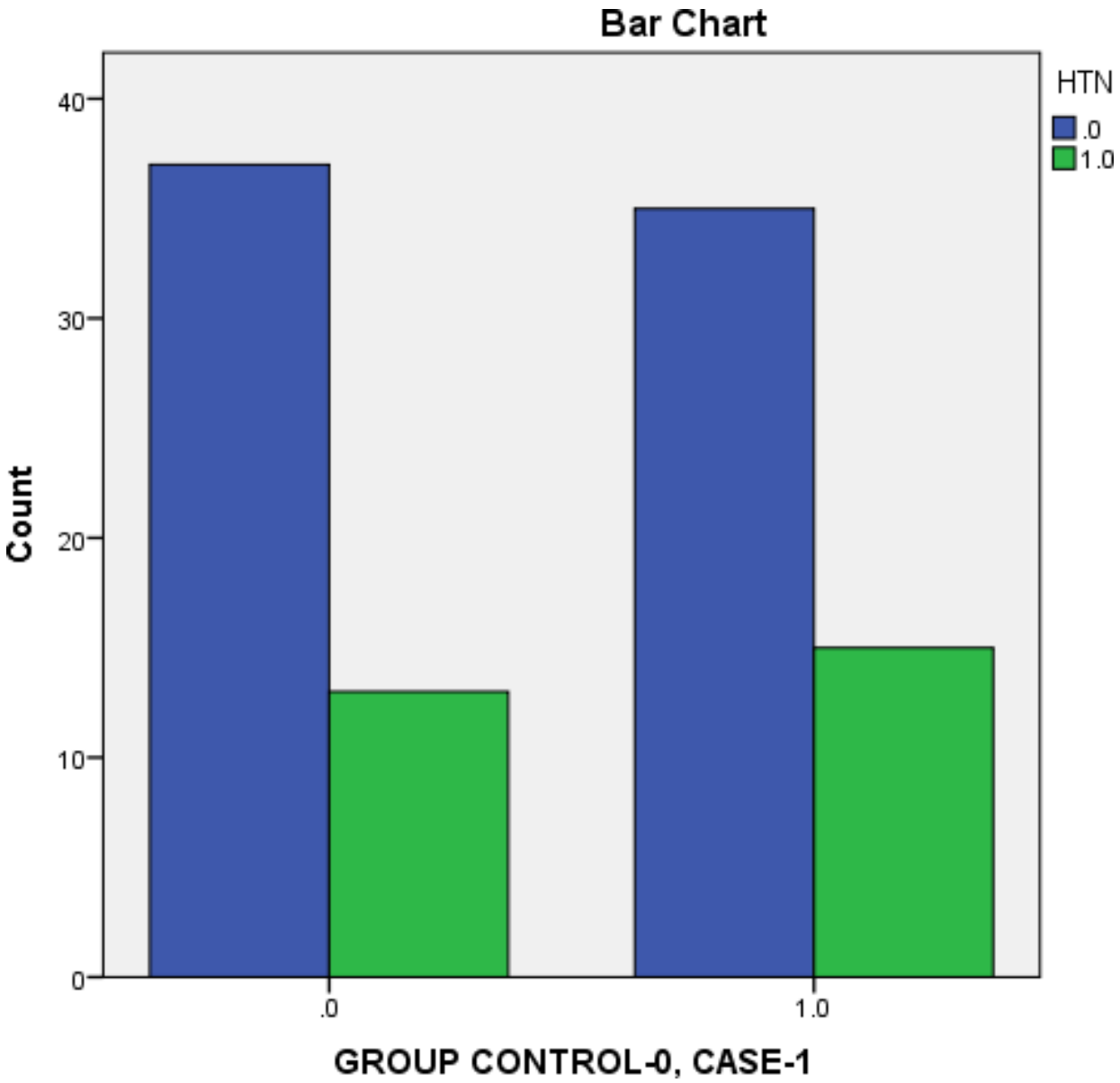

Figure 2: Distribution of Hypertensive patients among cases & controls

Figure 2 depicts the distribution of Hypertension among cases & controls. Though the number of hypertensives were higher among cases, compared to controls, it was not statistically significant.

