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Research Article

Interpreting low normative bone mineral density among Saudi Arabian women

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ABSTRACT

Background: Although results from prior publications have indicated that normative bone mineral density (BMD) in Saudi Arabian women is significantly lower than their North American and European counterparts, there has been no systematic attempt to study these differences across the age-spectrum.

Objectives: To explore these issues in more detail, a new Saudi Arabian normative BMD dataset was systematically derived from patient data at King Faisal Specialist Hospital & Research Centre in Riyadh. Changes in mean BMD were studied with respect to both age and years-since-menopause.

Methods: A retrospective analysis of BMD was carried out among 858 Saudi Arabian women who had undergone routine dual-energy x-ray absorptiometry. In addition to the usual patient details collected at each scan, information from questionnaires summarizing the patient's medical, lifestyle and menopause history was also used to identify a subset of 179 presumed-normal women.

Results: The normative BMD results for the L2-L4 AP-spine scans agree very closely with published data describing Jeddah women and indicate that during their postmenopausal years, the BMD of an average Saudi Arabian woman drops from a premenopausal plateau (i.e. peak bone mass) of 1.14 g cm^{-2}, to a residual postmenopausal plateau of 0.92 g cm^{-2}. The time-constant for this loss is 4.64 years.

Conclusions: We conclude that the average BMD of normal Saudi Arabian women is approximately 0.1 g cm^{-2} lower than European women across the entire adult age-range, but that the extent and rate of postmenopausal bone loss appears to lie within the normal European range. This suggests that osteoporosis is first manifested in young adults.

Keywords: osteoporosis, bone mineral density, Saudi Arabia

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INTRODUCTION

Although there have been a number of relevant publications in this area [1–9], there are no population-based estimates of normative bone mineral density (BMD) values among Saudi Arabian women - probably for logistical reasons, given that the country covers some two million square kilometers and not all regions have easy access to the expensive and cumbersome dual-energy x-ray absorptiometry (DXA) technology necessary for a valid diagnosis [10]. However most publications in this area have concluded that Saudi Arabian women have lower bone mineral density than women in the "West" [1–3] and consequently that there is likely to be an elevated burden of osteoporosis in the Kingdom [4–9].

Various explanations have been advanced to explain this apparent low bone mineral density. These have focused on nutritional issues (e.g. calcium intake [11], cultural differences such as multiparity and extended lactation [12], and the likelihood of vitamin-D insufficiency or deficiency [13] (presumed to be due to the tendency of many women to cover-up when outdoors, paradoxically almost eliminating their sun-exposure in spite of regular daily sunshine [14–20]. Although there is no shortage of candidate hypotheses, little headway has been made in identifying the principal cause. However this may become easier if the specifics of this population-based difference can be more clearly defined. Prior publications have contributed important observations, but have fallen short of providing robust comparisons between the bone mineral status of Saudi Arabian women and their Western counterparts.

Our intention here is to introduce a new Saudi Arabian BMD dataset - normative data systematically derived from the patient files at King Faisal Specialist Hospital and Research Centre (KFSH&RC) - and to use this to compare the BMD status of Saudi Arabian women with "western" women across the adult age-range. The particular western population which was selected for as a basis for comparison has already been extensively described in the literature [23,24] and comprises one of the largest volunteer studies in Europe - 8,789 women from Oxford, UK. One important (and unique feature) of these data is that they have been described on a year-by-year basis, offering a detailed profile of BMD across the various age-groups and thereby providing an ideal vehicle for comparison purposes.

METHODS

A retrospective analysis of BMD was carried out among all Saudi Arabian women who had undergone routine DXA scans at the KFSH&RC between 1st December 1995 and 31st October 2000. All scans were performed using a Lunar DPX Bone Densitometer (Lunar Corp, Wisconsin, USA) according to the manufacturer's operations manual. The calibration of the absorptiometer was confirmed on a daily basis. BMD measurements were obtained at the AP lumbar spine (L2-L4), the left femoral neck, Ward's triangle and trochanter. In addition to the details of each scan (routinely stored in the manufacturer's database), the scan protocol also required the completion of a questionnaire which summarized the patient's medical, lifestyle and menopause history. The combined data from the manufacturer's database and patient questionnaire constitute the source material for this study.

