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Serum vitamin-D and osteoporotic hip fractures association with Singh's index and comminution

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Abstract
Background: Osteoporosis is mostly an age related process which is characterized by presence of decreased bone mass and microstructural status of the bone. Vitamin D deficiency is one of the factors responsible for development of osteoporosis and proximal muscle weakness adversely affecting the mobility and functional ability to put an elderly person at increased risk of falling and sustaining hip fractures.
Aim: To estimate the prevalence of decreased serum vitamin - D levels and investigate its correlation with Singh's index and comminution at the fracture site in patients admitted with hip fractures due to trivial trauma at R.D. Gardi Medical College (CRGH), Ujjain, M.P.
Material and Methods: An observational study was done on 100 patients admitted with hip fractures due to trivial trauma, their serum Vitamin D was estimated using enhanced chemiluminiscence. Digital radiograph of pelvis with both hips antero-posterior and lateral views of involved side was taken. Singh's index and comminution at the fracture site was observed. Hypovitaminosis D was correlated with Singh's index and comminution at the fracture site.
Results: Study showed 84% of patients had osteoporosis with Singh's index grade 3 or below, 90% of patients had low serum vitamin D levels with average of 16.93 ng/ml and 40% had comminution at the fracture site. Statistical significance was seen between the variables.
Conclusion: There was a strong association seen between low serum vitamin D, Osteoporosis, low Singh's index and comminution at the fracture site. Measures should be taken to improve awareness and pharmacological management for low serum Vitamin D levels.

Keywords: Vitamin D, Singh's index, osteoporosis, hip fractures, fracture site comminution

Introduction
Since many years, the Vitamin D story has been involved with the calcium story. This is totally mistaken, as the two need to be separated. Calcium is not completely free of problems, with the possibility to cause cardiovascular complications [1]. Combination of Vitamin D with calcium has been shown to be far too low to exert any remarkable pharmacological effect [2]. Therefore, Vitamin D needs to be considered independently.
Almost all tissues and cell type in the human body has receptors for Vitamin D. This has warranted us to readdress its role not only in osteoporosis but also in the problems ranging from cardiovascular disease, oligospermia, and breast cancer prevention [3, 4, 5]. It has also led to re-estimating the current dose required to prevent the Vitamin D deficiency condition, as to the therapeutic dose required to treat various Vitamin D responsive conditions. Considerable proof has arisen over the past decade that conversion of 25(OH)D3 to 1,25(OH)2D3 via the 1 Alpha hydroxylase enzyme in osteoblasts, osteocytes, chondrocytes and osteoclasts mediates other processes like maturation and cell proliferation, bone resorption and mineralisation. These processes are dependent on VDR (Vitamin D receptor) [6].
Circulating Vitamin D3 - cholecalciferol, mainly originates from synthesis in the skin from a cholesterol derivative, 7-dehydroxycholesterol, under the effect of sunlight and its UV radiation.(7) Although a small percentage of the total circulating Vitamin D also arises from dietary intake and is essentially found in foods like fish, eggs and milk. Daily dietary intake of Vitamin D is approximated to be as low as 3.7–5.9 mcg [8]. The amount of circulating Vitamin D predominantly originates from cutaneous synthesis, while dietary Vitamin D intake minimally contributes to the total concentration.

Osteoporosis is a diffuse reduction in bone density which results from the increased rate of bone resorption compared to the rate of bone formation. It is most commonly associated with the ageing process in which bone formation generally proceeds the normal rate but bone removal occurs at an increased rate [9].

