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Prevalence of osteoporosis in otherwise healthy Indian males aged 50 years and above

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Abstract

Summary Bone mineral density was studied in 200 healthy Indian men above 50 years age, without fractures or osteoporosis. Mean vitamin D was 18.96 ng/ml; other biochemical evaluations were normal. Bone density (femur neck) decreased with age; there was osteoporosis in 8.5 %, osteopenia in 42 %, while 49.5 % were normal. Vitamin D deficiency may have caused osteoporosis.

Purpose Osteoporosis is recognized as the disease of females; however, males are also affected and have serious consequences thereof. The present study aimed at studying the prevalence of osteoporosis in otherwise healthy Indian males aged 50 years or more and studying the factors affecting bone mineral density (BMD).

Methods With informed consent, 200 healthy males aged 50 years or more without the history of fractures or diseases affecting the BMD were evaluated clinically (including anthropometry) and biochemically (serum calcium, phosphate, alkaline phosphatase, creatinine, albumin, 25-OH Vitamin D, intact parathyroid hormone (iPTH), and testosterone). The BMD was measured by single observer on Lunar DPX-NT at right proximal femur for least effects of artifacts. Calculation of *T* score and categorization as osteoporosis, osteopenia, and normal BMD was done as per WHO classification.

Results The mean age was 62.61 ± 7.64 years, and BMI was 23.90 ± 3.73 kg/m². The testosterone levels were normal in 84 % subjects. The mean 25-OH vitamin D level was 18.96 ± 10.23 ng/ml; only 13.5 % subjects had normal levels. The mean iPTH level was 72.60 ± 43.77 pg/ml; 57 % subjects had normal iPTH (12–72 pg/ml). The other parameters studied

were normal. The osteoporosis and osteopenia were more prevalent when BMD was evaluated at neck of femur (osteoporosis 8.5 vs 8 % at trochanter and 7.5 % at total right hip; osteopenia 42 vs 37 % at trochanter and 41 % at total right hip). The BMD deteriorated with age.

Conclusion The osteoporosis affects 8.5 % of otherwise healthy males aged 50 years and above. Vitamin D deficiency is common in such group and maybe responsible for osteoporosis.

Keywords Osteoporosis · Male · Bone mineral density · Elderly · Vitamin D deficiency · Secondary hyperparathyroidism

Introduction

Osteoporosis is “a systemic skeletal disease characterized by low bone mass and micro-architectural deterioration of bone tissue with a consequent increase in bone fragility and susceptibility to fracture” (WHO, 1994). Worldwide, osteoporosis is a serious public health concern, estimated to affect over 200 million people [1]. In the USA, in 2002, estimated 2 million men had osteoporosis, and approximately 30 % of hip fractures and 20 % of clinical vertebral fractures occurred in men. Clearly, osteoporosis is a serious health problem in men but remains underdiagnosed and undertreated [2]. Osteoporotic fracture in men is commoner than myocardial infarction and prostate cancer. Osteoporosis and osteoporotic fractures increase with advancing age [3] with loss of bone mineral density (BMD) at 1 % per year [4]. An osteoporotic fracture may occur in one fifth men above 50 years age during their life time [3, 5]. Whenever osteoporosis is discussed, the focus is on women; men are far less likely to receive a diagnosis of osteoporosis or osteoporotic fracture because of considerable gaps in knowledge on male

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osteoporosis [6]. In terms of back pain, kyphosis, height loss, and emotional difficulties, the clinical outcome of osteoporotic fracture in men is similar to women; however, morbidity following hip fracture is profound in males, with over 50 % of men requiring institutionalization and only 20 % returning to their previous level of function. The mortality after osteoporosis-related fracture is higher in men than women; mortality ratio after hip fracture was found to be 3.2 for men and 2.2 for women [7].

Similar to west, osteoporotic fractures are a major cause of morbidity and mortality in elderly Indians. The osteoporosis and osteopenia may occur at a relatively younger age in Indian population [8, 9]. Despite being a common cause of morbidity and mortality in male, available data on male osteoporosis in Indian perspective are very few. In this study, we evaluated the prevalence of osteoporosis in healthy adult males without history of fractures.

Methods

The study was conducted between January 2010 to September 2011 in the Department of Endocrinology and Metabolism, Institute of Medical Sciences, Banaras Hindu University, Varanasi, India.

