Effect of androgens on bone mineral density in Saudi Arabian males above the age of 50 years

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Osteoporosis is a generalized metabolic disease characterized by deterioration in the microarchitecture of the bone structure leading to fractures, with increased morbidity and mortality. Over the years, attention was meted out to the postmenopausal women and the prevalence of osteoporosis in men remained underestimated. This has changed recently, and reports indicate that 1-3 million men in the USA have osteoporosis, and another 8-13 million have osteopenia. Looker and his associates assessed the incidence of osteoporosis in men and reported that men suffer from osteoporosis in the range of 3-6%, and osteopenia in up to 47%. In the ethnic Saudi Arabian population, the prevalence was higher, so much that osteoporosis was found in 27.6%, and osteopenia in 57.5%.

Earlier it was well accepted that in women, estrogen, and in men, testosterone, were the main sex hormones related to osteoporosis, but this concept is being challenged lately. Studies indicate that estrogen is the key player in the prevention of osteoporosis in men, and reported that men suffer from osteoporosis in the range of 3-6%, and osteopenia in up to 47%. In the ethnic Saudi Arabian population, the prevalence was higher, so much that osteoporosis was found in 27.6%, and osteopenia in 57.5%.

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Methods. Saudi Arabian male patients over the age of 50 years, attending the outpatient clinics of King Fahd Hospital of the University, Al-Khobar, Kingdom of Saudi Arabia, comprised the study subjects. Between May 2005 and 30 January 2006, and after a verbal consent, patients had their weight and height measured to calculate the body mass index (BMI). A detailed history was taken with meticulous examination, followed by appropriate investigations, to rule out secondary osteoporosis.

Blood was extracted for serum level of androgens, gonadotropins, and thyroid stimulating hormone, albumin, calcium, phosphorus, and alkaline phosphatase. Bone mineral density measurement of hip and spine was carried out using dual energy x-ray absorptiometry. Osteopenia and osteoporosis were defined per the World Health Organization description.

Results: We analyzed the data of 181 patients with an average age of 61.76±0.75. Ninety-nine (54.7%) were osteopenic (Group B) and 54 (29.8%) were osteoporotic (Group C). Osteoporotic patients (Group C) had a higher testosterone level, 486.85ng/dl±17.18 versus 424.84ng/dl±20.93; p=0.001, and lower estradiol levels, 22.3pg/ml±0.73 versus 28.55pg/ml±1.82, p=0.001, compared to the non-osteoporotic patients (Group A). Compared to the non-osteoporotic group, the osteopenic patients had higher levels of testosterone (p=0.05) and lower estradiol levels (p=0.001).

Conclusions: Our study indicates that serum levels of testosterone in Saudi Arabian males of over 50 years have little influence on the protection against the development of osteoporosis and osteopenia, and secondly males who have a low level of estradiol are more likely to have low bone mineral density, osteopenia, or osteoporosis.


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secondary osteoporosis. Patients, who were on steroids, with chronic obstructive lung disease, cardiac, renal, liver, hematological diseases, or any malignancy, were excluded from the study. Blood for albumin, calcium, phosphorous, alkaline phosphatase, thyroid stimulating hormone (TSH), luteinizing hormone (LH), follicle stimulating hormone (FSH), total estrogen (E2), and total testosterone (Tt) was taken, and the hormonal assay was carried out by an Architect, model i 2000 (Abbott Laboratories, Illinois, USA) machine using chemiluminescent microparticle immuno-assay (CMIA). As the test for free testosterone was not available at our laboratory, the total testosterone level was taken for analysis. Bone mineral density (BMD) measurement of the hip area and the lumbar spine using dual energy x-ray absorptiometry (Dexa scan, Hologic Inc, Waltham, MA, USA) was performed. Patients with a T-score of <2.6 SD or above were taken as osteoporotic and those between <-1 to -2.6 SD was taken as osteopenic for analysis. The data were entered in the database and analyzed using a t-test to compare means between the non-osteoporotic, osteopenic, and osteoporotic patients. All tests were performed using the Statistical Package for Social Sciences, version 11.0, Chicago, Illinois, with statistical significant p value of <0.05, and with confidence of 95%.

