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Testosterone and DHEA Levels in Osteoporosis in Males Above The Age Of 60 Years.

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ABSTRACT

Background: A cross sectional study in which 100 male patients of 60 years and above were evaluated for Osteoporosis. **Methods:** Out of enrolled 100 men above 60 years suspected of Osteoporosis, 46 % is diagnosed as Osteoporosis, 32% as Osteopenia and 22% were observed to be normal based on BMD T-Score value. **Results:** The average level of Total Testosterone and DHEA in entire suspected osteoporosis patients were 2.74 ± 1.04 ng/ml and 1.45 ± 1.08 µg/ml respectively. The level across Osteoporotic cases (n=46), the average Total Testosterone and DHEA were 2.20 ± 0.77 ng/ml and 1.55 ± 0.91 µg/ml respectively. Abnormally low serum testosterone (<2.0 ng/ml as per society of andrology) were found in 19 (41%) cases out of 46 osteoporotic men compared with normal testosterone level men. Testosterone deficiency was seen in 39 (84%) cases of osteoporosis. This study has shown that the men with low testosterone levels had decreased BMD T-scores across entire cases (p<0.001). The men with decreased DHEA level also had decreased BMD T-scores BMI was inversely associated with testosterone and DHEA levels. It was found that decreased plasma testosterone had a 14 fold higher risk for decreased BMD compared with their peer with normal testosterone level. Age and BMD has shown significant association with testosterone levels (p<0.001).In this study, the incidence of osteoporosis increases with advancing age. **Conclusion:** There was significant decline in Testosterone and DHEA with advancing age and more over decrease in BMD value indicates the pathogenesis of osteoporosis in the patients. But still further study with large sample size is needed to clearly identify the role of testosterone in osteoporosis.

Keywords: Osteoporosis, BMD, Testosterone, DHEA, Males

INTRODUCTION

Osteoporosis is often described as the silent epidemic as it is a pain-free, symptomless disease in which bone becomes progressively porous, fragile and loses strength.[1,2] As bone strength decreases the outcome is often broken bones (fractures), even occurring after a minor bump or fall. There was significant decline in Testosterone and DHEA with advancing age and more over decrease in BMD value indicates the pathogenesis of osteoporosis in the patients. In men there is a gradual reduction in testosterone and estradiol with aging.[3] It is estimated that between the age of 40 and 70 years, male bone density falls by up to 15 percent. DHEA stands out as a multitalented star with amazing ways of outsmarting osteoporosis.

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DHEA is the only hormone that can both inhibit bone breakdown and stimulate bone formation. Plus, DHEA is a precursor to estrogen, progesterone and testosterone, all of which prevent bone loss in their own rights.[4] This study shows the relation of low Testosterone and DHEA levels in males and weakening of bone due to decreased bone mineral density which may lead to fragility fracture in males aged more than 60 years. It also provides scope for further interventional approach in large population with testosterone and DHEA therapy which may be a boon for male patients having low BMD.

MATERIALS AND METHODS

In this study, the patient attending outpatient camp organized by Department of Orthopedic surgery and those admitted to UCMS were included. Male patients above the age of 60 years presenting mostly for backache, fragility fractures of bone and follow up cases of previous fracture were enrolled in this study. A detailed history was taken and relevant clinical examination was done in all the patients.

BMD Measurement: It is measured at distal radius using peripheral technique by quantitative ultrasound. It involves the measurement of the average speed of sound (SOS) and broadband ultrasound assessment (BUA) through distal radius to provide a clinical measure called the stiffness index (SI). The radial QUS measurement were performed using a commercial device (Omni-sense 8000XP) which is specifically designed for assessing speed of sound (m/s) of ultrasonic waves, which travel axially along the bones at a center frequency of 1.25 MHz

Anthropometric measurement: Body weight was recorded in minimal clothing to the nearest 0.1 kg on a 880 electronic scale and height without shoes was measured to the nearest 0.1 cm using a standiometer. Body mass index (BMI) was expressed as the ratio of weight in kg to the square of height (kg/m2), and BMI for age T-scores (BAZ) were calculated using WHO AnthroPlus software version 1.01 (World Health Organization, Geneva, Switzerland).

Testosterone and DHEA measurement: The principle of the following enzyme immunoassay test follows the typical competitive binding schematic. For testosterone and DHEA, the protocol study has been adapted from HUMAN ELISA KIT, Germany and from Labor Diagnostika Nord DHEA-S ELISA Kit, Germany respectively.