Osteoporosis is a pandemic. Over a lifetime a female loses 30% of cortical bone and 50% of trabecular bone; males loose two-thirds of above values. Endosteal diameter of bone grows quickly than periosteal diameter due to more trabeculation present in cortical bone. Peak bone mass is achieved in second decade (20% > in men), with age the bone mass is lost gradually in both sexes more in females (Females: Males = 4:1). After crossing 80 years of age, there is no gender associated difference in prevalence of osteoporosis. With more life expectancy the old people are increasing into osteoporotic age group and bearing with complications. Primary undesirable consequence of osteoporosis is fragility fracture. Fracture will occur after a failing force is applied to bone. The strength of failing force needed is inversely proportional to bone strength. More fragile the bone, hence more will be chance of fracture. This is at the best a rough correlation. Elderly people gradually lose balance during walk and later may fall even during standing. Fall from standing height has been reported the most common cause of osteoporotic fractures. But there are various factors affecting each of the three variables (bone strength, the fall and the impact of fall) intrinsic to cause a fracture. This explains the less prevalence of fractures despite extensively prevalent osteoporosis. Nearly one-third of women aged between 60 years and 70 years and around 70% older than 80 years have osteoporosis (rest have osteopenia).

Deficiency of Vitamin D is also known to cause proximal muscle weakness adversely affecting the mobility and functional ability to put an elderly person at increased risk of falling and sustaining hip and other fractures. Prevention of such eventualities is feasible by adequate sunlight exposure, food fortification and supplementation of Vitamin D for at risk population as a cost-effective measure in prevention of hip and other geriatric fractures [10, 11].

Materials and Methods

The study was conducted in the Department of Orthopaedics of R.D. Gardi Medical College and associated C.R.G.H, Ujjain during the year January 2021 to August 2022. In this study, 100 cases of Hip Fractures (femoral neck and trochanteric region fractures) were evaluated and Serum Vitamin D levels were estimated along with the assessment of degree of osteoporosis using Singh's Index (a classification system for bone density of the femoral neck based on the visibility of the trabecular types) in view of feasibility, cost effectiveness and ease of assessment based on the readily available radiographs of pelvis, taken for the purpose of fracture care and Fracture Site Comminution using AO/OTA (Association for the Study of Internal Fixation/Orthopaedic Trauma Association) fracture and dislocation classification for Femur, proximal end segment, trochanteric region fracture (31a) and femoral neck fracture (31b).

Patients with fracture following a slip or fall while standing/walking and all patients of age >45 years were included in the study. Patients with significant history of trauma like road traffic accidents/ fall from height and pathological fractures and those receiving therapeutic interventions that might influence serum vitamin D and calcium status were excluded from this study.

Written Informed consent was taken from the patients after explaining all the details of the study including the risks and benefits involved. Clinical history (Signs & Symptoms) and detailed history of the patient and exact nature of the injury were recorded. Past history of falls/trauma, fractures, surgeries, drug history and medical co-morbidities were recorded. Digital radiograph of pelvis with both hips antero-posterior and lateral views of involved side were taken. Singh's index grade1, 2, 3 was considered as osteoporotic and grade 4, 5, 6 was considered as non osteoporotic. In addition to the routine investigations, serum levels of 25-hydroxyvitamin D (25-OH Vitamin-D) was measured. 4-5ml Venous blood of the patient, collected in plain vial. Serum level of Vitamin D < 20 ng/ml was considered as deficiency, Vitamin D level between 20–29 ng/ml was considered as insufficiency, and Vitamin D level 30–100 ng /ml was considered as normal. The serum was used for analyzing Vitamin D by enhanced chemiluminiscence on virus Eci auto analyzer.

All the data observed on individual case was entered in case record pro-forma that was entered in master chart of observation for calculations and analysis.

Statistical analysis was done by using SPSS (Statistical Package for Social Sciences) version 21.0. t-test and ANOVA (Analysis of Variance) were employed for testing significance, Chi-square test was used for analysis of categorical variables, normal distribution was tested using D'Agostino- Pearson test. Pearson's correlation was done for estimating the degree of correlation between the variables. Mean of the variables is expressed as mean±SD (SD denotes standard deviation) and 95% CI (CI denotes confidence interval) for the mean, P value < 0.05 was considered significant.