**Results.** We analyzed the data of 181 patients with an average age of 61.76 ±0.75 (50-76) with a mean BMI of 24.74±0.35 (18.5-31). Patients were divided based on the result of the BMD and T-score into 3 groups. Group A with normal BMD and T-score, Group B with osteopenia and Group C with osteoporosis. The primary demographic data are given in **Table 1.** It indicates that there was no significant difference in serum levels of albumin, calcium, phosphorous, alkaline phosphatase, and TSH. Patients in group C were at least a decade older and had significantly lower BMI (p=0.001). Analysis of the scans of the hip revealed that 25 (15.5%) of the patients were normal with an average BMD of 1.07±0.02 gm/cm² (0.898-1.326), and mean T-score of -0.1±0.13 (0.8 to -1). Ninety-nine (54.7%) were osteopenic with an average BMD of 0.920±0.007 gm/cm², and 54 (29.8%) were osteoporotic with a mean BMD of 0.817±0.01 gm/cm² (0.764-0.859) and T-score of -3.15±0.05 (-2.9 to -3.4). **Table 2 shows** the relationship of osteoporosis to the sex hormonal profile. The total testosterone level was higher in the osteoporotic patients (Group C) as compared to the non-osteoporotic (Group A), 486.85ng/dl±17.18 (395.5-552.3) versus 424.84ng/dl±20.93 (203.9-525.6), p<0.001, while estradiol level was lower in group C compared to group A, 22.3 pg/ml±0.73 (19-25) versus 28.55 pg/ml±1.82 (11-37.5), p<0.001. The comparison between non-osteoporotic and osteopenic patients showed higher levels of testosterone (p<0.05) and lower estradiol levels (p<0.001). The LH level was also higher in group C compared to group A, 8.63±1.4 (2.3-14.21) versus 5.77±0.24 (1.84-6.93), while FSH level showed no significant difference between the groups.

**Discussion.** In recent years, the important role of estrogen in the maintenance of bone architecture and development of osteoporosis in males has been considered seriously. The previous belief that testosterone is the main hormone that protects males from being susceptible to develop osteoporosis has come under dramatic scrutiny. Our study showed that patients with osteoporosis had low estrogen and normal testosterone as compared to those patients whose BMD and T-score were within the normal range. Studies have shown the importance of estrogen in adult males for the maintenance of bone mass, and this study further highlights the need for adequate levels of estrogen for the prevention of

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**Table 1** - Demographic data of the screened patients, and relation of bone mineral density to the baseline investigations.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Normal range</th>
<th>Non osteoporotic (Group A) n=28</th>
<th>Osteopenic (Group B) n=99</th>
<th>Osteoporotic (Group C) n=54</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>Mean±SD (range)</td>
<td>64±0.84 (52-70)</td>
<td>62.8±0.75 (50-75)</td>
<td>65.28±0.76 (67-76)</td>
</tr>
<tr>
<td>BMI Kg/M²</td>
<td>20-25</td>
<td>30.05±1.55 (26.9-36)</td>
<td>24.06±3.67 (18.42-35.4)</td>
<td>23.65±3.42 (19.94-28.91)</td>
</tr>
<tr>
<td>Albumin g/dl</td>
<td>3.5-4.8</td>
<td>3.93±0.56 (3-4.8)</td>
<td>3.83±0.37 (3.1-4.8)</td>
<td>3.95±0.39 (3.2-4.8)</td>
</tr>
<tr>
<td>Calcium level mg/dl</td>
<td>8.5-10.5</td>
<td>9.36±0.31 (8.9-9.7)</td>
<td>9.42±0.403 (8.8-10.9)</td>
<td>9.39±0.28 (9.0-9.7)</td>
</tr>
<tr>
<td>Phosphorus mg/dl</td>
<td>2.5-4.9</td>
<td>3.51±0.29 (3.3-4.1)</td>
<td>3.63±0.433 (2.6-4.5)</td>
<td>3.41±0.47 (2.6-3.9)</td>
</tr>
<tr>
<td>Alkaline phosphatase IU/L</td>
<td>48-277</td>
<td>68.87±18.17 (38-101)</td>
<td>86.22±22.4 (45-140)</td>
<td>77.65±16.13 (50-97)</td>
</tr>
<tr>
<td>TSH (UIU/ml)</td>
<td>0.35-4.94</td>
<td>2.16±0.93 (0.79-5.41)</td>
<td>2.05±1.56 (0.585-8.58)</td>
<td>1.69±0.62 (0.74-2.85)</td>
</tr>
</tbody>
</table>

