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ORIGINAL ARTICLE

Bone mineral density of the spine and femur in healthy Saudis

M. Salleh M. Ardawi · Abdulraouf A. Maimany
Talal M. Bahksh · Hasan A. N. Nasrat
Waleed A. Milaat · Raja M. Al-Raddadi

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Abstract The reference values of bone mineral density (BMD) were determined in healthy Saudis of both sexes and compared with US / northern European and other reference data. BMD was determined by dual-energy X-ray absorptiometry (DXA) at the lumbar spine and femur including subregions: trochanter, Ward's triangle, and neck, in 1,980 randomly selected Saudis (age range 20–79 years; 915 males and 1,065 females) living in the Jeddah area. Age-related changes in BMD were similar to those described in US / northern European and Lebanese reference data. Decreases in BMD of males were evident (% per year): 0.3–0.8 (lumbar spine), 0.2–0.4 (femoral trochanter), 0.2–1.4 (Ward's triangle), and 0.2–0.7 (femoral neck). Also, decreases in BMD of females were observed (% per year): 0.8–0.9 (lumbar spine), 0.7–0.9 (Ward's triangle), and 0.3–0.7 (femoral neck). Using stepwise multiple regressions that included both body weight and height, the former had 2–4 times greater effect on BMD than the latter. Using the mean BMD of the <35-year-old group the *T*-score values were calculated for Saudis. The prevalence of osteoporosis in Saudis (50–79 years) at the lumbar spine using the manufacturer's vs Saudi reference data was 38.3–47.7% vs 30.5–49.6 ($P<0.000$), respectively. Similarly, based on BMD of total femur, the prevalence of osteoporosis using the manufacturer's vs Saudi reference data was 6.3–7.8% vs 1.2–4.7% ($P<0.000$), respectively. Saudis (≥50 years) in the lowest quartile of body weight exhibited higher prevalence of osteoporosis (25.6% in females and 15.5% in males) as compared to that of the highest quartiles (0.0% in females and 0.8% in males). The present study underscores the importance of using population-specific reference values for BMD measurements to avoid overdiagnosis and/or underdiagnosis of osteoporosis.

Keywords Age · Bone densitometry · Osteoporosis · Saudis · *T*-score

M. S. M. Ardawi · A. A. Maimany · T. M. Bahksh
H. A. N. Nasrat · W. A. Milaat · R. M. Al-Raddadi
Saudi Osteoporosis Research Group, Jeddah, Saudi Arabia

M. S. M. Ardawi
Department of Clinical Biochemistry, Faculty of Medicine,
King Abdulaziz University Hospital,
King Abdulaziz University, Jeddah, Saudi Arabia

A. A. Maimany
Department of Radiology, Faculty of Medicine,
King Abdulaziz University Hospital,
King Abdulaziz University, Jeddah, Saudi Arabia

T. M. Bahksh
Department of Surgery, Faculty of Medicine,
King Abdulaziz University Hospital,
King Abdulaziz University, Jeddah, Saudi Arabia

H. A. N. Nasrat
Department of Obstetrics and Gynecology,
Faculty of Medicine, King Abdulaziz University Hospital,
King Abdulaziz University, Jeddah, Saudi Arabia

W. A. Milaat
Department of Family and Community Medicine,
Faculty of Medicine, King Abdulaziz University Hospital,
King Abdulaziz University, Jeddah, Saudi Arabia

R. M. Al-Raddadi
Primary Health Care Directorate,
Ministry of Health, Jeddah, Saudi Arabia

M. S. M. Ardawi (✉)
Department of Laboratory Medicine,
New Jeddah Clinic Hospital, PO Box 20724,
21465 Jeddah, Saudi Arabia
E-mail: ardawims@yahoo.com
Tel.: +966-2-6932705
Fax: +966-2-6403203

Introduction

Dual-energy X-ray absorptiometry (DXA) is a widely used technique to assess bone mineral density (BMD) at different skeletal sites and thus to stratify individuals with low bone mass who are at risk of osteoporosis and fractures [1]. BMD is influenced by several factors of which age and sex have such a strong impact that reference values for BMD should be age-and sex-specific, and, accordingly, for a reliable interpretation of such values, they need to be expressed in terms of established reference values derived from an appropriate healthy population [2] Comparisons can be achieved either by the use of T-scores which indicate the deviation from the mean BMD value of the young healthy population, or in terms of age-matched standard deviation scores, which are known as Z-scores [1]. However, it is considered that T-scores provide the be t information on the extent of bone loss and, thus, the best estimate of risk of fractures [1, 2]. The World Health Organization (WHO) defined a diagnostic criteria for osteoporosis in terms of BMD as measured by DXA [3], and although such criteria are based on observations in postmenopausal Caucasian females, they are widely used and applied to other at-risk populations to confirm a diagnosis of osteoporosis and/ or to estimate fracture risk [4] The WHO criteria allow classification of individuals into normal (T-score ≥ -1), with osteopenia (T-score < -1 and > -2 5), with osteoporosis (T-score ≤ -2 5), and with severe or established osteoporosis (T-score < -2 5 in the presence of one or more fragility fractures) [3]. These cutoff points have no inherent biological meaning: they were created to allow comparisons of the prevalence of osteopenia and osteoporosis in different populations and were not intended to be used to make treatment decisions [2] However, there are at least three difficulties facing the interpretation of the BMD data generated by DXA systems Firstly, there is an apparent discrepancy between reference values used by different DXA manufacturers: thus, when used in the same patients, DXA systems from different manufacturers differ in the proportion of patients diagnosed to have osteoporosis, by 6% to 15% [5, 6, 7, 8, 9, 10]. Secondly, all manufacturers use reference values based on a US and/or northern European adult population which will influence the interpretation of BMD data in other populations with different genetic, geographic, and socioeconomic characteristics from those of the US and/or northern European population [11]. Thirdly, ethnic variations in BMD values are well documented: indeed, it is known that the BMD values of African-Americans and Latinos are higher than those of whites [12], while Asians show lower values than Americans or northern Europeans [13, 14] because of their smaller size. Hence, there is a need to develop and use local reference BMD values rather than those provided by the manufacturers of DXA systems, something that has been emphasized by several studies in other populations [6, 15, 16, 17]

Osteoporosis is characterized by low bone mass and structural deterioration of bone tissue, leading to enhanced fragility and a consequent increase in fracture risk [18]. It is a common disease and often occult. yet it causes significant morbidity and mortality and in many cases may be preventable [19]; however, very limited information is available on either the prevalence of osteoporosis or on the BMD reference values in Saudis [20] To correctly categorize normal from abnormal, to avoid misdiagnosis with attendant risks of creating patient anxiety and subsequent overtreatment, reliable reference values for BMD appropriate to the observed population are required. Therefore, the main objectives of the present study are: (1) to determine the reference values of BMD for the lumbar spine (L2–L4) and the femur (including the femoral subregions of trochanter, Ward's triangle, and neck) in a randomly selected sample of healthy Saudi males and females—these reference values are used to estimate the prevalence of osteoporosis and osteopenia in Saudis 50 years of age and older, (2) to examine the influence of age, body weight, and height on BMD· and (3) to compare the results of the present study with those for Caucasians and other reference values