Fig 1: Pre-operative radiographs

Table 1: Corresponding Vitamin D levels, Singh's Index and Fracture Site Comminution of Cases

	A	B	C	D
• Vitamin D Level	8 ng/ml	8 ng/ml	24.7 ng/ml	37.1 ng/ml
• Singh's Index Grade	Grade 1	Grade 2	Grade 3	Grade 4
• Fracture Site Comminution	Yes	Yes	No	No

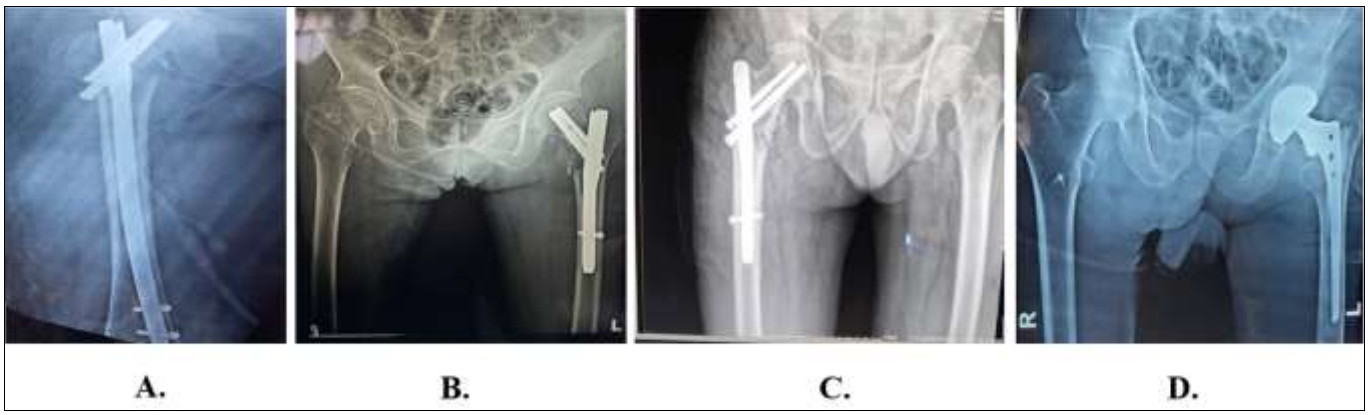

Fig 2: Post-operative radiographs

Results

100 cases of Hip Fractures (femoral neck and trochanteric region fractures) after a trivial trauma were admitted and serum Vitamin D levels were estimated along with the assessment of degree of osteoporosis using Singh's Index and Fracture Site Comminution. In the present study, mean age of the cases was 63.62±11.10 years, median age 65 years, mode 65 years, minimum age 46 years and maximum age 90 years. Majority of cases were belonging to 61-70 years age group (35%) followed by less than 50 years age group (21.0%), followed by 71-80 years age group (20.0%), followed by 51-60 years age group (19%) and followed by more than 80 years age group (5.0%). Out of 100 cases 57(57.0%) cases were male and 43(43.0%) female. Out of 100 cases majority of cases - 40(40.0%) were farmer, 31(31.0%) housewife, 24(24.0%) labour and 5(5.0%) involved in business. Majority of cases 88(88.0%) cases had low socioeconomic status and 12(12.0%) middle socioeconomic status. Most common affected side was left 51(51.0%) and then 49(49.0%) right side. 50(50.0%) cases had # Intertrochanteric Femur, 38(38.0%) # Neck of Femur and 12(12.0%) # Subtrochanteric Femur.

Out of the 100 patients 14(14.0%) cases had Singh's Index grade of 1, 33(33.0%) grade-2, 33(33.0%) grade-3, 15(15.0%) grade-4, and 1 grade-5. Out of the 100 patients studied, 40(40.0%) patients had fracture site comminution. In this study we found 75(75.0%) cases were Vitamin D deficient, 15(15.0%) were Vitamin D insufficient and 10(10.0%) were Vitamin D sufficient. No significant association was found between age groups and gender of the cases with $p>0.05$. Majority of male 76.2% cases were belonging to less than 50 years. The female (57.9%) were belonging to 51 – 60 years age group. Thus, more Active Males were affected than less active females. No significant association was found between Vitamin D category and gender of the cases with $p>0.05$. The males 66.7% had Vitamin D deficiency and 86.0% females had Vitamin D deficiency. In low-income group 78.4% cases had Vitamin D deficiency, and in middle income group 50.0%. There is no significant association was found between Vitamin D category and side affected of the cases with $p>0.05$. There is no significant association was found between Vitamin D category and type of fracture (femoral neck or trochanteric region fracture) of the cases with $p>0.05$.