Inclusion criteria

The study included healthy males at or above 50 year of age who were free from apparent illness studied.

Exclusion criteria

- Patients with previous history of fractures, hip replacement, kyphosis, or scoliosis.
- Patient currently on bisphosphonates, thyroxine, steroids, immunosuppressive therapy, antiepileptics, calcitonin, or teriparatide.
- Pre-existing fracture, malignancy, stroke, hemi/paraplegia, chronic kidney disease, chronic liver disease, rheumatoid arthritis, ankylosing spondylitis, primary hyperparathyroidism, hyperthyroidism, chronic obstructive pulmonary disease, chronic smokers, follow-up case of organ transplantation, or bed ridden patients.

The subjects fulfilling the selection criteria gave written informed consent, and history of smoking, alcohol intake, nutritional history, possible interfering diseases, and anthropometric parameters (height, weight, and BMI (weight (kg) / height (m²))) were recorded. In fasting state at 9–10 a.m., blood samples from every subject were drawn for estimation of serum calcium, phosphate, alkaline phosphatase, creatinine, albumin, 25-OH Vitamin D (RIA, Diasorin S.p.A.

Italy), intact parathyroid hormone (iPTH) level, and serum testosterone (IMMULITE 1000, Siemens Limited, Mumbai, India). The samples for serum iPTH were collected in the laboratory in cold syringes and kept cold till assayed.

The BMD was measured by dual energy X-ray absorptiometry (DXA; Lunar DPX-NT, GE Medical System, USA) at right proximal femur. The DXA scan was done by a single person. Before every scan, machine was calibrated and proper positioning of subjects was ensured. The proximal femur has no artifacts and the information regarding the association with fracture risk is most abundant for this site [10]. A *T* score was calculated as (*T* score=(subject's BMD–young adult mean BMD) / (1 SD of adult mean BMD)) at neck of femur, trochanter, and right total hip for the diagnosis of osteoporosis or normal BMD (WHO classification).

Results

The study included 200 male subjects with mean age 62.61±7.64 years, mean height 163.79±6.93 cm, mean weight 64.20±11.30 kg and mean BMI 23.90±3.73 kg/m²; 14 (7 %) were underweight, 75 (37.5 %) had normal BMI, 33 (16.5 %) were overweight, 17 (8.5 %) were mildly obese, and 61 (30.5 %) were moderately obese [11]. The biochemical parameters and mean BMD of the group at neck, trochanter, and total right hip are as shown in Table 1.

The mean total testosterone level was 360.43±176.69 ng/dl; 32 (16 %) had level below 180 ng/dl, while 168 (84 %) subjects had levels above 180 ng/dl. The mean vitamin D level in study population was 18.96±10.23 ng/ml (range 3–49 ng/ml); it was low (below 10 ng/ml) in 49 (24.5 %) subjects, deficient (10–19 ng/ml) in 67 (33.5 %) subjects, insufficient (20–29 ng/ml) in 57 (28.5 %) subjects while only 27 (13.5 %) subjects had sufficient serum 25-OH vitamin D levels (above 30 ng/ml). The mean iPTH level was 72.60±43.77 pg/ml; 114

Table 1 The biochemical characteristics and *T* score of the study population

Parameters	Mean	SD
Serum calcium (mg/dl)	9.50	0.77
Serum phosphate (mg/dl)	3.24	0.58
Serum alkaline phosphatase (U/l)	210.35	103.15
Serum total protein (g/dl)	7.02	0.56
Serum albumin (g/dl)	3.94	0.46
Serum total testosterone (ng/dl)	360.43	176.69
Serum 25(OH) Vit. D (ng/ml)	18.96	10.23
Serum iPTH(pg/ml)	72.60	43.77
<i>T</i> score (right femur)		
Neck	−0.92	1.22
Trochanter	−0.59	1.41
Total hip	−0.55	1.37

(57 %) subjects had normal iPTH (12–72 pg/ml), while remaining 86 (43 %) had elevated iPTH level (>72 pg/ml). The mean *T* scores although normal for the group at neck, trochanter, and total right hip, subdivision of the group into normal and abnormal (osteopenia and osteoporosis) could be done (shown below).

The study subjects were subdivided in age groups: 50–60 years, 61–70 years, 71–80 years, and 80 years and above. The study parameters were compared between these age groups is shown in Table 2.