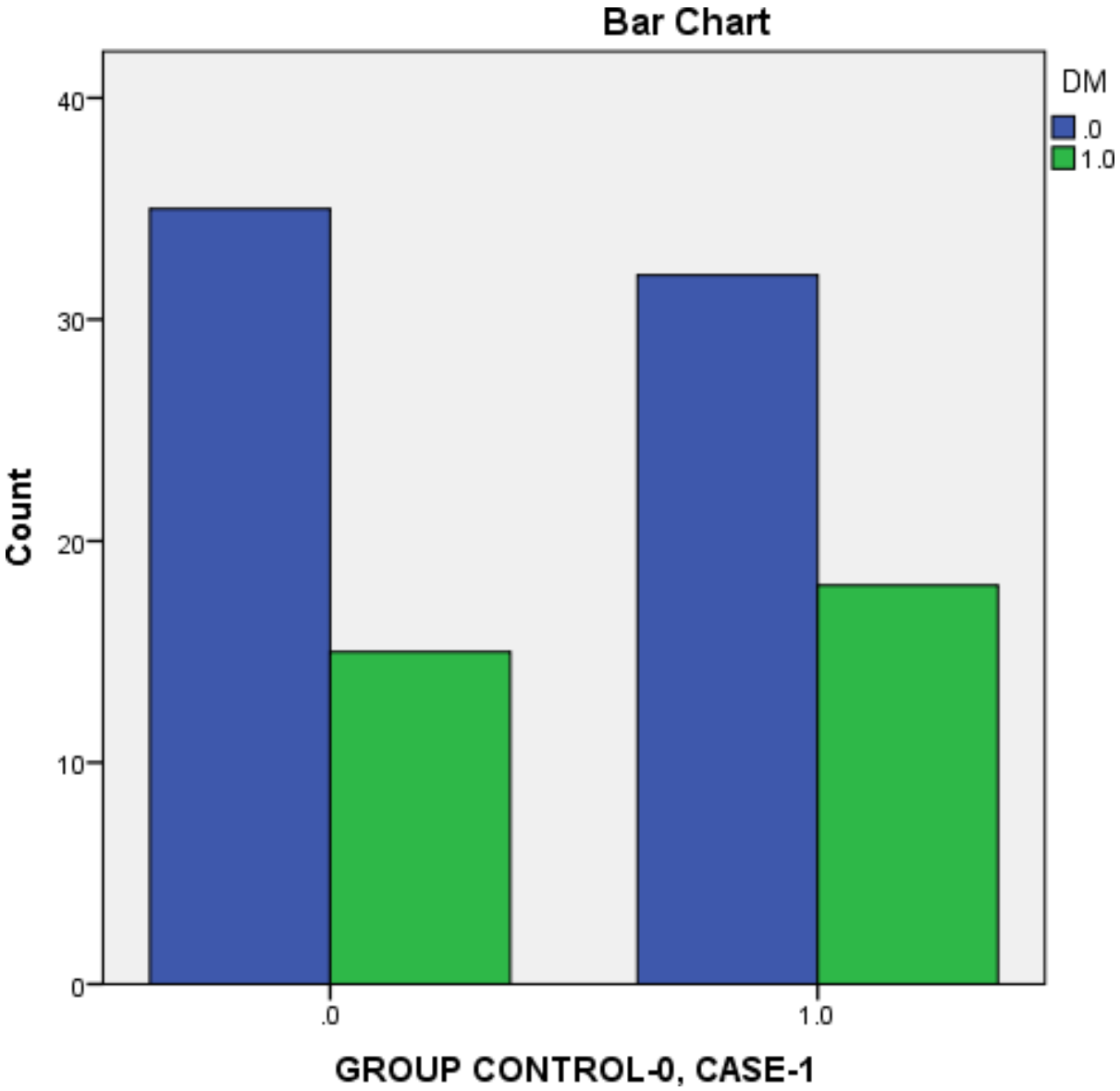

Figure 3: Distribution of Diabetic patients among cases & controls

Figure 3 depicts the distribution of Diabetes among cases & controls. Though the number of diabetic patients were higher among cases, compared to controls, it was not statistically significant.