Out of the 100 cases, 75 cases (75%) had Vitamin D deficiency with mean Vitamin D level of 12.06±4.26 ng/ml, 15(15.0%) insufficient Vitamin D with mean Vitamin D level of 24.51±2.91, and 10(10.0%) sufficient Vitamin D with mean Vitamin D level of 42.03±20.55 ng/ml. Mean difference in Vitamin D level is also statistically significant with $p<0.05$. Out of the 100 cases, 57 cases (57%) were male with mean Vitamin D level of 19.1±14.21 ng/ml and 43(43.0%) cases were female with mean Vitamin D level 14.05±7.36 ng/ml. Mean difference in Vitamin D level is also statistically significant with $p<0.05$.

Table 2: Association between Singh's index grade and Vitamin D category

Singh's Index Grade	Outcome			Total
	Vitamin D Deficient	Vitamin D Insufficient	Vitamin D Sufficient	
I	14	0	0	14
	100.0%	0.0%	0.0%	100.0%
II	31	1	1	33
	93.9%	3.0%	3.0%	100.0%
III	29	6	2	37
	78.4%	16.2%	5.4%	100.0%
IV	1	8	6	15
	6.7%	53.3%	40.0%	100.0%
V	0	0	1	1
	0.0%	0.0%	100.0%	100.0%
Total	75	15	10	100
	75.0%	15.0%	10.0%	100.0%

Chi-square=58.407, p=0.000

Study further indicated that there is significant association present between Vitamin D category and Singh 's index grade of the cases with $p<0.05$. Singh 's index grade was negatively associated to Vitamin D category. In Singh 's index grade-1 cases 100% cases had Vitamin D deficiency, in grade-2 93.9% cases had Vitamin D deficiency, in grade-3 78.4% cases had Vitamin D deficiency and in grade-4 6.7% cases had Vitamin D deficiency.

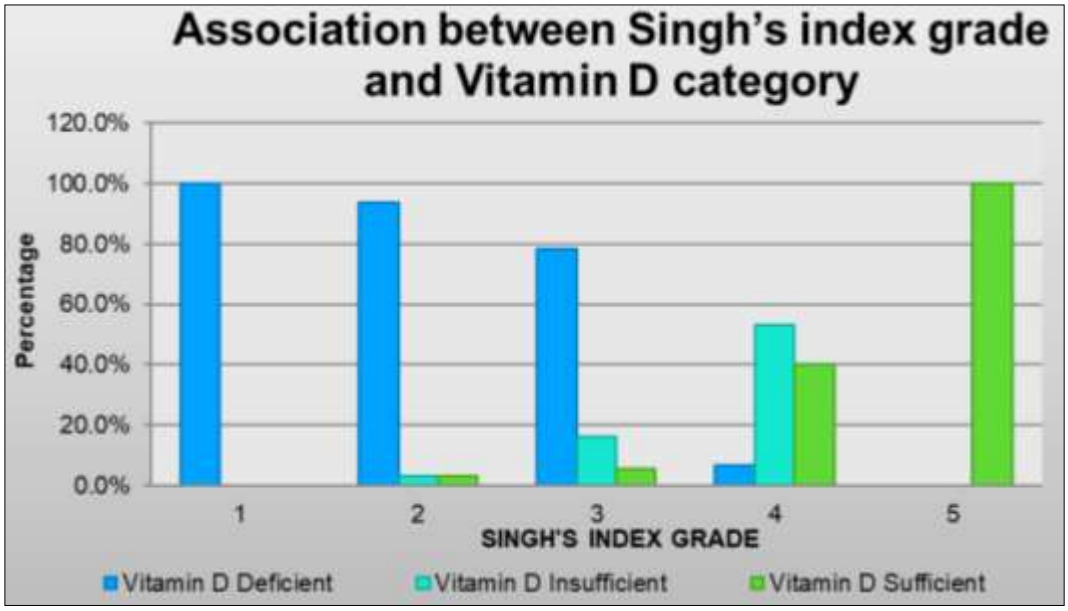

Fig 3: Association between Singh's index grade and Vitamin D category

Table 3: Association between Fracture site comminution and Mean Vitamin D levels

Fracture site comminution	N	Mean Vitamin D	SD	t	p
Yes	40	14.12	8.05	1.944	0.04
No	60	18.8	13.75		