Subjects and methods

Study design

A total of 1,980 healthy Saudis (age range 20–79 years), males ($n=915$) and females ($n=1,065$) living in the Jeddah area, participated in the present study. Jeddah is the second most populated city (population 2.1 million) in Saudi Arabia with a diverse population representing most Saudis [21]. Originally, a total of 5,000 subjects were randomly selected during a health survey from 18 primary health care centers scattered around the city of Jeddah from April 2000 until April 2003 to ensure that the average health status of the study group would reflect a normal adult population A representative sample size was calculated using the sample-size determination option in Epi-Info Statistical Package (Version 6) supplied by USD, West Park Place, Stone Mountain, GA, USA. Subjects who agreed to participate in the survey were asked to visit a special clinic at the King Abdulaziz University Hospital (KAUH) to be enrolled in the present study Age, body weight, height, body mass index (BMI) (kg/m^2), and waist-to-hip ratio (WHR) were recorded Age and anthropometric data of the subjects studied are presented in Table 1 Each subject was medically examined and interviewed using a standardized questionnaire to collect information on life style, smoking habits, and level of physical activity in leisure time; coffee and tea consumption and the use of vitamins and medications. Subjects with chronic diseases including osteoarthritis or established osteoporosis or with evident endocrine disorders or on any form of drug treatment with possible effect on bone metabolism (e g , glucocorticoids, anticonvulsants, and/or thyroid hormones) were excluded. Subjects who are cigarette or sheesha smokers or are on vitamin supplement(s) were also excluded from the present study and, accordingly, a total of 3,020 males and females were excluded by the exclusion criteria. In addition, all subjects included exhibited (1) normal blood counts; (2) normal values for renal creatinine (serum creatinine in females <105 µmol/l and males < 116 µmol/l), and (3) normal values for liver function tests (serum aspartate aminotransferase [AST] < 30 U/l; alanine aminotrasnferase [ALT] < 30 U/l; alkaline phosphatase [ALP] between 80 and 280 U/l; and gamma-glutamyl transferase [GGT] < 60 U/l). Females on hormonal replacement therapy together with subjects who were vitamin D deficient (a total of 425 out of 3,020 [14.1%] subjects: 276 [9.2%] females and 149 [4.9%] males) with calcidiol levels < 20 nmol/l [22] were also excluded. Since the body weight affects BMD [23, 24, 25, 26], subjects with a BMI > 30 kg/m^2 were also excluded. The study protocol was in agreement with KAUH ethical standards and the Declaration of Helsinki of 1975, as revised in 1989. The study was approved by the Ethics Committee of KAUH, and informed written consent was obtained from all participants in the present study

Bone mineral densitometry measurements

BMD (g/cm^2) was determined for the anteroposterior lumbar spine (L2–L4) and mean of proximal right and left femur (total and subregions) by dual-energy X-ray absorptiometry (DXA) using a Lunar DPX-IQ (Lunar, Madison, WI, USA), according to standard protocol. BMD of the femur was expressed as the mean of the BMD values for the subregions: trochanter, Ward's triangle, and femoral neck. Quality control procedures were carried out in accordance with the manufacturer's recommendations. Instrument variation was determined regularly by a daily calibration procedure using a phantom supplied by the manufacturer Precision error of the phantom was 0.3% and for in vivo measurements was less than 1 2% for the spine and less than 2% for femoral regions In addition, there was no significant drift over the period of the study using the DXA system The standard deviation scores, which indicate the deviation from normal values [1], were calculated by the following equations

- Number of standard deviations = [(measured BMD) – (mean BMD of young reference population)] / [standard deviation]
- Number of standard deviations = [(measured BMD) – (mean BMD of sex- and age-matched population)] / [standard deviation]

BMD values were classified according to WHO criteria a *T*-score between −1 and −2 5 is indicative of osteopenia, while a *T*-score < −2 5 reflects osteoporosis, and a *T*-score > −1 is considered normal [3] Although, these criteria were based on observations in postmenopausal Caucasian females, they are now generally applied to other at-risk populations including men without thorough investigation of the utility or validity in these groups. Nevertheless, apart from an existing fragility fracture, BMD is considered to be the most robust determinant of fracture risk in men [1, 2, 4, 16, 18].

Statistical analysis

Results are presented as means (± SD) and categorical variables are expressed as frequencies. Data were analyzed using SPSS Statistical Package (version 11 0 for Windows Smart Viewer) supplied by SPSS 2000, Mapinfo, Tokyo, NY, USA Results that were not normally distributed were log-transformed before analysis. Associations between continuous variables were examined by Pearson correlation coefficient. ANOVA was used to examine differences among the groups for different variables, and the Bonferroni criterion was used when significance tests were made. The two-sided Student's *t*-test was used to compare the mean BMD values of the manufacturer's DXA reference values with those of the present study

Results

The basic anthropometric characteristics of the 915 males and 1,065 females studied are presented in Table 1. The body weight and BMI increased with age the weight difference$_{20–79}$ was 13.88 kg (P < 0.000) and 7.21 kg (P < 0.000) for males and females, with a corresponding BMI difference$_{20–79}$ 3.5 (P < 0.000) and 6 1 (P < 0.000), respectively. Height declined with age: the height difference$_{20–79}$ was 7 6 cm (P < 0 000) and 7 6 cm (P < 0.000) for males and females, respectively. WHR

Table 1 Anthropometric characteristics of Saudis studied. Results are presented as means + SD. *M* male, *F* female, *BMI* body mass index, *TSF* triceps skinfold, *MAC* midarm circumference, *WHR* waist-to-hip ratio

Age group	Sex (M/F)	Number	Age (years)	BMI (kg/m^2)	TSF (mm)	MAC (cm)	WHR
20–29	M	206	22.2 ± 1.7	22.6 ± 4.1	16.5 ± 5.9	23.1 ± 2.4	0 813 ± 0.06
	F	226	24.3 ± 3.5	22.4 ± 3.8	28.4 ± 9.9	25.0 ± 4.2	0.751 ± 0.05
30–39	M	110	33.9 ± 3.0	26.2 ± 2.6	32.9 ± 8.2	30.3 ± 3.3	0.934 ± 0.07
	F	243	34.1 ± 3.1	25.1 ± 3.0	32.2 ± 8.4	28.6 ± 3.2	0.782 ± 0.07
40–49	M	221	43.9 ± 2.3	25.5 ± 3.6	30.2 ± 11.1	28.8 ± 4.1	0.937 ± 0.05
	F	276	43.1 ± 2.9	26.2 ± 3.3	32.7 ± 7.4	29.9 ± 5.3	0.817 ± 0.09
50–59	M	154	53.7 ± 2.5	24.5 ± 2.4	31.4 ± 8.2	29.7 ± 2.8	0.959 ± 0.03
	F	143	52.9 ± 2.6	27.2 ± 2.1	33.6 ± 6.3	32.1 ± 9.8	0.857 ± 0.08
60–69	M	117	64.9 ± 2.6	26.1 ± 3.2	30.4 ± 6.2	28.7 ± 2.8	0.990 ± 0.05
	F	102	62.9 ± 2.3	25.9 ± 2.7	29.6 ± 7.3	29.3 ± 2 3	0.884 ± 0.09
70–79	M	107	73.3 ± 2.6	24.8 ± 3.5	25.0 ± 7.6	27.2 ± 3.9	0.971 ± 0.07
	F	75	74.4 ± 2.1	27.2 ± 1.6	29.3 ± 6.1	29.8 ± 1.4	0.818 ± 0.07
20–79	M	915	45.7 ± 16.9	24.8 ± 3.5	27.2 ± 10.3	27.7 ± 4.1	0.924 ± 0.08
	F	1,065	39.5 ± 13.7	24.9 ± 3.6	31.1 ± 8.5	28.4 ± 5.3	0.801 ± 0.09

increased with age: the WHR difference$_{20–79}$ was 0 187 ($P < 0.000$) and 0.102 ($P < 0\ 001$) for males and females, respectively.