At right femoral neck, 99 (49.5 %) subjects had normal BMD, 84 (42 %) subjects had osteopenia, while 17 (8.5 %) had osteoporosis. At trochanter of right femur, normal BMD was found in 111 (55.5 %) subjects, osteopenia in 74 (37 %) subjects, while 15 (7.5 %) had osteoporosis. BMD was normal at right hip (total) in 104 (52 %) study subjects, while 82 (41 %) subjects had osteopenia and 14 (7.0 %) subjects had osteoporosis (Table 3). *T* score at wards triangle overestimates osteoporosis incidence [10] and so it was excluded.

A relationship of BMD *T* scores and serum 25-OH vitamin D level, serum iPTH, and serum total testosterone is shown in Table 4. The subjects were classified in three categories of based on total testosterone level, according to assay kit range: <180 ng/dl, 180–788 ng/dl, and above 788 ng/dl. The characteristics of study subjects were analyzed in relation to BMD at femoral neck (Table 4, Fig. 1).

Discussion

The study included 200 males between 50 and 84 years (mean 62.61 ± 7.64 years) of age visiting endocrinology services as healthy relatives or patients free from apparent

illness studied or healthy male Banaras Hindu University staff. The mean serum calcium, phosphate, alkaline phosphatase, total protein, and albumin levels were normal.

The mean vitamin D level was lower, and mean iPTH, testosterone, and BMD were normal. However looking closely, only 13.5 % subjects had sufficient 25(OH) vitamin D levels, while out of rest, 58 % had either low or deficient level. Vitamin D deficiency is quite prevalent in India. Goswami et al. [12], in a study from Delhi, reported that up to 90 % of apparently healthy urban office workers and hospital staff had moderate to severe vitamin D deficiency. Tandon et al. [13] evaluated young healthy men ($n=40$) and women ($n=50$) between 20 and 30 years of age from the Indian paramilitary forces and found a mean vitamin D level 18.4 ng/ml in men. Arya et al. [14] reported that 78.3 % subjects were diagnosed to be vitamin D deficient/insufficient from study done at Lucknow (North India). Zargar et al. [15] from Kashmir valley studied 92 healthy natives; out of them, 64 were men. They observed that 49 of the 64 males (76.56 %) were vitamin D deficient. Vupputuri et al. [16] reported 25-OH D levels below 20 ng/ml in 94.3 % of study subjects from north India.

The mean iPTH level was 72.60 ± 43.77 pg/ml. Arya et al. [14] found that mean serum iPTH level was $72.3 (\pm 21.0)$ pg/ml among subjects in whom also vitamin D deficiency was seen, but Tandon et al. [15] reported that mean iPTH level were 19.3 pg/ml in young men from paramilitary forces, despite 25-OH vitamin D levels below 20 ng/ml. The study subjects were younger than our study population. The younger age and less deficient vitamin D level may have been responsible for the difference.

The mean total testosterone level was 360.43 ± 176.69 ng/dl. Out of total 200 subjects, 32 (16 %) had level below 180 ng/dl, while 164 (82 %) subjects had levels above 180

Table 2 Relations between age and other study parameters

Parameters		Age group (years)				<i>p</i> value
		50–60 (<i>n</i> =85)	61–70 (<i>n</i> =84)	71–80 (<i>n</i> =28)	>80 (<i>n</i> =3)	
BMI (kg/m ²)		24.38±3.61	23.59±3.71	23.77±4.07	19.88±1.69	0.141
Serum calcium (mg/dl)		9.60±0. 81	9.51±0. 68	9.27±0. 83	8.59±0. 26	0.044
Serum phosphate (mg/dl)		3.31±0. 56	3.26±0. 59	3.0±0. 53	2.80±0. 20	0.041
Serum alkaline phosphatase (U/l)		202.95±93.23	204.20±111.17	238.04±92.65	333.67±165.19	0.069
Total protein (g/dl)		7.12±0.55	7.03±0.5166	6.71±0.57	6.50±0.10	0.003
Serum albumin (g/dl)		3.97±0.43	4.01±0.41	3.62±0.53	3.40±0.26	0.000
Serum testosterone (ng/dl)		428.87±176.89	323.75±161.45	285.89±150.43	144.0±33.04	0.000
Serum 25(OH) Vit D (ng/ml)		19.41±10.59	20.56±9.92	14.23±8.22	5.50±3.04	0.003
Serum iPTH(pg/ml)		69.12±46.33	68.56±34.29	89.0±55.28	130.33±19.85	0.014
<i>T</i> score (right femur)	Neck	−0.77±1.29	−0.91±1.20	−1.12±0.89	−2.87±0.40	0.016
	Trochanter	−0.44±1.49	−0.58±1.39	−0.82±1.10	−2.57±0.45	0.056
	Total hip	−0.35±1.44	−0.56±1.35	−0.88±1.00	−2.57±0.32	0.018