A stringent procedure was subsequently used to classify patients as normal, based on 24 different items of information contained in the patient database and questionnaire. These describe the patient's fracture history, chronic disease history, relevant medication, current treatment (if any) and additional ad-hoc comments and observations. Seven independent binary indices of normality were generated to describe each patient: (1) any history of fracture, (2) any history of chronic disease (including diabetes), (3) prior or existing use of steroids or oral contraceptives, (4) prior or existing use of estrogen replacement therapy, (5) prior or existing use of bone-related medication, including thyroid hormone, (6) prior or existing use of vitamin-D, (7) prior or existing use of calcium. Only those patients who scored zero for all seven indices were presumed to be normal.

All statistical analyses were carried out using the JMP statistics package (v5.1.2, SAS Institute Inc) running under Microsoft Windows XP Professional (SP2) on a Hewlett-Packard workstation XW4200. Curve-fitting and scientific plotting were performed by Origin v5.1 (Microcal Software Inc.). A 5-point adjacent-averaging technique was used to smooth selected (specified) curves which were drawn using a B-spline technique. Intercomparisons of lumbar AP DXA measurements of BMD were facilitated by converting all measurements to their approximate L2-L4 equivalent L2-L4 Lunar values. Hologic 1000 results were converted using the following equation:

$$DPX = (1.074 * (QDR1000 / 1.019)) + 0.054 (21,22).$$

Table 1. Referral distribution of female DXA patient population.

Hospital Department	Number of Referrals
Family Medicine	615
Medicine: Endocrinology	242
Other Sections	252
Obstetrics & Gynecology	116
Others	92
Missing or Ambiguous	229
Total	**1,546**

Table 2. Current residence of female Saudi Arabian patient population.

Current Residence	Number of Women
KSA: Riyadh	404
Elsewhere	161
Non-specific	93
Abroad	5
Missing or Ambiguous	195
Total	**858**

Table 3. Application of study exclusion criteria.

Women Who Presented for DXA Scans	Excluded	Remaining
All women who presented for at least 1 DXA scan at KFSH&RC between 1st December 1995 & 31st October 2000.	–	1,546
Not Saudi Arabian	683	863
First scan outside study-time-frame	5	858
Invalid scan	6	852
Uncorroborated first-scan	9	843
No lumbar AP scan	22	821
Only women ages 20-80 years	17	804

Table 4. Seven exclusion criteria used to establish normality.

Disease Category	Non Normals	Remaining Normals
—	-	804
Any Fracture	43	761
Chronic Disease + Diabetes	361	424
Steroids + Oral Contraceptives	171	375
ERT	137	293
Bone Medication + Thyroid Hormone	71	270
Vitamin-D	247	211
Calcium	315	179

This work was part of a larger DXA study and was approved by the Research Advisory Council at King Faisal Specialist Hospital and Research Centre.

RESULTS

1,546 women presented for Lunar DXA scans at KFSH&RC between the 1st December 1995 and the 31st October 2000. The referring department could be clearly identified for 1,317 of these women (Table 1); 47% were from the Family Medicine department, which provides primary health care for hospital employees and their extended families. The Hospital Information System identified 863 women as Saudi Arabian, but 5 had their first scans outside the study time-frame, leaving 858 women which constituted the principal material for this study. Typical of the KFSH&RC patient population, these women were drawn both from Riyadh and from many outlying regions. In conjunction with our rigorous screening process (see methods) and the fact that many patients were referred from well-women clinics and the Family Medicine Department, it seems unlikely that significant selection bias remains in the final dataset which is presented here.

BMD-related information was extracted from the Lunar database for all the DXA scans of these 858 patients. 404 were known to be resident in Riyadh at the time of their scan (Table 2). Six patients had

Table 5. Comparison of mean BMI (and standard-deviation) across different publications.