Subjects were divided into six decade subgroups for cross-sectional analysis. The mean BMD values are grouped according to age and are given in Table 2 with the corresponding *T*-scores for the lumbar spine and femur with its various subregions (trochanter, Ward's triangle, and neck) Saudis exhibited a similar pattern of decrease in BMD to that described for US [11, 27], northern European [28, 29, 30, 31, 32, 33, 34, 35] and Lebanese populations [36], and Kuwaiti [37], Japanese [38], and Chinese [39] (females only) reference values (Figs. 1 and 2) BMD of the femur was consistently higher in males than in females between 20 and 79 years, except for Ward's triangle in females of 40–49 years of age. Females exhibited higher BMD lumbar spine values in the age groups of 50–59 and 70–79 years than in the corresponding males of the same age-matched groups (see Table 2)

Age showed highly significant negative correlations with all skeletal sites examined in both males (Table 3) and females (Table 4). With respect to BMI, there were positive correlations with BMD which were significant for all skeletal sites examined in both males and females with the exception of femoral neck in females studied (Table 4) Significant negative correlations were also evident between WHR and the skeletal sites examined in both males and females except in femoral trochanter and total femur in females studied (see Tables 3 and 4)

Every anatomical region has a different rate of bone loss The lumbar spine BMD values were relatively stable from 20 to 49 years in the females studied, but decreases by about 0.9% per year between 60 and 69 years and by 0 8% per year between 50 and 79 years were evident Significant decreases were observed in the femur BMD (per year). 0.3% in neck and 0 7% in Ward's triangle, in females between 20 and 49 years, respectively, with no significant changes in femoral

Table 2 Measured bone mineral density (BMD) of healthy Saudis of both sexes with calculated *T*-scores based on the mean bone mineral density of the age group of <35 years

Age (years)	Females			Males		
	Number	BMD (g/cm^2)	*T*-score	Number	BMD (g/cm^2)	*T*-score
Spine (L2–L4)						
20–29	226	1.116 ± 0.12	0.00 ± 1.0	206	1.137 ± 0.09	0.00 ± 1.0
30–39	243	1.128 ± 0.11	−0.59 ± 0.93	110	1 116 ± 0.15	−0.21 ± 1.46
40–49	276	1.110 ± 0.15	−0.70 ± 1.23	221	1.013 ± 0.18	−1.23 ± 1.78
50–59	143	0.993 ± 0.17	−1.73 ± 1.41	154	0.982 ± 0.13	−1.54 ± 1.29
60–69	102	0.884 ± 0.15	−2.60 ± 1.20	117	0.972 ± 0.22	−1.64 ± 2.16
70–79	75	0.764 ± 0.09	−2.74 ± 0.94	107	0.728 ± 0.09	−4.07 ± 0.96
20–79	1,065	1.075 ± 0.161	−0.99 ± 1.28	915	1.019 ± 0.19	−1.16 ± 1.92
Femur (total)						
20–29	226	0.992 ± 0.17	0.00 ± 1.0	206	1.098 ± 0.19	0.00 ± 1.0
30–39	243	0.973 ± 0.11	−0.24 ± 0.89	110	1 07 ± 0.16	−0.55 ± 0.86
40–49	276	0.979 ± 0.13	−0.21 ± 1.05	221	0.98 ± 0.16	−1.04 ± 0.91
50–59	143	0.893 ± 0.15	−0.92 ± 1.12	154	0.95 ± 0.13	−1.16 ± 0.72
60–69	102	0.817 ± 0.12	−1.51 ± 0 99	117	0.95 ± 0.13	−1.16 ± 0.74
70–79	75	0.808 ± 0.11	−1.57 ± 0.92	107	1.03 ± 0.10	−0.76 ± 0.56
20–79	1,065	0.953 ± 0.15	−0.43 ± 1.14	915	1.01 ± 0.1.17	0.92 ± 0.65
Femur (trochanter)						
20–29	226	0 807 ± 0.16	0.00 ± 1.0	206	0.879 ± 0.15	0.00 ± 1.0
30–39	243	0.774 ± 0.10	−0.36 ± 0.71	110	0.878 ± 0.14	−0.105 ± 1.09
40–49	276	0.784 ± 0.13	−0.29 ± 0.89	221	0.796 ± 0.12	−0.749 ± 0.95
50–59	143	0.703 ± 0.096	−0.846 ± 0.66	154	0.811 ± 0.09	−0.631 ± 0.78
60–69	102	0.648 ± 0.11	−1.226 ± 0.76	117	0.797 ± 0.11	−0.739 ± 0.85
70–79	75	0 598 ± 0.04	−1.565 ± 0.25	107	0.826 ± 0.09	−0.513 ± 0.69
20–79	1,065	0.800 ± 0.19	−0.452 ± 0.95	915	0.829 ± 0.13	−0.484 ± 1.01
Femur (Ward's triangle)						
20–29	226	0.949 ± 0.18	0.00 ± 1.0	206	1 058 ± 0.20	0.00 ± 1.0
30–39	243	0.846 ± 0.13	−0.605 ± 0.71	110	0.931 ± 0.19	−0.599 ± 1.07
40–49	276	0.794 ± 0.17	−0 898 ± 0.94	221	0 753 ± 0.14	−1.610 ± 0.79
50–59	143	0.662 ± 0.12	−1.634 ± 0.61	154	0.759 ± 0.13	−1.577 ± 0.71
60–69	102	0 548 ± 0.11	−2.272 ± 0.61	117	0 691 ± 0.16	−1.961 ± 0.91
70–79	75	0.481 ± 0.04	−2.648 ± 0.21	107	0.722 ± 0.12	−1 788 ± 0 70
20–79	1,065	0.800 ± 0.19	−1.65 ± 0.58	915	0.831 ± 0.21	−1.369 ± 1.19
Femoral neck						
20–29	226	0.963 ± 0.16	0.00 ± 1.0	206	1.045 ± 0.20	−0.059 ± 1.24
30–39	243	0.934 ± 0.10	−0.427 ± 0.68	110	1.049 ± 0.15	−0.027 ± 0.92
40–49	276	0.916 ± 0.13	−0.552 ± 0.89	221	0 983 ± 0.13	−1.06 ± 0.82
50–59	143	0.829 ± 0.11	−1.134 ± 0.74	154	0.942 ± 0.14	−0.698 ± 0.86
60–69	102	0.733 ± 0.12	−1.779 ± 0.77	117	0.892 ± 0.13	−1.009 ± 0.83
70–79	75	0.696 ± 0.03	−2.026 ± 0.19	107	0.908 ± 0.11	−0.913 ± 0.72
20–79	1,065	0.901 ± 0.15	−1.156 ± 0.99	915	0 951 ± 0.17	−0.642 ± 1.03