Table 3 Relation between BMD and vitamin D, iPTH, and serum testosterone

Parameter		T score (right femur)			25(OH) Vit. D (ng/ml)
		Neck	Trochanter	Total hip	
25(OH) Vit. D (ng/ml)	<10	-1.68±1.15	-1.38±1.30	-1.40±1.21	—
	10-19	-1.07±1.08	-0.66±1.41	-0.62±1.30	—
	20-29	-0.43±0.95	-0.18±1.07	-0.06±1.11	—
	>30	-0.207±1.34	0.20±1.55	0.18±1.44	—
	<i>p</i> value	0.000	0.000	0.000	—
Serum iPTH (pg/ml)	12-72	-0.514±1.09	-0.08±1.32	-0.07±1.27	23.88±9.79
	>72	-1.46±1.18	-1.25±1.26	-0.07±1.27	12.40±6.50
	<i>p</i> value	0.000	0.000	0.000	0.000
Serum total testosterone (ng/dl)	≤180	-1.83±0.95	-1.58±1.01	-1.60±0.97	—
	181-788	-0.77±1.19	-0.42±1.39	-0.36±1.33	—
	>788	0.75±1.02	0.62±1.55	0.62±1.41	—
	<i>p</i> value	0.000	0.000	0.000	—

ng/dl. This finding is similar to various cross sectional and longitudinal studies in men indicating consistent age-related declines in total and free testosterone levels from the age of 30–40 years onwards [17, 18].

The iPTH level was higher with lower vitamin D levels and BMD *T* scores. The BMD was significantly lower at lower vitamin D levels than that at normal vitamin D levels.

Osteoporosis was more prevalent if BMD at femur neck was considered for classifying subjects (8.5 vs 8 % at trochanter and 7.5 % at total right hip). The slight difference in percentage at neck, trochanter, and total hip is normal variation found at different site. The site with lowest BMD is chosen to classify patients [10]. In US NHANES III study [19], prevalence of osteoporosis was 3–6 % in older U.S. men over age 50 year, whereas 28–47 % had osteopenia, prevalence estimates being highest using the femoral neck BMD of all proximal femur sites measured. El-Desouki et al. [20] from Saudi Arabia studied 429 healthy Saudi men

from the community and reported 11.4 % osteoporosis prevalence at femoral neck. In recent Indian study by Marwaha et al. [21], prevalence of osteoporosis ranged from 2.6 to 18.0 % in males. Their study subjects also included those with past history of fractures, while our study excluded any subject with past or present osteoporotic fracture(s). All these studies suggest that osteoporosis in men is not uncommon as previously believed, and the prevalence rates might be different because of various DXA machines used, or difference in selection criteria.

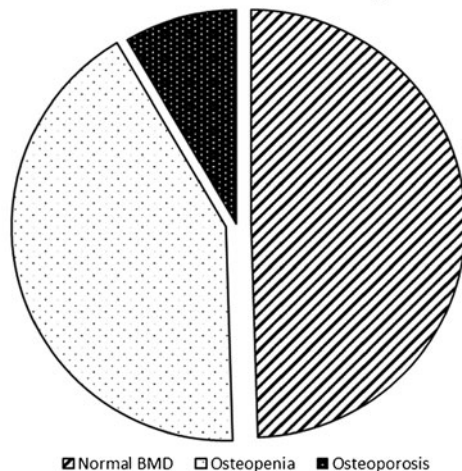
The BMI insignificantly decreased with advancing age. Marwaha et al. [21] also reported reduced mean BMI with advancing age in Indian men and women.