TABLE 2: METABOLIC PROFILE OF THE STUDY SUBJECTS

S.No.	Parameters	Cases n=50	Controls n=50	p value≠
1.	Weight	64.54 ± 7.11	64.28 ± 6.19	0.846
2.	Height	156.08 ± 4.27	155.56 ± 5.83	0.612
3.	BMI	26.53 ± 3.13	26.54 ± 1.79	0.986
4.	Waist Circumference	86.38 ± 9.15	84.31 ± 9.50	0.270
5.	Hip circumference	92.74 ± 9.47	93.51 ± 8.68	0.673
6.	Waist Hip ratio	0.93 ± 0.06	0.90 ± 0.06	0.007
7.	Systolic Blood Pressure	122.54 ± 7.89	118.66 ± 7.08	0.011
8.	Diastolic Blood Pressure	77.56 ± 5.86	73.56 ± 4.84	0.0001

≠ Student t test

Table 2 : Describes the anthropometric parameters and blood pressure among the study subjects. There was no significant difference in weight, height, BMI, waist circumference, hip circumference and waist hip ratio. Blood Pressure – both systolic and diastolic were significantly higher in cases, compared to controls

TABLE 3: BIOCHEMICAL PARAMETERS OF THE STUDY SUBJECTS

S.No.	Parameters	Cases n=50	Controls n=50	p value ≠
1.	Fasting Blood glucose (mg/dl)	112.58 ± 18.93	92.76 ± 28.44	0.0001
2.	Total cholesterol (mg/dl)	170.02 ± 26.33	154.60 ± 27.89	0.005
3.	Triglycerides (mg/dl)	129.72 ± 46.66	90.94 ± 25.03	0.0001
4.	High Density Lipoprotein (HDL)-cholesterol (mg/dl)	34.72 ± 7.29	48.22 ± 8.42	0.0001
5.	Low Density Lipoprotein (HDL)-cholesterol (mg/dl)	109.36 ± 24.53	88.19 ± 28.04	0.0001
6.	Very Low Density Lipoprotein (HDL)-cholesterol (mg/dl)	25.94 ± 9.33	18.19 ± 5.01	0.0001
7.	Metabolic syndrome	30 (60%)	12 (24%)	0.0001
8.	Vitamin D (ng/dl)	16.13 ± 9.20	21.54 ± 10.10	0.006

≠ **Student t test**

Table 3: Shows the biochemical parameters among the study subjects. The fasting blood glucose, total cholesterol, triglycerides, LDL and VLDL levels and metabolic syndrome were significantly higher in cases, compared to controls. HDL levels and Vitamin D levels were significantly lower in cases, compared to controls In this study, we observed that 68% of the elderly hip fracture patients were vitamin D deficient and 24% were vitamin d insufficient.