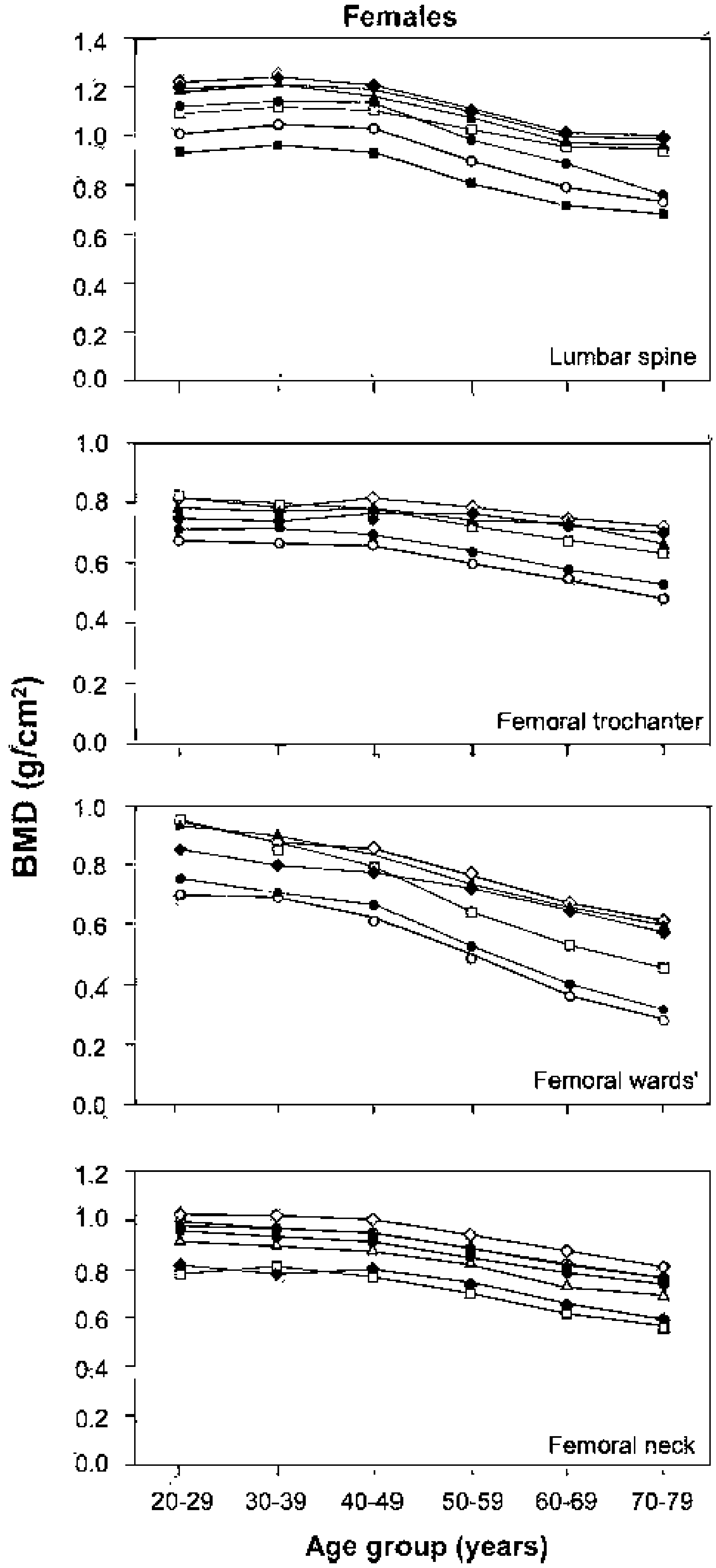

Fig. 1 The age change in BMD of lumbar spine, trochanter, Ward's triangle, and femoral neck in Saudi females *(solid diamond)* as compared to Lebanese [34] *(open diamond)*, US [11, 27] *(solid triangle)*, Kuwaitis [37] *(open square)*, northern Europe [28, 29, 30, 31, 32, 33, 34, 35] *(solid circle)*, Japanese [38] *(open circle)*, and Chinese [39] *(solid square)* females