The mean BMD at neck, trochanter, and total hip was normal in age groups 50–60 and 61–70 years, osteopenic in age 71–80 years, while osteoporotic in age above 80 years. Since there were only three subjects in the fourth group (>80 years age), results cannot be generalized. The difference

Table 4 Relations between BMD at neck of femur and other study parameters

Parameters	Neck of femur (<i>n</i> =200)			<i>p</i> value
	Normal BMD (<i>n</i> =99; 49.5 %)	Osteopenia (<i>n</i> =84; 42 %)	Osteoporosis (<i>n</i> =17; 8.5 %)	
BMI (kg/m ²)	25.27±3.42	22.77±3.62	21.41±2.90	0.000
Serum calcium (mg/dl)	9.86±0.67	9.20±0.70	8.92±0.66	0.000
Serum phosphate (mg/dl)	3.46±0.58	3.10±0.48	2.67±0.32	0.000
Serum alkaline phosphatase (U/l)	184.13±83.47	214.99±87.05	340.12±167.58	0.000
T. protein (gm/dl)	7.18±0.46	6.91±0.59	6.54±0.45	0.000
Serum albumin (gm/dl)	4.08±0.34	3.84±0.51	3.54±0.43	0.000
Serum testosterone (ng/dl)	424.32±163.47	318.81±170.85	194.00±96.95	0.000
Serum 25(OH) Vit. D (ng/ml)	23.40±10.22	15.77±7.73	8.75±8.07	0.000
Serum iPTH (pg/ml)	53.73±30.24	87.52±48.75	108.64±33.73	0.000

Distribution of BMD at neck of right femur

**Fig. 1** Distribution of BMD at neck of right femur

in neck and total BMD was significantly negative between younger groups and more than 70 years age groups. In the MINOS cohort, an age-related increase in prevalence of vertebral deformity has been reported [22]. The prevalence of vertebral deformity was also noted to increase with decreasing bone density at the total hip [22]. Looker AC et al. [19] and El-Desouki et al. [20] based their results on femoral BMD in men over 50 years age. Similarly, Lekamwasam et al. [23] reported 5.8 % prevalence of osteoporosis among men older than 50 years in Sri Lanka, and it increased with advancing age. Marwaha et al. [21] observed that prevalence of osteoporosis increased with age in females, but not in males.

In the present study, with advancing age, fewer subjects had sufficient vitamin D level (more than 30 ng/ml) and more subjects had low (less than 10 ng/ml) or deficient level. This can be due to decreased formation of vitamin D in skin and poor absorption in gastrointestinal tract with age [24].

Mean iPTH level was on higher side of normal in age groups of 50–60 and 61–70 years (69.12 ± 46.33 and 68.56 ± 34.29 pg/ml) while elevated in elderly 71–80 (89.07 ± 55.28 pg/ml) and above 80 years age (130.33 ± 19.86 pg/ml) groups. There was a trend of increasing iPTH with advance age, and the *p* value was significant. This finding is expected in our study as subnormal (below 30 ng/ml) vitamin D level was seen in 86.5 % of study subjects. According to Basaran et al. [25] with vitamin D levels below 30 ng/ml, parathyroid hormone (PTH) level increases. So, as the age advanced and vitamin D levels decreased, serum iPTH was increased.

Mean serum testosterone level was higher in younger subjects in comparison to elderly study subjects. The mean serum testosterone in 50–60 years age group was 428.87 ± 176.90 ng/dl, in 61–70 years age was 323.75 ± 161.45 ng/dl, in 71–80 years age was 285.89 ± 150.44 ng/dl, and in subjects above 80 years age was 144.0 ± 33.05 ng/dl. The *p* value was significant between these groups. This finding

elaborates the decreasing testosterone seen in such age group [26].

The level of total protein and serum albumin also decreased with advancing age. Similar trend was seen in serum calcium and phosphorus level with age, and *p* value was significant, while serum alkaline phosphatase showed opposite trend but here, *p* value was not significant. This could be due to vitamin D deficiency prevalent in the study population and possibly increased malabsorption with increasing age.

In our study, BMD has significant positive correlation with BMI. Murillo-Urbe et al. [27] also reported similar finding in a study done at Mexico. Morin et al. [28] also reported strong association between high BMD and high BMI although these studies included women subjects. Marwaha et al. [21] also reported that BMD at all sites, except distal radius, was positively correlated with BMI in both women and men.