Statistical Analysis

The data were fed in the Microsoft Excel and analyzed by Statistical package for social service (SPSS)-IBM 20. Descriptive data were expressed in mean ± SD along with the frequency table. Means of continuous variables were compared by using the two-tailed independent Student's t–test and analysis of variance (ANOVA). The correlations were computed by Pearson's correlation. The multiple regression (β) value was calculated for the independent predictive value of the variable. The p-value of <0.05 was considered to be statistically significant.

RESULTS

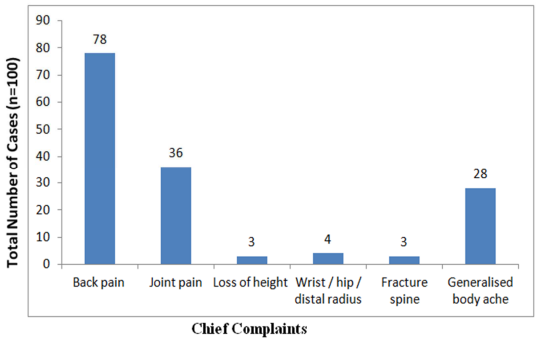

Figure 1: Demographic features of Cases (n=100)

Out of 72 cases with low back pain 10 had unilateral and 6 had bilateral radiculopathy. 33 cases had large joint pain and 11 cases had pain in small joint. Among the patients with back pain there were 3 more cases with clinically evident loss of height due to stoopy posture.

Table 2: Age wise Distribution of Cases (n=100)

Age Groups (Years)	Frequency				p-value
	Osteoporosis (-2.5 & Above)	Osteopenia (- 1.0 to -2.4)	Normal (-0.9 to 2.5)	Total	
60-64	17 (29.82%)	25 (43.85%)	15 (26.31%)	57	0.01
65-69	14 (63.63%)	3 (13.63%)	5 (22.72%)	22	
70-74	9 (81.81%)	1 (9.09%)	1 (9.09%)	11	
75-79	2 (50.00%)	2 (50.00%)	0 (0%)	4	
80-84	3 (75.00%)	1 (25.00%)	0 (0%)	4	
85-89	1 (50.00%)	0 (0%)	1 (50.00%)	2	
Total	46	32	22	100	

Table 3: Comparison (Mean ± SD) of study variables of Cases (n=100)

Variables	Osteoporosis	Osteopenia	Normal	Total Cases	p value
Age (years)	64.95 ± 6.57	69.90 ± 15.22	67.22 ± 11.27	67.06 ± 6.61	>0.05
BMD (T-scores)	-2.96 ± 0.58	-1.63 ± 0.78	-0.10 ± 0.73	-1.91 ± 1.31	0.001
BMI (Kg/m2)	21.21± 3.45	22.06 ± 4.80	19.95 ± 4.55	20.9 ± 4.45	>0.05
T. Testosterone (ng/ml)	2.20 ± 0.77	2.71 ± 0.74	3.93 ± 0.95	2.74 ± 1.04	0.001
DHEA (µg/ml)	1.23 ± 1.20	1.45 ± 1.21	1.55 ± 0.91	1.45 ± 1.08	0.01

It represents that incidence of osteoporosis increases with age. Almost 50% of men were subjected to osteoporosis after the age of 65 years. The peak of osteoporosis is seen in the age groups from 70 years to 74 years. The statistically significant difference was observed in BMD (p<0.001), Total Testosterone (p<0.001) and DHEA (p<0.01) respectively.

It shows with age the number of cases increased in osteoporotic cases in comparison to the normal. A maximum frequency of 20 men (52.63%) with osteoporosis were recorded having Total Testosterone levels between 2.1- 3.0 ng/ml. The maximum of 100% osteoporosis cases is recorded in the men having Total Testosterone level less than 1.0 ng/ml.

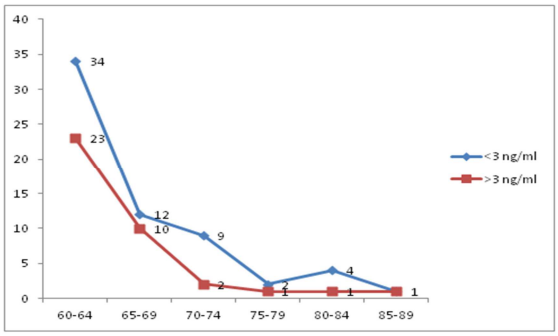

Figure 3: Proportion of cases and normal with total testosterone with cut off 3ng/ml