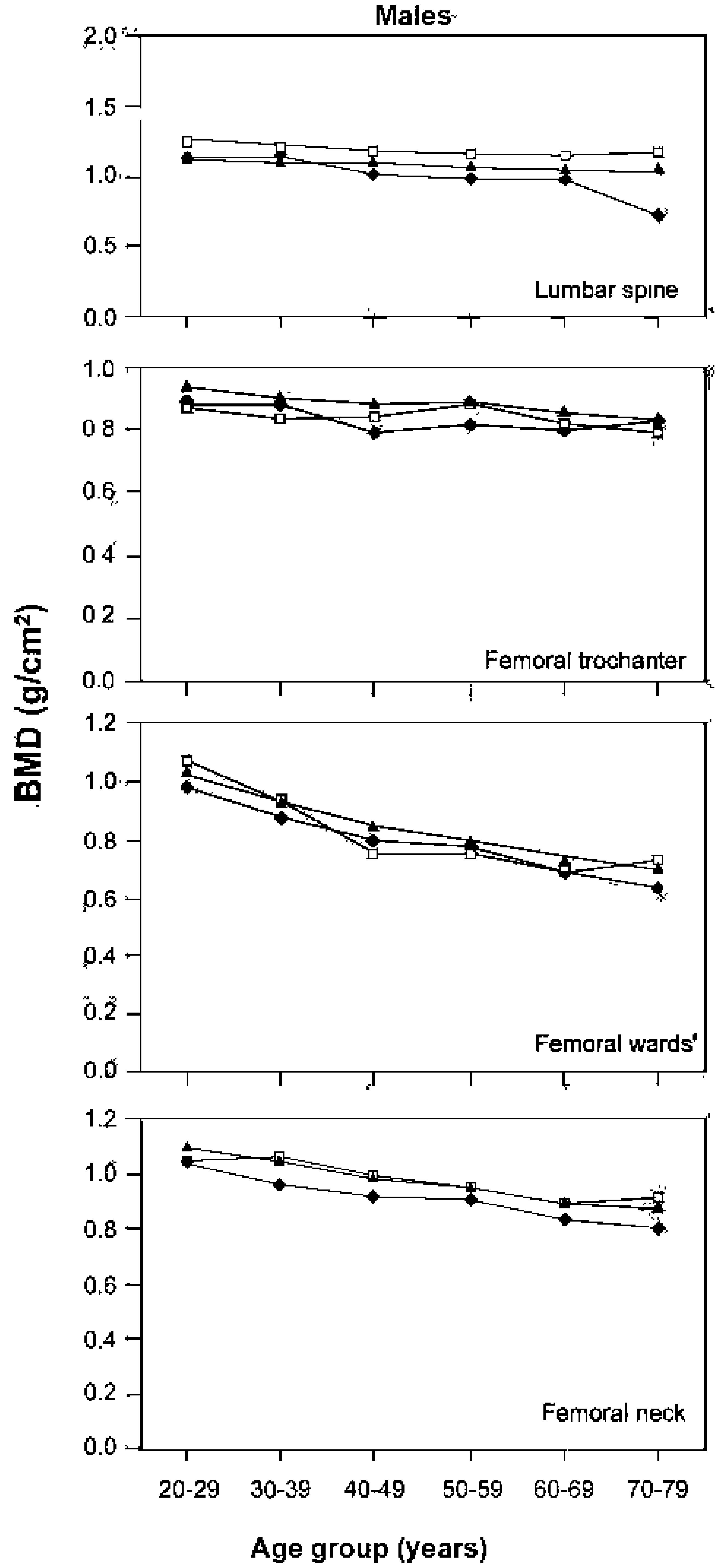

Fig. 2 The age change in BMD of lumbar spine, trochanter, Ward's triangle, and femoral neck in Saudi males *(solid diamond)* as compared to US/European [28, 29, 30, 31, 32, 33, 34, 35] *(open square)*, and Lebanese [36] *(solid triangle)* males

trochanter. In females of 50 to 79 years of age, significant decreases (% per year) in femoral BMD subregions were observed: neck (0.7%), Ward's triangle (0.9%), and trochanter (0.5%), respectively. Significant changes were also evident in the lumbar spine (0.3% per year) and femur BMD subregions (% per year): neck (0 7%), Ward's triangle (1 4%), and trochanter (0 4%), in males between 20 and 49 years of age, respectively. Males of 50 to 79 years, exhibited significant decreases in lumbar spine BMD (0.8% per year) and 0.2% per year in both the femoral neck and Ward's triangle with no significant changes in femoral trochanter

The influence of age, height, and body weight on the BMD results was examined by regression analysis (Tables 5, 6, 7, and 8) The effects of age, weight and

Table 3 Pearson correlation coefficient of bone mineral density (BMD) at different skeletal sites with age, BMI, and WHR in males studied

	Age	BMI	WHR	Spine (L2–L4)	Femur (total)	Femur (trochanter)	Femur (neck)	Femur (Ward's triangle)
Age	-							
BMI	0.19**	-						
WHR	0.65**	0.33**	-					
Spine (L2–L4)	−0.50**	0.23**	−0.25**	-				
Femur (total)	−0.25**	0.49**	−0.12**	0.42**	-			
Femur (trochanter)	−0.19**	0.54*	−0.05	0.86**	0.86**	-		
Femur (neck)	−0.32**	0.41**	−0.11*	0.41**	0.87**	0.90**	-	
Femur (Ward's triangle)	−0.57**	0.28**	−0.38**	0.84**	0.84**	0.83**	0.92**	-

Statistically significant at $*P < 0.05$; $**P < 0.001$

Table 4 Pearson correlation coefficient of bone mineral density (BMD) at different skeletal sites with age, BMI, and WHR in females studied

	Age	BMI	WHR	Spine (L2–L4)	Femur (total)	Femur (trochanter)	Femur (neck)	Femur (Ward's triangle)
Age	-							
BMI	0.42**	-						
WHR	0.44**	0.32**	-					
Spine (L2–L4)	−0.48**	0.19*	−0.15**	-				
Femur (total)	−0.33**	0.09*	−0.01	0.72**	-			
Femur (trochanter)	−0.36**	0.09*	−0.03	0.66**	0.92**	-		
Femur (neck)	−0.49**	0.04	−0.11**	0.71**	0.89**	0.88**	-	
Femur (Ward's triangle)	−0.65**	−0.11*	−0.24**	0.72**	0.83**	0.83**	0.93**	-

Statistically significant at $*P < 0.05$; $**P < 0.001$

Table 5 Regression of BMD for spine ($n = 745$) and femur ($n = 745$) regions on age, weight and height in females age 20–49 years

Region	Regression equation	r^2	P
Spine (L2–L4)	1.117–0.000 Age	0.002	NS
Femur (neck)	1.019–0.003 Age	0.144	0.002
Femur (Ward's triangle)	1.120–0.007 Age	0.358	0.000
Femur (trochanter)	0.808–000 Age	0.035	NS
Spine (L2–L4)	0.901 + 0.004 Weight	0.286	0.000
Femur (neck)	0.694 + 0.004 Weight	0.304	0.000
Femur (Ward's triangle)	0.709 + 0.026 Weight	0.148	0.002
Femur (trochanter)	0.547 + 0.004 Weight	0.302	0.000
Spine (L2–L4)	0.571 + 0.003 Height	0.183	0.000
Femur (neck)	−0.051 + 0.006 Height	0.317	0.000
Femur (Ward's triangle)	−0.146 + 0.006 Height	0.253	0.000
Femur (trochanter)	0.037 + 0.005 Height	0.241	0.000
Spine (L2–L4)	0.928–0.002 Age + 0.004 Weight + 0.000 Height	0.307	0.000
Femur (neck)	0.303–0.004 Age + 0.005 Weight + 0.003 Height	0.437	0.000
Femur (Ward's triangle)	0.466–0.010 Age + 0.005 Weight + 0.003 Height	0.480	0.000
Femur (trochanter)	0.294–0.002 Age + 0.004 Weight + 0.002 Height	0.354	0.000

height on BMD for Saudi females are presented in Table 5 (age group 20–49 years) and Table 6 (age group 50–79 years). Tables 7 (age group 20–49 years) and 8 (age group 50–79 years) show the effects of age, weight, and height on BMD of the corresponding age-matched Saudi males. The lumbar spine BMD in females exhibited increases from 0.4% to 0.9% per kilogram of body weight; whereas, in males, lumbar spine BMD increased from 0.3% to 0.7% per kilogram of body weight. Femoral subregions, however, showed significant increases in both males (per kg) (neck 0.7% to 0.8%, Ward's triangle 0.5% to 0.7%, and trochanter 0.6%) and females (per kg) (neck 0.4% to 0.9%, Ward's triangle 0.2% to 0.9%, and trochanter 0.4% to 0.7%). In both males and females studied, height was a predictor of BMD, however, using stepwise multiple regressions that included both weight and height, the former had about 2–4 times greater effect on BMD than the latter. In addition, BMI was a significant predictor of BMD at all sites examined in both males and females (results not shown). Moreover, WHR was found to be a predictor of lumbar spine BMD in males (age group 20–49 years) and in both males and

Table 6 Regression of BMD for spine ($n = 378$) and femur ($n = 378$) regions on age, weight, and height in females age 50–79 years