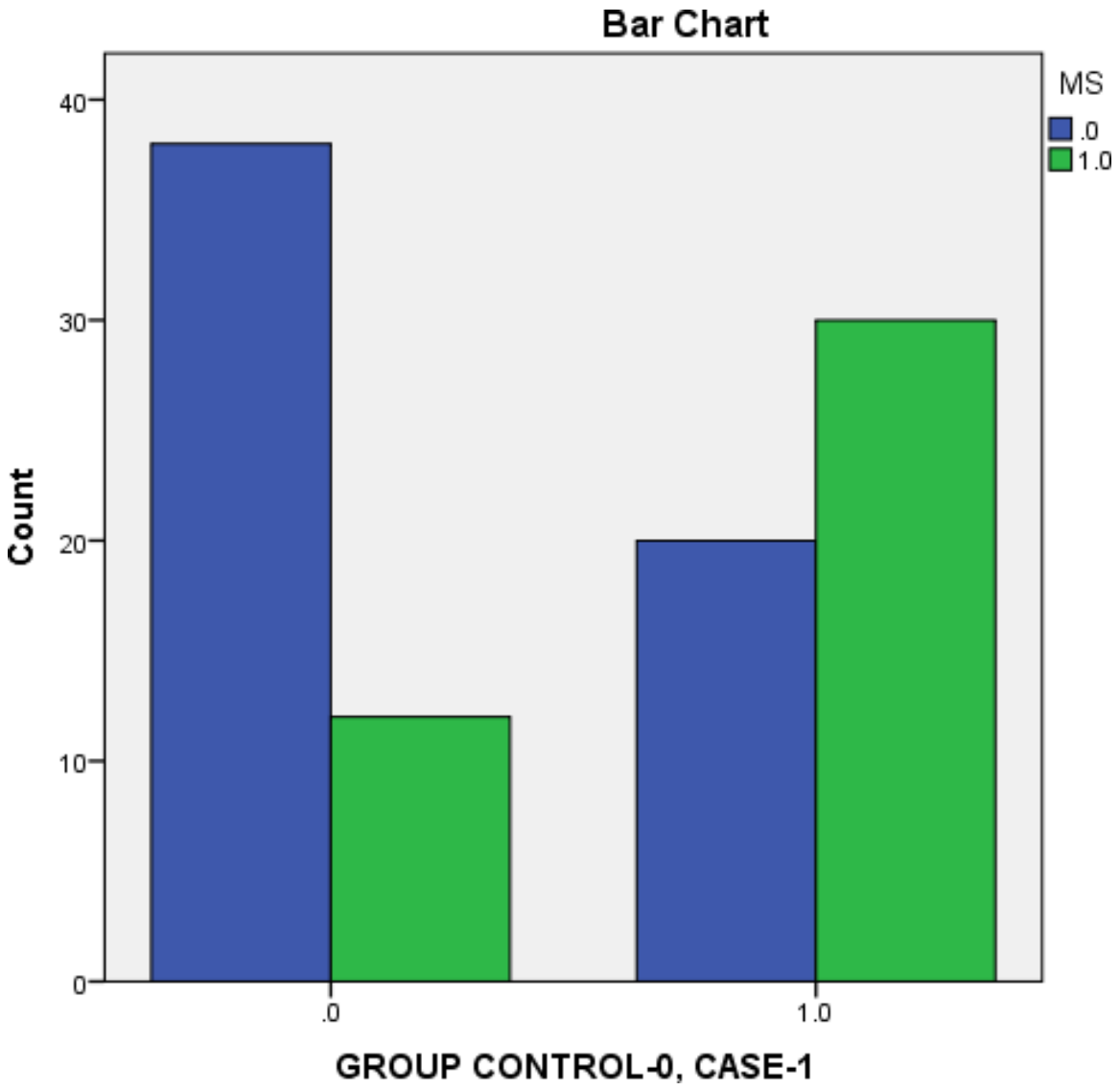

Figure 4: Distribution of metabolic syndrome among cases & controls

Figure 4: Depicts the distribution of metabolic syndrome among the study subjects. The frequency of presence of metabolic syndrome was significantly higher among cases, compared to controls.