Age-Group	El-Desouki	Ghannam et al.	Ardawi et al.	KFSH&RC	
				Normals	All
30–39	29 (6)	26.8 (4.1)	25.1 (3.0)	27.8 (7.6)	28.3 (6.4)
40–49	30 (6)	28.2 (5.5)	26.2 (3.3)	28.4 (5.9)	29.6 (6.1)
50–59	31 (5)	30.8 (5.8)	27.2 (2.1)	31.9 (5.4)	31.2 (5.7)
60–69	31 (6)		25.9 (2.7)	31.0 (5.0)	30.9 (5.1)

Note that Ardawi et al. used an exclusion criterion of BMI > 30, and Ghannam used slightly different groupings for ag (21–30, 31–40 etc.).

Table 6. A comparison of the magnitude of postmenopausal decline between the observed KFSH&RC data, the predicted result (using a 3-parameter exponential decay) and the publication of Shipman et al. [23].

Author	Mean Premenopausal BMD Age-Range	Mean Residual BMD Age-Range	Difference	% Drop
Shipman et al. (1999)	1.22 30-39(inc)	0.99 70-73 (inc)	0.27	19
KFSH&RC (data)	1.15 30-39(inc)	0.92 70-75 (inc)	0.23	20
KFSH&RC (model)	1.14	0.92	0.22	19

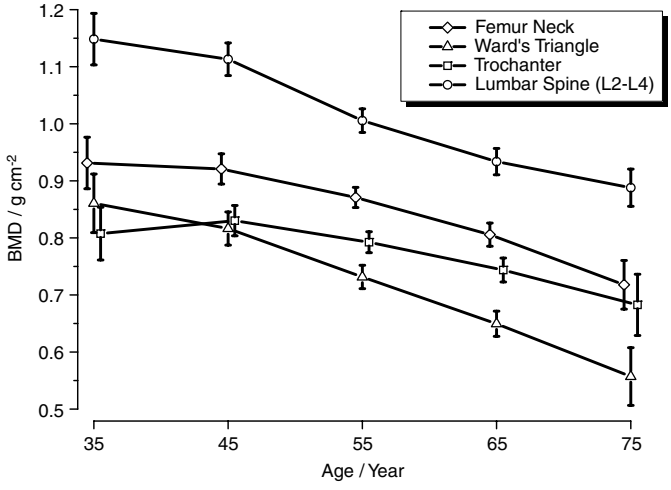


Figure. 1 The change in mean BMD (and associated standard-error) with age at four different anatomical sites (AP Lumbar Spine L2-L4, Femur Neck, Ward's Triangle and Trochanter) for 179 apparently-normal Saudi Arabian women. The patients were categorized into 5 different age-groups: 30–39, 40–49, 50–59, 60–69 years. Note that the x-coordinates on the plot have been staggered slightly, in order to avoid overlapping the standard errors.

no valid scans, leaving 17,290 BMD measurements (multiple measurements were associated with each scan) and 852 patients (Table 3). To eliminate any treatment effect, only those scans from each patient's first visit were retained. These were identified using the *sequence-number* field within the Lunar database and confirmed by examining the sequence of *scan-dates* for each patient. These were in agreement for 843 patients who had 13,654 measurements altogether. Six women who were older than 80 years and 11 who were younger than 20 years were eliminated at this stage, leaving a final patient dataset of 804 women who had a lumbar DXA scan. 782 of these women also had a scan of the femur.

According to the criteria described earlier, there were 179 normal Saudi Arabian women between the ages of 20 and 80 years (Table 4). For this subgroup, the relationship between mean BMD at the lumbar spine (L2-L4) and age is shown in Fig. 1. Comparable results for BMD decline with age at the three femur sites (neck, Ward's triangle and trochanter) are also shown in the same figure. The normative curve for BMD at the lumbar spine is redrawn in Fig. 2, where it is compared with all three previously-published normative results for Saudi Arabia. The smoothed year-on-year results for 8,789 female volunteers from Oxford, UK [23] are also shown.