BMD was positively correlated with 25-OH vitamin D level. Subjects with osteoporosis at neck and trochanter had mean 25-OH vitamin D level below 10 ng/ml. The subjects with normal mean BMD at neck, trochanter, and total hip had mean 25-OH vitamin D level above 22 ng/ml while subjects with osteopenia at neck, total hip had mean 25-OH vitamin D level just above 15 ng/ml, and at trochanter above 16 ng/ml. Arya et al. [14] also reported that low serum 25-OH D level is possibly one of the reasons for lower BMD among Indians. Several investigators from west had reported significantly lower hip BMD in subjects with low serum 25-OH D concentrations [29, 30]. Besides, vitamin D supplementation led to beneficial effect on hip BMD [31–33].

The subjects with normal mean BMD at neck, trochanter, and total hip had mean iPTH just above 53 pg/ml, while subjects with osteopenia at neck and total hip had mean iPTH above 86 pg/ml but subjects with osteoporosis at trochanter and total hip had mean iPTH above 122 pg/ml. In our study, the subjects with iPTH in normal range (less than 72 pg/ml) had mean 25-OH vitamin D level 23.88 ± 9.80 ng/ml, while subjects with iPTH level above 72 pg/ml had mean 25-OH vitamin D level 12.41 ± 6.50 ng/ml. This finding can be explained as vitamin D deficiency causes secondary hyperparathyroidism which can cause increased resorption of bone and decreases BMD. Recently Marwaha et al. [21] showed that total body BMD is negatively correlated with iPTH levels.

The subjects with normal mean BMD at neck, trochanter, and total hip had mean serum testosterone level above 400 ng/dl, while subjects with osteopenia at neck, and total hip had mean serum testosterone level just above 300 ng/dl and subjects with osteoporosis at neck, trochanter, and total hip had mean serum testosterone level near 200 ng/dl. So in our study, level of serum testosterone has positive correlation with BMD at neck, trochanter of femur, and total hip, and subjects with osteopenia or osteoporosis has lower mean serum testosterone than subjects with normal mean BMD; *p* value was

significant. However, limitation of study is that we measured only total testosterone not free testosterone. Fink HA et al. [26] reported that androgen deficiency had an effect on bone health. In men aged 65 years or more, low total testosterone levels (<200 ng/dl) are associated with increased prevalence of osteoporosis at either the hip or the femoral neck, and increased incidence of rapid bone loss at the hip. Decreased total testosterone levels are also associated with increased incidence of fractures, particularly of hip fractures and non-vertebral fractures in men older than 60 years [34]. Kenny et al. [35] reported that 52 % of older men with low bioavailable testosterone levels had BMD levels below the young adult normal range and are likely at an increased risk of fracture.

Subjects with osteoporosis at neck, trochanter, and total hip had mean total protein level 6.54 ± 0.45 , 6.47 ± 0.48 , 6.47 ± 0.50 , respectively, and mean serum albumin level 3.54 ± 0.43 , 3.47 ± 0.45 , 3.49 ± 0.46 g, respectively. As total protein and serum albumin level is related to nutritional status along with other factors, the relation between BMD and mean total protein or mean serum albumin may partly reflect relation with nutrition as well. The mean serum calcium level and mean serum phosphorus level also followed the similar trend in this study, and the mean total serum calcium level and mean serum phosphorus level were more in subjects with normal mean BMD than subjects with osteopenia or osteoporosis. This finding may also be related to nutritional status and vitamin D level as the deficiency of vitamin D also contributes to malabsorption of calcium and phosphorus. According to nutritional hypothesis by Gupta [36], low peak bone mass results from continued dietary deficiency of calcium, since early life and consequently osteoporosis at early age. New et al. [37] also reported relationship between nutrition and BMD. Similarly, Kazutoshi Nakamura et al. [38] also reported strong relationship between BMD at neck of femur and level of nutrition.

Subjects with normal mean BMD at neck, trochanter, and total hip had mean serum alkaline phosphatase level were towards lower range than in subjects with mean BMD in osteopenic and osteoporosis range. But the p value was not significant. Similar finding has also reported by Marwaha et al. [21], they showed that total body BMD was negatively correlated with alkaline phosphatase.

The study has some lacunae. The testosterone levels were done once, and free levels were not calculated. The half of apparently healthy male above 50 years of age may have lower BMD (8.5 % osteoporosis and 42 % osteopenia) and vitamin D deficiency. The bone mineral density decreased with advancing age. The effect of vitamin D is evident by higher iPTH and alkaline phosphatase levels with lower bone mineral density.

Conflicts of interest None

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