Out of the 100 cases, 40 cases had fracture site comminution with mean Vitamin D level of 14.12±8.05 ng/ml and mean Vitamin D level for patients without comminution (60 cases) was 18.8±13.75 ng/ml.

Mean difference in Vitamin D level also statistically significant with $p<0.05$.

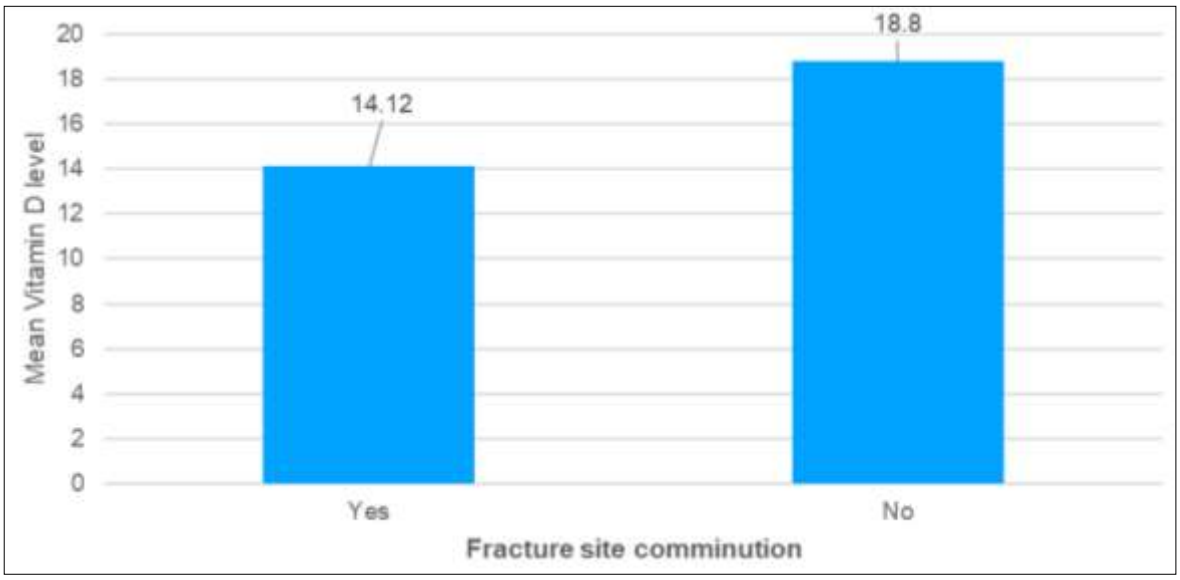

Fig 4: Association between Fracture site comminution and Mean Vitamin D levels

Table 4: Association between fracture site comminution and Singh's Index

Fracture site comminution	Singh's index grade		Total
	Normal	Osteoporotic	
Yes	3	37	40
	7.5%	92.5%	100.0%
No	13	47	60
	21.7%	78.3%	100.0%
Total	16	84	100
	16.0%	84.0%	100.0%
Chi-Square = 3.58, p = 0.058			

Out of 40 cases of fracture site comminution 37(92.5%) were found to be osteoporotic based on Singh's Index Grade 1,2 and 3.