The relationship between BMD and Years-Since Menopause (YSM) was studied for the 115 postmenopausal women whose detailed menopausal status was known at the time of their scan

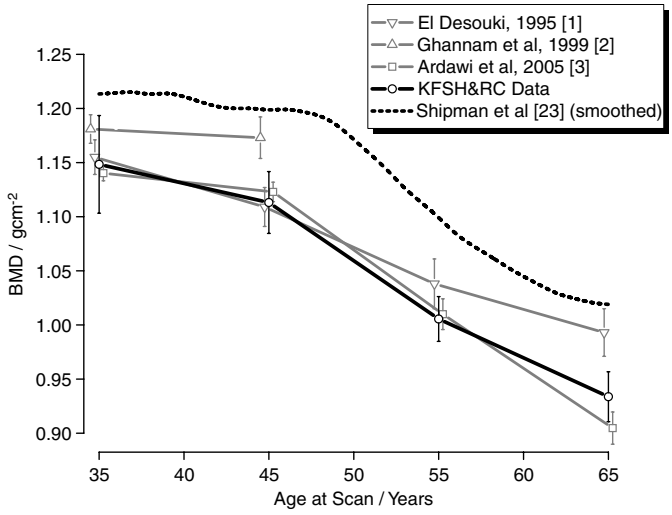


Figure. 2 A comparison of the trend in mean BMD (and associated standard error) with age, for all four normative Saudi Arabian datasets. For comparison purposes, these are also compared with smoothed results from a large North European dataset (Oxford, UK) [23].

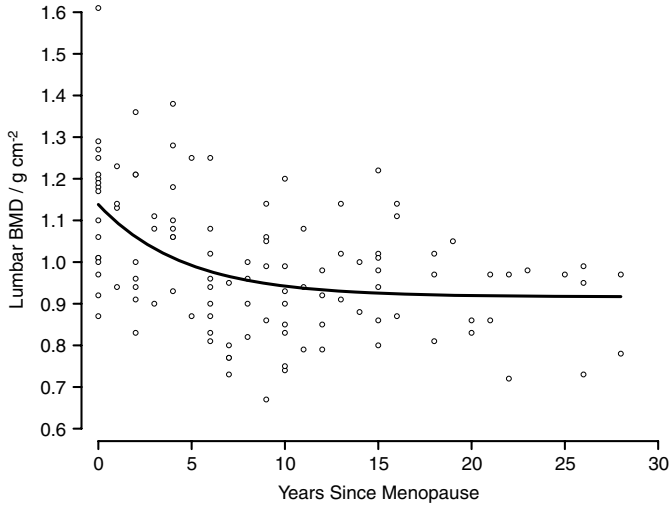


Figure. 3 An exponential fit to the relationship between BMD at the Lumbar Spine and Years Since Menopause. The curved line is the theoretical exponential decline.

(Fig. 3); these included 97 postmenopausal women with natural menopause and 18 premenopausal women. Note that the zeroth time-point on this graph can be calculated by averaging the premenopausal BMD results because we have previously demonstrated that there is no detectable change in lumbar BMD prior to menopause [24]. A detailed analysis of the Age-At-Menopause (AAM) distribution which underlies these results can also be found in our other previous publication [25]. The least-squares exponential fit to these data is also shown in Fig. 3, revealing a time-constant of 4.64 years, a premenopausal plateau (i.e. peak bone mass) of 1.14 g cm^{-2}, and a residual BMD (i.e. when postmenopausal decline is almost complete) of 0.92 g cm^{-2}. This implies that the average Saudi Arabian woman experiences a postmenopausal decline in BMD of ~0.22 g cm^{-2}.

DISCUSSION

We have presented a new normative BMD dataset for Saudi Arabian women. Three prior publications [1–3] have attempted to provide similar normative data, and these have disagreed. The results of Ghannam et al. [2] (Riyadh, N = 321) are limited to women younger than 50 years of age, and are consistently higher than the other two. The estimates by El-Desouki et al. [1] (Riyadh, N = 249) and

Ardawi et al.[3] (Jeddah, N = 1,065) agree well with each other below the age of 50 years but diverge markedly for older women, eventually resulting in a discrepancy of 0.1 g cm^{-2} (~10%) by the age of 70 years.