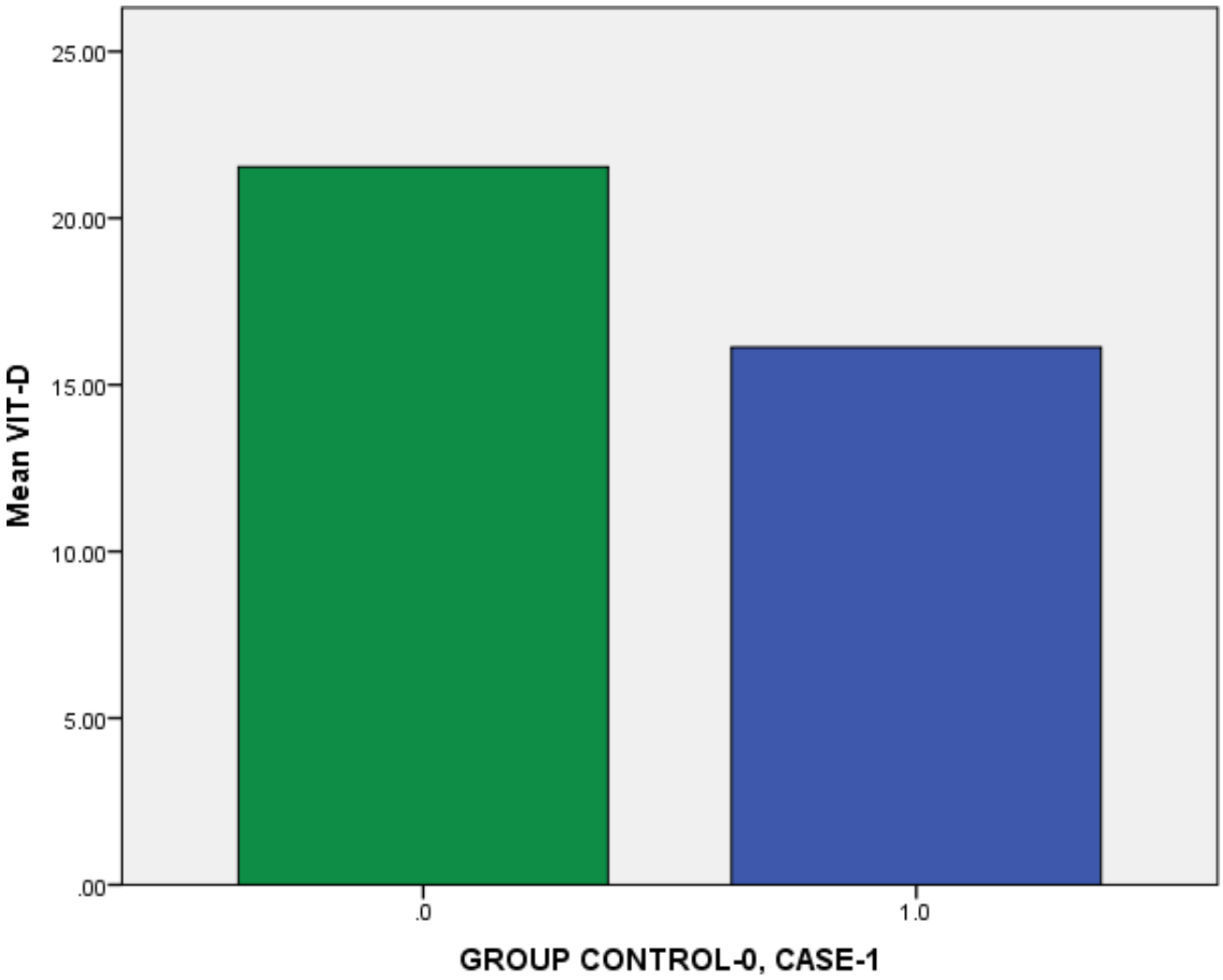

Figure 5: Comparison of Vitamin D levels among cases & controls

Figure 5 depicts the Vitamin D levels among the study subjects. It was significantly lower in cases, compared to controls

TABLE 4: CORRELATION BETWEEN METABOLIC SYNDROME AND ITS COMPONENTS WITH VITAMIN D AMONG THE STUDY SUBJECTS

S.No.	Parameters	r value	p value#
1.	Fasting Blood glucose (mg/dl)	-0.329	0.001
2.	Total cholesterol (mg/dl)	-0.115	0.255
3.	Triglycerides (mg/dl)	-0.348	0.0001
4.	High Density Lipoprotein (HDL)-cholesterol (mg/dl)	0.280	0.005
5.	Low Density Lipoprotein (HDL)-cholesterol (mg/dl)	-0.113	0.262
6.	Very Low Density Lipoprotein (HDL)-cholesterol (mg/dl)	-0.348	0.0001
7.	Metabolic syndrome	-0.719	0.0001*

*** Spearman correlation, # Pearson correlatio**

Table 4 shows the correlation between metabolic syndrome and its components with vitamin D levels among the study subjects. Fasting blood glucose, Triglycerides, HDL and presence of metabolic syndrome showed significant negative correlation with vitamin D levels