Region	Regression equation	r	P
Spine (L2–L4)	1.111–0.008 Age	0.518	0.000
Femur (neck)	1.163–0.007 Age	0.456	0.000
Femur (Ward's triangle)	1.124–0.009 Age	0.573	0.000
Femur (trochanter)	0.969–0.005 Age	0.400	0.000
Spine (L2–L4)	0.303 + 0.009 Weight	0.398	0.000
Femur (neck)	0.238 + 0.009 Weight	0.510	0.000
Femur (Ward's triangle)	0.024 + 0.009 Weight	0.498	0.000
Femur (trochanter)	0.242 + 0.007 Weight	0.459	0.000
Spine (L2–L4)	−1.97 + 0.014 Height	0.441	0.000
Femur (neck)	−0.334 + 0.007 Height	0.370	0.000
Femur (Ward's triangle)	−0.542 + 0.007 Height	0.349	0.000
Femur (trochanter)	0.370 + 0.007 Height	0.393	0.000
Spine (L2–L4)	0.064–0.007 Age + 0.000 Weight + 0.008 Height	0.573	0.001
Femur (neck)	0.626–0.004 Age + 0.007 Weight – 0.000 Height	0.584	0.000
Femur (Ward's triangle)	0.639–0.007 Age + 0.006 Weight – 0.000 Height	0.648	0.000
Femur (trochanter)	0.537–0.003 Age + 0.005 Weight – 0.000 Height	0.520	0.000

Table 7 Regression of BMD for spine ($n = 537$) and femur ($n = 537$) regions on age, weight, and height in males age 20–49 years

Region	Regression equation	r	P
Spine (L2–L4)	1.273–0.003 Age	0.263	0.001
Femur (neck)	1.220–0.007 Age	0.398	0.000
Femur (Ward's triangle)	1.359–0.014 Age	0.605	0.000
Femur (trochanter)	0.968–0.004 Age	0.257	0.000
Spine (L2–L4)	0.874 + 0.003 Weight	0.270	0.000
Femur (neck)	0.536 + 0.007 Weight	0.505	0.000
Femur (Ward's triangle)	0.598 + 0.005 Weight	0.279	0.000
Femur (trochanter)	0.470 + 0.006 Weight	0.540	0.000
Spine (L2–L4)	0.631 + 0.003 Height	0.139	0.004
Femur (neck)	−0.245 + 0.008 Height	0.327	0.000
Femur (Ward's triangle)	0.333 + 0.005 Height	0.122	0.012
Femur (trochanter)	−0.043 + 0.005 Height	0.299	0.000
Spine (L2–L4)	1.014–0.009 Age + 0.005 Weight + 0.000 Height	0.572	0.000
Femur (neck)	0.739–0.012 Age + 0.010 Weight + 0.000 Height	0.812	0.000
Femur (Ward's triangle)	1.439–0.018 Age + 0.011 Weight – 0.004 Height	0.822	0.000
Femur (trochanter)	1.135–0.007 Age + 0.009 Weight – 0.004 Height	0.748	0.000

Table 8 Regression of BMD for spine ($n = 378$) and femur ($n = 378$) regions on age, weight, and height in males age 50–79 years

Region	Regression equation	r	P
Spine (L2–L4)	1.477–0.008 Age	0.404	0.000
Femur (neck)	1.027–0.002 Age	0.131	0.030
Femur (Ward's triangle)	0.867–0.002 Age	0.156	0.009
Femur (trochanter)	0.758–0.001 Age	0.083	NS
Spine (L2–L4)	0.456 + 0.007 Weight	0.353	0.000
Femur (neck)	0.379 + 0.008 Weight	0.591	0.000
Femur (Ward's triangle)	0.229 + 0.007 Weight	0.516	0.000
Femur (trochanter)	0.403 + 0.006 Weight	0.600	0.000
Spine (L2–L4)	−0.546 + 0.009 Height	0.305	0.000
Femur (neck)	−0.383 + 0.008 Height	0.420	0.000
Femur (Ward's triangle)	−0.379 + 0.007 Height	0.337	0.000
Femur (trochanter)	0.001 + 0.005 Height	0.349	0.000
Spine (L2–L4)	1.004–0.008 Age + 0.007 Weight + 0.000 Height	0.544	0.000
Femur (neck)	0.525–0.003 Age + 0.088 Weight – 0.000 Height	0.621	0.000
Femur (Ward's triangle)	0.904–0.004 Age + 0.009 Weight – 0.004 Height	0.569	0.000
Femur (trochanter)	0.668–0.001 Age + 0.007 Weight – 0.002 Height	0.609	0.000

females (age group 50–79 years). Also WHR predicted femoral trochanter in males (age group 50–79 years) and females (age group 20–79 years) (results not shown)

The T-scores indicate the deviation of BMD from the mean BMD of a young healthy reference population and are therefore widely used for testing for osteopenia and osteoporosis (see "Methods"). Using the mean BMD of the <35 year-old group of the Saudis studied, T-scores were calculated (Table 2) and the percentage of subjects presenting with BMD indicative of osteopenia (T-score between −1 and −2.5) or osteoporosis (T-score <−2.5), differed substantially depending on using the lumbar

Table 9 Prevalence of osteopenia and osteoporosis in Saudis (≥50 years), using US/European and Saudi reference data. Data are presented as percentages with osteopenia (> −2.5 SD to < −1 SD below young adult BMD) and osteoporosis (< −2.5 SD below young adult BMD), for spine (L2–L4) and femur (total)

	Females		Males	
	US/European reference	Saudi reference	US/European reference	Saudi reference
Spine (L2–L4)				
Osteopenia	39.1%	42.2%	32.8%	19 1%
Osteoporosis	47.7%	30.5%	38.3%	49.6%
Femur (total)				
Osteopenia	57.0%	58.6%	32.3%	56.7%
Osteoporosis	7.8%	4.7%	6.3%	1.2%
Either (spine or femur)				
Osteopenia	41.4%	43.4%	46.5%	54.1%
Osteoporosis	44.5%	28.2%	33.2%	37 8%

Table 10 Anthropometric measurement, BMD spine and femur with corresponding *T*-score values stratified by body weight quartiles and sex in Saudis. Results are presented as means ± SD. *T*-scores are based on manufacturer's reference values. *M* male, *F* female, *BMI* body mass index, *WHR* waist-to-hip ratio

	Sex (M/F)	Quartile			
		1	2	3	4
Age (years)	M	60.7 ± 8.7	63.5 ± 9.3	67.2 ± 6.0	62.9 ± 7.9
	F	62.2 ± 4.2	65.1 ± 8.8	58.7 ± 7.3	55.3 ± 4.3
Weight (kg)	M	51.7 ± 4.1	65.7 ± 3.2	72.9 ± 0.4	80.7 ± 2.6
	F	48.1 ± 4.2	56.9 ± 1.7	63.1 ± 1.5	69 9 ± 3.7
BMI (kg/m^2)	M	20.9 ± 1.9	24.9 ± 1.4	26.8 ± 1 7	27.7 ± 1.1
	F	22.1 ± 2.4	25.8 ± 1.7	27.6 ± 1.0	28.6 ± 0.8
WHR	M	0.935 ± 0.042	0.971 ± 0.062	0.984 ± 0.024	0.997 ± 0.048
	F	0.917 ± 0.079	0.851 ± 0.103	0.855 ± 0.082	0.871 ± 0.080
Spine (L2–L4) (g/cm^2)	M	0.859 ± 0.096	0.865 ± 0.147	0.954 ± 0.248	1.064 ± 0.258
	F	0.867 ± 0.116	0.858 ± 0.123	0.892 ± 0.189	1.054 ± 0.186
T-score spine	M	−2.80 ± 0.39	−2.03 ± 1.29	−0.873 ± 0.592	−0.563 ± 1.28
	F	−2.81 ± 0.96	−2.53 ± 0.71	−2.20 ± 1.56	−1.23 ± 1.49
Femur (total) (g/cm^2)	M	0.880 ± 0.128	0.956 ± 0.110	0.943 ± 0.093	1.065 ± 0.089
	F	0.796 ± 0.087	0.798 ± 0.074	0.842 ± 0.147	0.969 ± 0.149
T-score femur	M	−1 66 ± 0.97	−1.13 ± 0.718	−0.833 ± 0 824	−0.158 ± 0.679
	F	−1.73 ± 0.75	−1.66 ± 0.61	−1.29 ± 1.21	−0.331 ± 1.120