Our normal data agree closely with the results of Ardawi et al. [3] suggesting both that the dataset of Ghannam et al. [2] is an outlier and that the difference between the other two does not simply reflect a "Riyadh-Jeddah" effect. The high BMD estimates produced by Ghannam et al. are particularly intriguing because our data originated from the same instrument and includes some data from the same time-period. All three prior publications presented various age-matched comparisons between the average BMD of Saudi Arabian and US/European women, demonstrating statistically-significant differences by which the authors concluded that the BMD of a Saudi woman is lower than her western counterpart. However the magnitude of this discrepancy is debatable since it depends upon which population was used as a reference and which age-group was tested. We should also mention that similar discrepancies also appear to exist between the average BMD of women in USA/Europe and almost all Middle-Eastern countries [26–30] although the magnitudes of these differences are also debatable.

We have clearly demonstrated that there is an almost constant difference between the average BMD of Saudi Arabian and UK women aged 30 and 70 years of age. It is unlikely that these estimates are significantly influenced by differences in BMI, because the BMI exclusion criterion implemented by Ardawi et al. [3] resulted in a sample of women with substantially lower BMI than is found in our normative sample (and also throughout the general Saudi Arabian population - Table 5) and yet our BMD results agree closely. The similarity between the KFSH&RC results and the much larger, population-based, sample of Ardawi et al. also supports the view that there is little residual bias within the hospital data.

There have already been several publications [4–7] describing the BMD status of postmenopausal Saudi Arabian women in Saudi Arabia. El-Desouki et al. [4,5] reported twice on different "snapshots" of the same dataset (Riyadh, N = 482 & N = 830) and in a third publication [6] explored the impact of diabetes mellitus (Riyadh, N = 205). Sadat-Ali et al. [7] (Al Khobar, N = 256) report an overall prevalence of osteoporosis. However these publications used an analytical approach more applicable to a mixed (premenopausal and postmenopausal) group. The principal advantage of focusing purely on postmenopausal women is that it facilitates an axis change - instead of plotting BMD against age, it can more properly be plotted against Years-Since-Menopause (YSM). When our BMD data for the lumbar spine were fitted to a single-exponential model with respect to YSM [30] the underlying postmenopausal decline was revealed to have a time-constant of just over 4.6 years. It would therefore appear that Saudi Arabian women lose bone at almost the same rate as Europeans (5.8 years [30]).

Furthermore, comparing the *magnitude* of this exponential decline (0.22 g cm^{-2}) with that reported for the Oxford women also suggests that during the 20 years or so of this postmenopausal period, Saudi Arabian women lose approximately the same amount of bone as Europeans (20%). This is very similar to the magnitude of decay manifested in the overall cross-sectional data (Table 6). Additional support for this estimate of 20% comes from the review in our previous publication [24] where we found that the average drop in BMD for 9 published European studies was approximately 19.5%.

That both the UK and Saudi Arabian women appear to lose the same amount of bone mineral during their postmenopausal years - and at the same rate - is also reflected in the almost constant difference in average BMD between the Saudi Arabian and the Oxford women across the entire postmenopausal age-range. This strongly suggests that the principal difference between European and Saudi Arabian women is simply the BMD level at which bone loss begins - i.e. their premenopausal BMD or peak bone mass. For Saudi Arabian women this is approximately 0.1 g cm^{-2} lower (~8%) than the Oxford female volunteers.

We therefore conclude that the BMD of Saudi Arabian women remains consistently lower than western women across the postmenopausal age-range, whereas the extent and rate of their postmenopausal bone loss lies close to normal European values. This suggests that the additional burden of osteoporosis in Saudi Arabia is primarily due to a decreased peak bone mass and is first manifested in young adults.

COMPETING INTERESTS

The authors have declared that there no competing interests.

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AUTHOR CONTRIBUTIONS

(i) WG: Contributed to the conception and design of the study and the acquisition, analysis and interpretation of the data, drafted the manuscript and gave final approval of the manuscript version submitted for publication.

(ii) MA: Contributed to the conception and design of the study, drafted the manuscript and gave final approval of the manuscript version submitted for publication.

(iii) AR: Contributed to the conception and design of the study, and revised the manuscript critically for content.

(iv) AF: Contributed to the acquisition, analysis and interpretation of the data, revised the manuscript critically for content and gave final approval of the manuscript version submitted for publication.All authors (apart from Dr. Rifai who passed away before this version of the manuscript was submitted) read and approved the final manuscript.

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