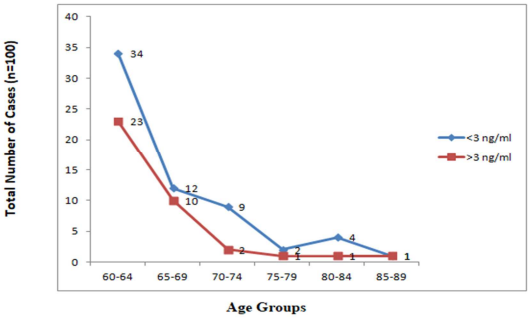

Figure 4: Proportion of cases and normal with the cut off value of DHEA 3 µg/ml

Table 6: Distribution of Cases (n=100) based on BMI (Kg/m2)

BMI (Kg/m2)	Frequency				p-value
	Osteoporosis (-2.5 & Above)	Osteopenia (- 1.0 to -2.4)	Normal (-0.9 to 2.5)	Total	
10-14	5 (71.54%)	1 (14.28%)	1 (14.28%)	7	0.089
15-19	14 (45.16%)	11 (35.48%)	6 (19.35%)	31	
20-24	20 (45.45%)	13 (29.54%)	11 (25.0%)	44	
25-29	7 (46.66%)	4 (26.66%)	4 (26.66%)	15	
30-34	0 (0%)	3 (100%)	0 (0%)	3	
Total	46	32	22	100	

Table 7: Pearson's Correlation of the study variables (n=100)

Variables	BMD	Age	BMI
Total Testosterone	0.57**	-0.061	-0.05
DHEA	-0.074	0.043	-0.037
BMD	1	-0.24*	0.12

**p<0.001, *p<0.01

Table 8: Comparison (Mean ± SD) of study variables of cases with low and Normal Testosterone level

Variables	Study groups	Number of Cases		Mean ± SD	Mean ± SD	p-value
		Low Testosterone	Normal Testosterone	Low Testosterone (<2 ng/ml)	Normal Testosterone (2-8 ng/ml)	
BMI (kg/m2)	Osteoporosis (n=46)	19	27	20.21 ± 4.43	19.78 ± 4.53	>0.05
	Osteopenia (n=32)	6	26	22.88± 3.09	21.87± 5.14	>0.05
BMD (T-Score)	Osteoporosis (n=46)	19	27	-3.01±0.66	-2.03± 0.53	<0.01
	Osteopenia (n=32)	6	26	-1.93± 0.57	-1.56±0.81	>0.05
Age (Years)	Osteoporosis (n=46)	19	27	65.11± 7.72	67.17± 5.94	>0.05
	Osteopenia (n=32)	6	26	62.33± 4.41	63.15± 6.37	>0.05
Testosterone (ng/ml)	Osteoporosis (n=46)	19	27	1.41±0.38	2.71 ±0.48	.0001
	Osteopenia (n=32)	6	26	2.93±0.65	2.71±0.74	.0001

Table 9: Comparison (Mean ± SD) of study variables of cases with low and Normal DHEA level

Variables	Study groups	Number of Cases		Mean ± SD	Mean ± SD	p-value
		Low DHEA	Normal DHEA	Low DHEA (<0.5 µg/ml)	Normal DHEA (0.5-4 µg/ml)	
BMI (kg/m2)	Osteoporosis (n=46)	6	40	21.61± 5.46	19.70 ± 4.30	>0.05
	Osteopenia (n=32)	4	28	19.88±4.39	22.37 ±4.85	>0.05
BMD (T-Score)	Osteoporosis (n=46)	6	40	-3.30± 0.89	-2.91±0 .52	>0.05
	Osteopenia (n=32)	4	28	-1.95 ±0.59	-1.59± 0.80	>0.05
Age (Years)	Osteoporosis (n=46)	6	40	65.16± 3.43	67.35±6.95	>0.05
	Osteopenia (n=32)	4	28	67.75 ±8.05	62.32 ±5.50	>0.05
DHEA (µg/ml)	Osteoporosis (n=46)	6	40	1.73±0 .84	1.55±0 .91	0.0001
	Osteopenia (n=32)	4	28	1.60 ±1.22	1.45 ±1.21	0.0001

Table 10: Independent predictive determinants of Bone Mineral Density (BMD) in males ≥60years (n=100)

Independent Variables	β	p-value
Total Testosterone	0.592	0.0001
DHEA	-0.101	0.206
BMI	0.165	0.042
Age	-0.159	0.05

It shows that with age the number of cases increased in osteoporotic cases in comparison with normal. Maximum number of cases 66.66% has been observed in DHEA interval between 3.1-4.0 µg/ml.