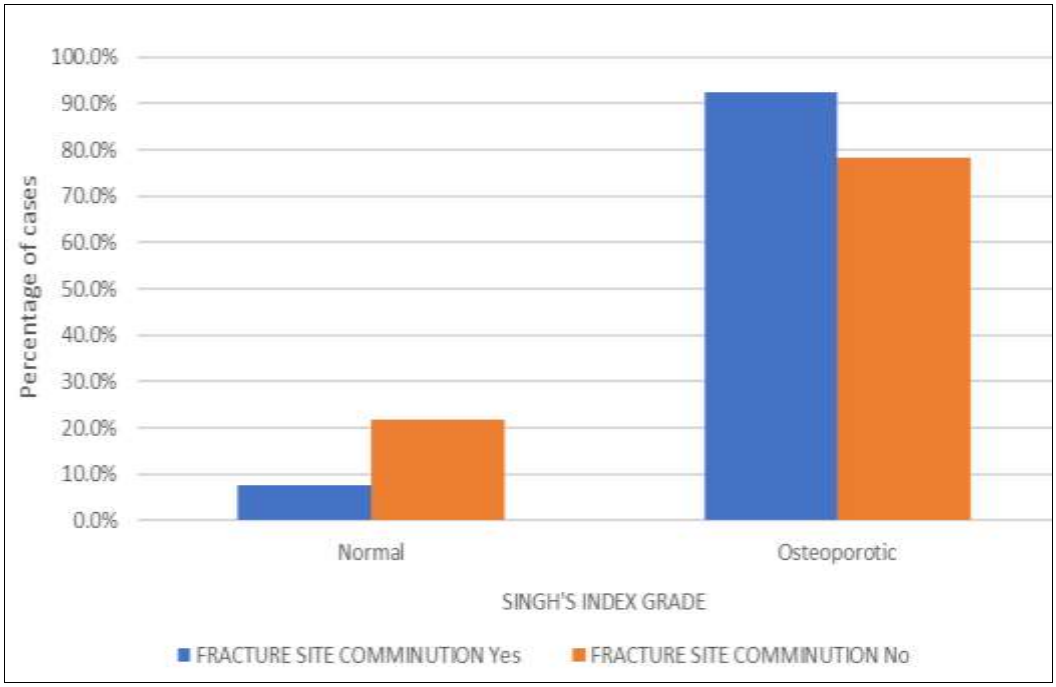

Fig 5: Association between fracture site comminution and Singh's Index

Discussion

Hip fractures are a leading cause of morbidity and mortality in the geriatric age group and are associated with chronic pain, disability and increased degree of dependence. These injuries have costly management and have a significant physical and social impact. Approximately 50 million people in India are either osteoporotic or osteopenic [12]. Most of the hip fractures in the elderly can be related to osteoporosis with a consequent increase in bone fragility [13]. The frequency of fractures of the proximal femur increases with age. In our study the mean age at presentation was 63.62±11.10 years and majority of the cases were belonging to 61-70 years (35%). This is considerably less compared to the western population (80years) [14]. There is a male preponderance (57%) in our study which is contrary to the reported literature in Ramason *et al*. having female preponderance (71.4%) [15]. Correlation of age with Vitamin D levels, osteoporosis and fracture site comminution in our study was insignificant when compared to the Lips *et al*. and Metcalfe at al. [16, 13].

The Endocrine society clinical practice guidelines defined Vitamin D deficiency as serum concentration of Vitamin D < 20 ng/ml and insufficiency as 21 to 29 ng/ml [17]. Decreased serum levels of Vitamin D are associated with muscle weakness, generalized body pains, reduced strength/balance, increased bone turnover, increased risk of falls and sustenance of hip fractures in older adults [18, 19, 20]. Apart from bone, Vitamin D is beneficial in decreasing the fracture risk by its anabolic effect on muscle mediated through highly specific nuclear receptors leading to denovo protein synthesis and myocyte growth. Muscular impairment precedes bony changes in cases of Vitamin D deficiency [20, 21].

In De Jong Andy *et al*., Vitamin D deficiency was reported in 51% and insufficiency in 40% of the population [22]. These results were comparable to our study with 90% of patients with hypovitaminosis D (75% deficiency and 15% insufficiency). Although 10% were labeled as normal for Vitamin D levels, their average Vitamin D level was marginally higher than the cutoff value to be defined as insufficient (42.03±20.55 ng/ml). The mean Vitamin D level in our study was 16.93±11.98 ng/ml. These are comparable with reports on fragility fractures from Moniz *et al*. and Beringer *et al*. with mean serum 25(OH) D level of 32.1 and 36.1nmol/L respectively with respect to the co-existence of osteoporosis and hypovitaminosis D as a co morbid condition for each of them [23, 24]. There was no significant difference in mean Vitamin D levels of patients with IT fractures, ST fractures and IC fracture neck of femur; though IT fractures were predominant. In total there were 50 IT, 38 NOF and 12 ST femur fractures.