BMI - body mass index, TSH - thyroid stimulating hormone.
male osteoporosis. In males, estrogens are produced from the adrenals; however, most of the estrogens in men come from aromatization of testosterone in the adipose tissue. Once in the circulation, it exerts an inhibition of the osteoclastic activity, and regulation of bone mass via specific α and β receptors located within osteoblasts. In this study, we observed that patients with higher BMI were less osteoporotic than their lean counterparts indicating the role of adipose tissue in the peripheral production of estrogens and the protection from the development of osteoporosis. Reports in the literature confirm that patients with higher BMI had lower incidence of osteoporosis, and its related fractures. The association of male hypogonadism and low bone mass with lower BMD is well-known. Researchers found lower testosterone levels in over 30% of elderly men, which we could not corroborate from our study, possibly because we measured total, and not the bioavailable testosterone. In the last decade, osteoporosis in men has become an important public health problem and secondary causes of osteoporosis are presumed to be common, and this needs a definite evaluation. It was suggested that as age advances estrogen levels drops in men causing low BMD. It appears that both androgens and estrogens are needed for the maintenance of bone deposition and prevention of bone resorption. The individual role of these 2 sex hormones needs to be clearly defined in the management of osteoporosis in men.

The present study has a few limitations. Although we ruled out most of the secondary causes of osteoporosis on a clinical and laboratory basis, still we did not perform all the investigations needed for the complete evaluation of osteoporosis in men. Secondly, we measured total estrogen and testosterone, as some may argue that the free form is more relevant than the total level and, thirdly, the higher age and the lower BMI possibly contributed to the increased prevalence of osteoporosis in group C. In conclusion, this study suggests that the level of estrogen correlates with BMD; hence, measurement of estrogen levels is essential in the evaluation of male osteoporosis in addition to the measurement of the androgens.

References


Table 2 - Data of the patients and the relationship between bone mineral density (BMD) and sex hormones.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Normal range</th>
<th>Non osteoporotic (Group A) n=28</th>
<th>Osteopenic (Group B) n=99</th>
<th>Osteoporotic (Group C) n=54</th>
<th>Means±SD (range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total testosterone &gt;50 years ng/dl</td>
<td>156-563</td>
<td>424.84±20.93 (203.9-525.6)</td>
<td>451.4±168 (106-906)</td>
<td>486.85±17.18 (395.5-552.3)</td>
<td></td>
</tr>
<tr>
<td>Total estradiol (pg/ml)</td>
<td>11-44</td>
<td>28.55±1.82 (11-37.5)</td>
<td>22.6±1.05 (10-52)</td>
<td>22.3±0.73 (19-25)</td>
<td></td>
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<tr>
<td>LH (MIU/ml)</td>
<td>1.26-10.05</td>
<td>5.77±0.24 (1.84-6.93)</td>
<td>6.30±0.35 (1.1-14.4)</td>
<td>8.63±1.4 (2.3-14.21)</td>
<td></td>
</tr>
<tr>
<td>FSH (MIU/ml)</td>
<td>1.37-13.58</td>
<td>7.05±3.02 (3.01-11.21)</td>
<td>6.19±2.84 (1.9-3.56)</td>
<td>5.96±2.16 (3.06-11)</td>
<td></td>
</tr>
<tr>
<td>BMD-hip</td>
<td>1.07±0.02</td>
<td>(0.898-1.326)</td>
<td>0.920±0.007 (0.697-1.065)</td>
<td>0.817±0.01 (0.764-0.859)</td>
<td></td>
</tr>
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<td>T-score</td>
<td>-0.1±0.13</td>
<td>(0.8 to -1)</td>
<td>-1.7±0.04 (-1 to -2.5)</td>
<td>-3.15±0.05 (-2.9 to -3.4)</td>
<td></td>
</tr>
<tr>
<td>BMD-spine</td>
<td>1.06±0.01</td>
<td>(0.862-1.123)</td>
<td>0.885±0.014 (0.527-1.25)</td>
<td>0.789±0.02 (0.713-0.931)</td>
<td></td>
</tr>
<tr>
<td>T-score</td>
<td>-0.29±0.10</td>
<td>(0.3-1.0)</td>
<td>-2.4±0.1 (-1.1 to -2.5)</td>
<td>-3.6±0.2 (-2.8 to -4.4)</td>
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</tbody>
</table>

LH - luteinizing hormone, FSH - follicle stimulating hormone.
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