The data represent that Osteoporosis increases with increasing BMI to a particular level and then document a decline in osteoporosis.

It represents the significant correlation between the BMD with Total Testosterone (p<0.001) and BMD with Age (P<0.01) respectively. The low degree correlation was observed between other variable which was statistically insignificant.

[Table 10] represents Multiple regression analysis demonstrated that Total Testosterone (β = 0.592, p < 0.0001), BMI (β = 0.165, p < 0.042) and Age (β = -0.159, p < 0.05) were independent predictive determinants of Decreased Bone Mineral Density (BMD) in enrolled osteoporotic cases.

DISCUSSION

Advancing age also means longer total exposure to chronic oxidant stress and inflammation, both of which contribute to development of osteoporosis.[5-7] One in five men over the age of 50 will suffer an osteoporotic fracture during their lifetime. The most serious fragility fracture is a hip fracture, and one-third of all hip fractures worldwide occur in men.[8] Furthermore, a study from Sweden, which followed a cohort of older men for 22 years, reported that 27% of men who had suffered a hip fracture sustained subsequent fractures in their remaining lifetime.[9] In Denmark, a national evaluation of the impact of fragility fractures concluded that almost 5,000 working days would be lost on account of fractures in men aged 50-65 years.[10]

Free health camp was organized for detection of Osteoporosis. The incidence of 46% men was diagnosed as osteoporosis, 32% as Osteopenia and remaining 22% men were found to be normal based on BMD T-Score. An additive explanation for higher proportion of osteoporotic men is represented by low physical activity and relative low calcium intake by public. In our study, maximum frequencies of 20 men (52.0%) were recorded as osteoporotic with total testosterone levels between 2.1-3.0ng/ml out of 46 osteoporotic cases and 15 men (39.47%) were recorded as Osteopenic out of 32 Osteopenic cases. Wishart and Colleagues demonstrated that 25% of men over 65 years old have serum testosterone levels less than 300ng/dl or 3 ng/ml.[11] The age- related decline in testosterone level was attributed to two factors, which were the degeneration of Leydig's cells and the increase of SHBG level with age.[12] In vitro studies demonstrated that androgen could increase the proliferation and decrease the apoptosis of osteoblast via regulation of protein kinase B.[13] Similar results were also observed in the study of Slemenda et al.[14] The maximum frequency of 18 osteoporotic men is recorded who were having DHEA level between interval 0.1-1.0 µg/ml. The same interval of DHEA level between 0.1 -1.0 µg/ml was observed in 18 men as osteopenic whereas 14 men as normal. The study is supported by DHEAS is by far the most abundant androgen in plasma. Its mean concentration in young males is about 220ng/dl or 2.2ng/ml is 10 to 20 times the concentration of cortisol, however decreasing rapidly with age.[15,16] Similar to our study, Kenny et al. (1998),[17] reported that serum DHEAS levels were inversely associated with BMD of the trochanter. The positive co-relation was observed between BMD and Age as well as Testosterone and BMD. It is estimated that the residual lifetime risk of experiencing an osteoporotic fracture in men over the age of 50 is up to 27%.[18] The multiple regression analysis also demonstrated that serum Total Testosterone level (p <0.0001) was an independent predictive determinant of decreased BMD level in Osteoporosis so as that of Age (< 0.05) and BMI (p< 0.042) as well. Hence this observation can be the preliminary data to show the decrease testosterone level can be independently involved in decreasing bone mineral leading to fragility fractures. The interventional study by administration of testosterone can be done in large population with blinded randomized control trial to see the effect of testosterone in bone.

Osteoporosis has long been considered to be exclusively a problem of women and now time has come for a radical reappraisal of osteoporosis management in men. In this study opportunity is taken to find the incidence of osteoporosis and its correlation with Testosterone and DHEA in males above the age of 60 years. This study has become the preliminary data analysis in south west region of Nepal to find out the incidence of osteoporosis to correlate with the androgens like Testosterone and DHEA which according to this study has shown testosterone plays an independent and fundamental role in regulating bone mineral resorption.

CONCLUSION

Our results show maximum cases of Osteoporosis in the age group of 60-64 years but the incidence recorded in the particular age group was maximum in 70-74 years i.e. 81.81%. Significant difference was observed in the level of serum Testosterone, DHEA and BMD among various groups viz a viz Osteoporosis, Osteopenia and Normal (p <0.0001). Thus, present study indicates an important role of testosterone and bone loss as measured by BMD of distal radius by ultrasonography technique.

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