spine or the femur (total) data (see Table 9) In Saudis, more females were defined as osteoporotic using the manufacturer's reference data as compared with that of the Saudi reference data (Table 9) The prevalence of osteoporosis at the lumbar spine using the manufacturer's reference data was 47.7%, as compared to 30 5% using the current Saudi reference data ($P < 0.000$) Similar differences were observed for the femur (total) 7 8% and 4 7% of the females were considered osteoporotic using manufacturer's and Saudi reference data, respectively ($P < 0.000$). (Table 10)

Since, there is no widely accepted definition of osteoporosis in males, we used the WHO criteria for testing for osteoporosis in the female population. The prevalence of osteoporosis at the lumbar spine in males at 50–79 years of age was 38 3% and 49 6% using the manufacturer's and the current Saudi reference data, respectively (Table 9). Differences were also evident for testing for osteoporosis at the femur (total): 6.3% and 1.2% of the males were osteoporotic using the manufacturer's and the Saudi reference data, respectively ($P < 0.000$) (Table 9)

T-scores were calculated according to body weight quartiles for Saudis of both sexes (Table 11). The heaviest subjects exhibited significantly higher *T*-scores than those for the thinnest subjects, with much higher prevalence of osteoporosis in the latter than the corresponding former subjects (see Table 11)

Table 11 The proportion of Saudis aged ≥50 years with lower than −2.5 SD, stratified by body weight quartiles and sex

Body weight quartile	Females ($n = 142$)	Males ($n = 125$)
1	25.6%	15.5%
2	18.1%	15.9%
3	1.5%	1.6%
4	0.0%	0.8%

Discussion

The present study is considered to be the first large-scale report on reference values on the BMD of the lumbar spine and the femur (including subregions of trochanter, Ward's triangle, and neck) in randomly selected healthy ambulatory Saudis of both sexes of various age groups (20–79 years) with defined exclusion criteria The changes in lumbar spine and femur BMD values with age in Saudis showed a similar pattern to that previously reported for US [11, 27], northern European [28, 29, 30, 31, 32, 33, 34, 35], and Lebanese [36] reference values The mean values for the lumbar spine BMD in both sexes of Saudis were lower than those reported previously for US and northern European populations [11, 27, 28, 29, 30, 31, 32, 33, 34, 35], and Kuwaitis [37], but similar to those reported for Lebanese males (except lower in the age groups 40–79 years) and females (except lower in the age groups 60–79 years) [36]. The mean BMD values for trochanter, Ward's triangle, and femoral neck subregions were similar to those reported for the US [11, 27] and northern Europe [28, 29, 30, 31, 32, 33, 34, 35], and higher than those of Lebanese [36] over the age range 20–49 years; but then, lower values than those for the US, northern European, and Lebanese populations were evident over the age range of 50–79 years However, Saudi females showed higher values for the lumbar spine and the femoral subregions than the corresponding Japanese [38] and Chinese [39] females (age 20–79 years). The mean values for femoral neck BMD in Saudi males were higher than the corresponding values reported for Lebanese [36], but were similar to those reported in US and northern European data [11, 27, 28, 29, 30, 31, 32, 33, 34, 35]. Saudi males showed similar values for Ward's triangle to those of US and northern European males [11, 26, 27, 28, 29, 30, 31, 32, 33, 34] However, lower femoral trochanter BMD values over the age group 40–69 years were evident in Saudi males as compared with the corresponding values in US, northern European and Lebanese males, but values similar to those of US and northern European males were achieved by the age group 70–79 years [11, 27, 28, 29, 30, 31, 32, 33, 34, 35].

Age-related bone loss follows different patterns in each site of the Saudis studied. For the lumbar spine, we observed little loss in young males (age 20–49 years), but a slight loss (0 3% per year) in the corresponding age-matched females, and a greater loss of 0.8% per year in older males and females (age 50–79 years). The three femoral subregions exhibited different rates of bone loss according to age in the Saudis studied. In females, Ward's triangle showed the greatest rate and the trochanter the lowest rate of bone loss Similarly, Saudi males showed the greatest rate of bone loss in Ward's triangle with a slight loss at the trochanter These findings are consistent with significantly negative correlations observed between BMD and age in both sexes (Tables 3 and 4). Although in Saudis studied, significant positive correlations between BMD values from different sites were observed; nevertheless, Ward's triangle and the femoral neck in both sexes, together with the lumbar spine, appeared to be the most sensitive skeletal sites for the detection of age-related bone loss in the population examined. These findings are consistent with those reported previously by Burger et al. [35], Kudlacek et al. [40], and others [11, 36]. Furthermore, longitudinal studies on the rate of bone loss at the lumbar spine and the femoral subregions have been published for American [41, 42], Australian [43, 44], and European [45] cohorts Among late postmenopausal and elderly Caucasian females, estimates of annual rates of bone loss at femoral subregions were 0.32–0.95% (total), 0 36–1 14% (trochanter), 0.35–0.96% (neck) [41, 42, 43, 44, 45] In males, fewer data are available; however, in Caucasian males, the annual rates of bone loss at femoral neck ranged from 0.06% to 0.82% [43, 44] In addition, data on the rates for femoral and lumbar spine loss ranged from 0.39% per year to gains of 0.94% per year, and for males there was a gain at the spine of 0 56% per year [45]. In this connection, methodological aspects of BMD measurement should be taken into consideration in the interpretation of DXA data: elderly subjects, who are shorter than young ones may have smaller bones, which augments spuriously the age-related decrease in BMD and tall subjects may have greater vertebral bodies, particularly ventrodorsal This will influence the measurements in that direction, so that smaller and thinner subjects may be diagnosed to be more osteoporotic [46] Technical difficulties in performing DXA are more common in the elderly, and measurement errors may be higher in this group problems with patient positioning, patients' inability to remain motionless for the duration of the scan, and the presence of radiopaque implants in the measurement areas, most commonly in the hip, are further sources of inaccuracy [47]. Further, at the lumbar spine, the increase of variability depends on the presence of osteophytes, aortic calcifications, reactive and degenerative disk diseases, and osteoarthritis which will falsely record an inaccurate increase in BMD values [48, 49, 50, 51] Additional causes of inaccuracy in DXA data are the inability to straighten the lumbar spine or internally rotate the thigh of an examined subject [47]. Another source of error is the known differences in the rates of loss of bone mineral content from different skeletal sites [52], so that the mean differences will differ according to different sites measured.