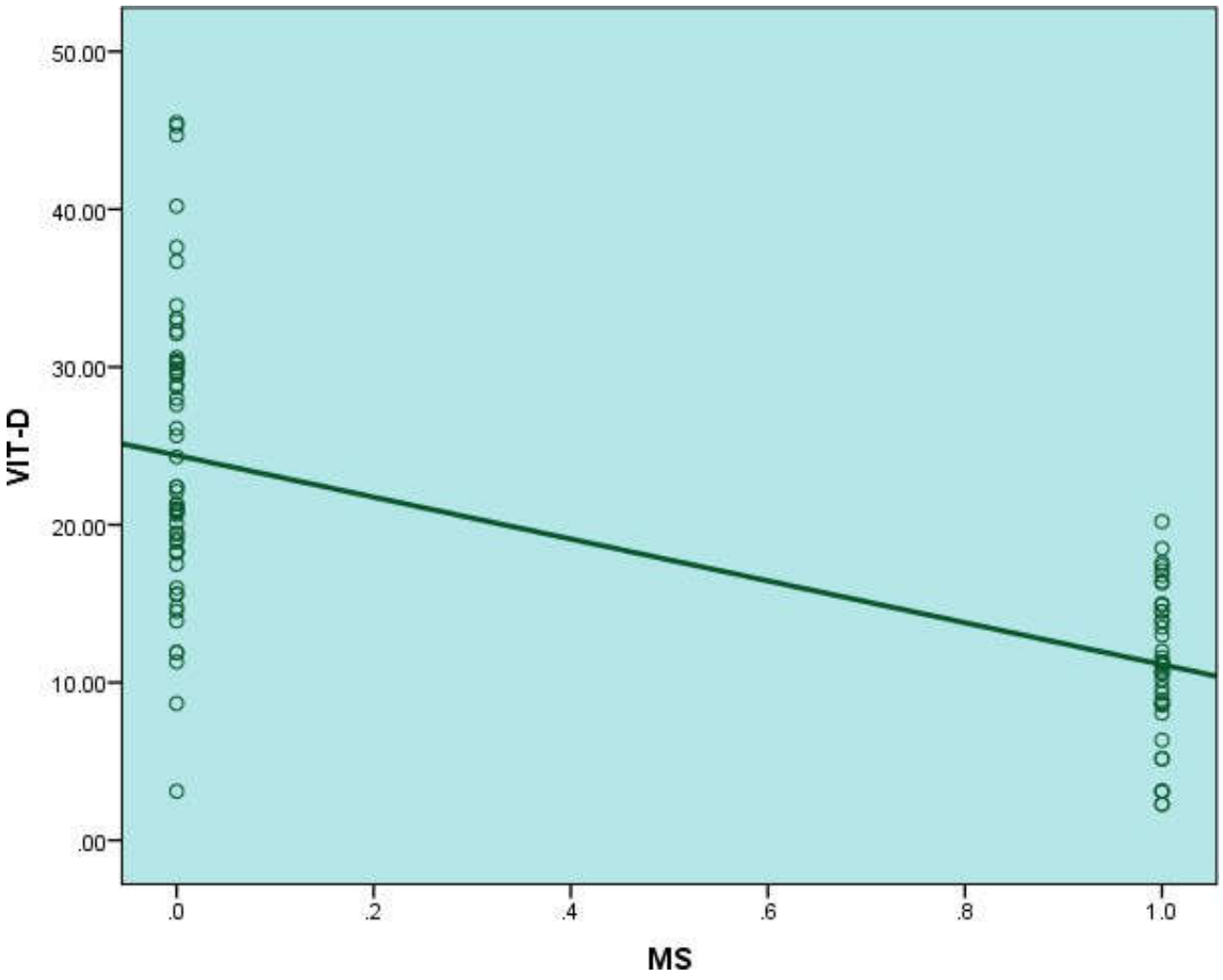

Figure 6: Correlation of Metabolic syndrome with Vitamin D levels among cases & controls

Figure 6 depicts the negative correlation between metabolic syndrome and vitamin D levels among the study subjects

Discussion:

Vitamin–D is very important in normal bone formation and good muscle health. The deficiency of vitamin- D has been associated with rickets, osteoporosis, an increased risk of fractures, and other tooth related disorders. About 2/3rd patients with acute hip fracture have been identified to have vitamin D insufficiency. [1] Vitamin –D deficiency is also found to be associated with various metabolic diseases like diabetes, hypertension and increased risk of cardiovascular diseases. Elderly patients are at increased risk of osteoporosis and hence low impact fractures, most common being hip fracture. They are also associated with low vitamin D levels and increased prevalence of hypertension, diabetes, obesity, the components of metabolic syndrome. Vitamin D deficiency in adults can precipitate or exacerbate osteopenia and osteoporosis, cause osteomalacia and muscle weakness, and increase the risk of fracture [5] Vitamin-D deficiency is highly prevalent among Asian Indians and has been reported in almost all age groups even among the healthy Indian subjects.[6] According to Khadgawat et al. significant prevalence of vitamin D deficiency (96.7 percent) is observed in patients from Asia and India with a fragile hip fracture.[31] In the present study, we observed that 68% of the elderly hip fracture patients were vitamin D deficient and 24% were vitamin d insufficient. Navarro et al. has shown that vitamin D levels were insufficient in 50% of people between the ages of 18 and 60 and in 87 percent of people over the age of 65. In our study, we also observed that the vitamin D levels were significantly lower in patients with hip fracture, compared to controls. According to a recent published study from Japan it's been reported that patients with hip fractures had deficiency of Vitamin-D. [36] Further studies observed that decreased levels of 25-OHD serves as a risk marker in hip fractures. [37, 38] A study by Melguizo et al has described the link between vitamin D insufficiency and obesity. They proposed volumetric dilution and vitamin D sequestration as the possible theories leading to decreased vitamin D levels in obese individuals. Poor dietary practices, reduced exposure to sunlight, the differential in gene expression in vitamin D metabolizing enzymes, and impaired hepatic 25-hydroxylation are some further possibilities for this association.[40] In this study, we did not observe significant association between body mass index or waist hip ratio with vitamin D levels. Further, we did not observe significant difference in BMI between cases and controls.