Singh *et al*. reported that, 80.6% of the studied cases (n = 40) had vitamin D deficiency and 42.5% had osteoporosis [25]. In our study, 84% of the patients had osteoporosis with significant male predominance (p = 0.033). 81% of the 84% osteoporotic patients had hypovitaminosis D with significant difference of mean Vitamin D levels when compared to normal patients without osteoporosis. This implies a high prevalence of hypovitaminosis D in patients with osteoporosis and vice versa.

Fracture site comminution gives an insight about the mode of injury and the bone strength. It adversely affects the fracture stability. As the mode of injury was same for all the patients (trivial trauma), the role of bone strength was looked for, as correlation of fracture site comminution with osteoporosis and concomitant Vitamin D deficiency. In our study, fracture site comminution was noted in 40% of cases (n = 22 in IT and n = 9 in IC NOF, n = 9 in ST femur fractures). The mean Vitamin D levels in these patients was 14.12±8.05 ng/ml (17.23±9.84 ng/ml in IT, 17.95±15.50 ng/ml in NOF and 12.42±5.07 in ST femur fractures) suggesting deficiency. The difference in the mean Vitamin D level between the cases with comminution compared to those without comminution was highly significant (p = 0.005). Similarly statistically significant number of patients with fracture site comminution had osteoporosis implying high prevalence and strong association of hypovitaminosis D and osteoporosis in patients with fracture site comminution making it necessary for prompt correction for a better functional outcome.

Table 5: Studies in population of different countries depicted different mean Vitamin D levels [Mean±SD (ng/ml)]:

Country	Mean±SD(ng/ml)	Study Population
UK	4.8±3.2	n = 43 [26]
Sweden	10	n = 47 [27]
Japan	8.8±3.2	n = 51 [28]
USA	12.8	n = 30 [29]
Canada	15.6	n = 186 [30]
New Zealand	20.8±9.2	n = 38 [31]
Saudi Arabia	3.6±1.2	n = 24 [32]
Europe	11.6	n = 410 [33]
Switzerland	7.2±7.2	n = 193 [34]
Italy	10.8±7.2	n = 42 [35]
Germany	20±10	n = 580 [36]
Belgium	11.6±8.4	n = 240 [37]
France	8.4±4.4	n = 104 [38]
Netherlands	11.2±5.2	n = 348 [39]
Denmark	9.6±8	n = 94 [40]
INDIA	23.4±10.6	n = 1648 [41]

Conclusion

This study confirms that Vitamin D deficiency is common in elderly patients with osteoporotic hip fractures and is commonly associated with being housebound. This also established a strong correlation between reduced Vitamin D levels, osteoporosis and fracture site comminution as coexisting factors. Identifying and treating these patients early with Vitamin D for osteomalacia and anti-osteoporotic regimens for osteoporosis will improve the bone density, muscle strength and overall health thereby reducing falls and fractures.

Therefore we conclude that, to prevent osteoporotic hip fractures, attention should be focused on high risk groups. Health measures in Indian population should include fortification of foods such as milk with Vitamin D_3, Vitamin D_3 supplementation to high-risk groups, and calcium supplementation when calcium intake is below daily intake levels.

This also warrants further larger scale studies of ethnic Vitamin D variations and potential causal interrelationship between function (housebound state), cognition, comorbidities, and Vitamin D deficiency state on osteoporotic hip fractures as well as the possible effect of styles of clothing(more covered body with clothing) on Vitamin D levels.

Conflicts of interest: None

Ethical Committee approval: For collection of data ethical clearance was taken from Human Research Ethical Committee of R.D. Gardi Medical College, Ujjain. Approved.

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