Several studies have shown that body weight correlates positively with BMD in both sexes [11, 19, 36, 40, 53, 54, 55], which is concurrent with the findings in the present study. Moreover, consistent with previous reports, BMI was found to positively correlate with BMD in both sexes [36, 40, 53]. In fact, increasing weight and BMI are known to be associated with higher bone density [23, 24, 25, 26, 27], and both lean and fat body masses appear to affect bone density in most such studies. However, low body weight was a significant risk factor for hip fracture in black [56] and Japanese [57] as well as in Caucasian females [58, 59, 60] Mechanisms for this relationship include diminished sex hormone–binding globulin levels that increase free sex steroid levels in obese females [23], and weight loss acting as a marker of illness and fragility [61]. In this connection, it is important to know the limitations of BMD measurements using DXA in obese subjects, particularly if the measurements are complicated by significant weight change BMD values correlated positively with body fat mass and BMD of the spine will thus be underestimated if the amount of overlying fat of the spinal column is higher than that on either side of the lumbar spine [62, 63]. Reid et al reported that a mean fat thickness difference of 2 cm resulted in a BMD error of 9–10% [62], this reached a value as high as 16% in other studies [63] However, in a small study by Tothill and Pye [64], changes in fat distribution during weight loss were independent of changes in spinal BMD measurement In the present study, in Saudis, body weight was the strongest predictor of both femoral and lumbar spine BMD values (Tables 5, 6, 7, and 8) which is similar to previous studies, in both males [33, 53, 54] and females [29, 55, 56]. However, using stepwise multiple regression analysis including both weight and height, the former had about 2–4 times greater effect on BMD than the latter. Body weight profoundly influenced the percentage of subjects with osteoporosis Males (age ≥50 years) in the lower body weight quartile exhibited almost 19-fold higher frequency of low BMD with a *T*-score value below −2.5 SD as compared to the corresponding age-matched males (age ≥50 years) in the highest body weight quartile (Table 11). Similarly, females (age ≥50 years) in the lowest body weight quartile exhibited a 25.6% prevalence of osteoporosis as compared to no osteoporosis in the corresponding age-matched females (age ≥50 years) in the highest body weight quartile (Table 11) These observations are similar to those reported previously in US females [11], but contrast with those reports which suggested that body weight had a slight influence [65, 66]. However, other studies have indicated that postmenopausal bone loss is minimal in overweight females, and enhanced in the corresponding thinnest females [66, 67]. Moreover, analysis of body weight quartiles showed that the *T*-scores in the lowest quartile were more than 1 SD lower than the corresponding *T*-scores of the highest quartile in both males and females ($P < 0.000$). These findings confirm the importance of considering body weight in the evaluation of patients in relation to the diagnosis of osteoporosis In this connection, body weight in both males and females could be used in providing guidance to asymptomatic individuals: indeed, studies in postmenopausal females have suggested that females weighing under 60 kg (as in the present study, i.e., the lowest quartile) would be a potential candidate for BMD measurement, even in the absence of other risk factors [26, 68]

The BMD values obtained in the present study were examined in relation to the prevalence of osteopenia and osteoporosis It must be emphasized, however, that the present study was cross-sectional with no data specifically related to fracture risk. Moreover, there is unfortunately no detailed information on the rate or types of fractures in Saudis or in other populations in the Gulf region, and future work is urgently needed in this connection. Reference BMD values should include both healthy young and older subjects in order to determine the peak BMD, and, consequently, so that an accurate estimate of the prevalence of osteopenia and osteoporosis in the population can be determined [69] In practice, reference ranges have been chosen variously from adults aged 20–29 or 20–39 years, and at the age of 50 years, which will influence the apparent prevalence of osteoporosis [5, 70, 71]. Reference BMD values are now available for many populations including Dutch [72], British [73, 74], German [75], French [76], American [77], and Australian [78, 79], and several other European populations [80, 81] Indeed, in the present study, the reference values for BMD in the young Saudis were identified to be in the age range of 20–35 years (i.e., ≤ 35 years). Thus, the *T*-scores were calculated accordingly as described in "Methods" and presented in Table 2. The results of the present study strongly support the notion that population-based variations in BMD values exist [82], which enforces the need to establish local reference BMD values for each population to allow correct interpretation of DXA measurements This is best illustrated by the results of the present study (see Table 9), which show the wide discrepancies in the percentage of Saudis (age ≥50 years) classified with osteopenia or osteoporosis, when data from the manufacturer's database or our current Saudi data were used for the calculation of *T*-scores. This is clearly seen when DXA data are converted to *T*-scores for BMD at the lumbar spine and the femur (Table 2): for example, the use of the manufacturer's reference values would classify 44 5% females with osteoporosis, as compared with only 28 2% when the Saudi reference values were used, thus overdiagnosing Saudi females with osteoporosis. In addition, fewer Saudi males (age ≥50 years) would be classified as osteoporotic based on the use of the manufacturer's reference values than the corresponding Saudi values (33 2% vs 37.8%), thus underdiagnosing Saudi males with osteoporosis. The cause(s) of high prevalence of osteoporosis in male Saudis as compared to other studies [83] is under investigation, but genetic, nutritional, endocrine, life-style, and environmental factors [83] could be involved; further studies are needed in this connection In addition minor differences in the reference data can have important effects on patient classification; indeed, Ahmed et al [5] applied two different normative data sets to their study data and found a twofold difference in the prevalence of osteoporosis (6% vs 15%). Moreover, previous studies have reported an inappropriately high incidence of osteoporosis when the *T*-scores were based on the manufacturer's reference data in various populations examined, including Spanish [17], Turkish [15], British [8], Greek [81], Lebanese [36], and Austrian [40] populations

In conclusion, the present study shows that Saudis of both sexes exhibited similar trends in the rates of bone loss in the lumbar spine and femoral subregions (trochanter, Ward's triangle, and neck) to that observed in Caucasians and Lebanese. However, Saudis showed lower BMD values at the lumbar spine and femoral subregions than the corresponding Caucasian reference values particularly in the older age group (50–79 years), but higher values than those reported for

Japanese and Chinese females Body weight was a significant predictor of BMD at all skeletal sites examined and was more important than height in multiple regression analysis The BMD values obtained in the present study resulted in higher prevalence of osteopenia (in both males and females) and osteoporosis (in females), but lower prevalence of osteoporosis in males according to WHO criteria if the manufacturer's reference values rather than Saudi reference values were used. The overdiagnosis (in females) and the underdiagnosis (in males) of the prevalence of osteoporosis in Saudis have obvious clinical implications for therapeutic intervention and prevention strategies. These variations in BMD values among different populations necessitate the use of local reference ranges for reliable and accurate interpretations of the individual DXA data Such information is essential if BMD data are used to predict fracture risks [80, 84], to avoid unnecessary patient anxiety or errors in diagnosis and hence treatment. Accordingly, a nationwide standardization of BMD measurements by DXA through the appropriate use of population-specific reference values is recommended to improve the quality of medical care provided in relation to the prevention and treatment of Saudis who are at risk of osteoporosis or are already osteoporotic

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