However, in this study, we found significant negative correlation of vitamin D with fasting blood glucose levels. This implicates the association of vitamin D with glycemic status. We also observed that fasting blood glucose levels were significantly higher in elderly patients with hip fracture, compared to controls. Another study has reported that patients with metabolic syndrome, diabetics are more prone to fractures because of low glycemic index. [42] Xu et al. found that people with genetically higher 25(OH)D concentration had a lower probability of developing type 2 diabetes. Various researchers have found that the reduced serum vitamin D levels have been linked to a higher risk of metabolic syndrome. [40, 43, 44, 45] In our study as well, we observed a significant negative correlation between vitamin D levels and presence of metabolic syndrome and all of its components. Barbalho et al had observed that 80% of the patients with metabolic syndrome admitted in cardiology unit also had hypovitaminosis D. Additionally, they found that individuals with vitamin D insufficiency had significantly greater levels of glycaemia, glycosylated hemoglobin, total cholesterol, LDLs, triglycerides, and atherogenic indices as well as a higher body mass index than those with appropriate vitamin D levels.[40] Serum vitamin D levels are found to be negatively correlated with metabolic syndrome parameters, such as abdominal obesity, insulin resistance, fasting blood glucose, arterial hypertension, and triglycerides.[46,47,48,49] Supplementing with vitamin D has been shown to have positive effects in the treatment of metabolic syndrome-related illnesses like high cholesterol, insulin resistance and hyperglycemia, obesity, and hypertension.[40]

The limitations of the study are listed below:

- This study was a cross-sectional study. Hence, we were not able to establish the causative role of vitamin D deficiency in metabolic disorders in elderly hip fracture patients, which would require a longitudinal study.

- We have not accounted for the variations in the daily intake of vitamin D in these subjects. However, we have accounted for seasonal bias and sunlight exposure, which seems to play a major role.

- We have not studied the effect of vitamin D supplementation in reducing the risk of fracture or reduction in metabolic derailments. A randomized controlled trial for the same will have to be carried out in the future to address this.

Conclusion:

This study showed that compared to elderly controls, elderly patients with hip fracture had significantly decreased vitamin D levels and increased frequency of metabolic syndrome or its components. These metabolic derangements were also significantly correlated with low vitamin D levels in these patients. This shows the role of vitamin D in increasing the risk of osteoporosis, frailty and falls and fractures as well as triggers metabolic changes with resultant increased risk of insulin resistance, metabolic syndrome, diabetes, hypertension and cardiovascular risk.

This emphasizes the need for screening of elderly people especially those with low impact fractures for possible vitamin D deficiency, increase their exposure to sunlight, provide vitamin D supplementation as necessary to prevent further risk of fractures, frailty and also improve the metabolic co-morbidities and improve their quality of life.

Conflict of interest: The authors do not have any conflict of interest

Acknowledgement / Declaration of Interest: We thank the host institute for providing facility to carry out this project.

Authors contribution: Author contributions Conceptualization: all authors; Data curation: SB, RG; Formal analysis: RG; Methodology, Project administration: RG; Investigation: SB; Software: RG Supervision: RG; Writing-original draft: SB; Writing-review & editing: , RG, SB

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