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Comparison of Bone Mineral Density in Isfahani Women with other Populations: The Impact on Diagnosis of Using Different Normal Ranges

[1]M.R. Salamat, [1]M.B. Tavakoli, [2]M. Salehi, [3]E. Pishva, [4]A.H. Salari and [5]F. Tabesh
[1]Department of Medical Physics, Isfahan University of Medical Sciences, Isfahan, Iran
[2]Department of Genetics and Molecular Biology,
Isfahan University of Medical Sciences, Isfahan, Iran
[3]Department of Microbiology, Isfahan University of Medical Sciences, Tehran, Iran
[4]Unit of Rheumatology Research, Tehran University of Medical Sciences, Tehran, Iran
[5]Faculty of Medicine, Isfahan University of Medical Sciences, Isfahan, Iran

Abstract: Bone Mineral Density (BMD) of 359 healthy Isfahani women aged 23-60 years were compared with the Caucasian's, Tehranis and some Arab women. BMD was determined using dual energy X-ray absorptiometry (DXA) at the lumbar spine and proximal femur. Age related changes in BMD were similar to those described in Lebanese and Saudis for the femur, Lebanese having the lowest femur BMD. However, the age related values for the spine were similar for all populations, having the lowest BMD values for the Isfahani women. The problem of using manufacture provided reference data was investigated. In fact using the manufacture provided reference data for the femoral neck diagnosed ouly 14.9% of the postmenopausal women as normal due to improper use of T-score, while using the Isfahan normative data 41.9% of the postmenopausal women were diagnosed as normal. The normative peak BMD values acquired for Iranian women in Isfahan and Tehran were different, in particular for the spine. The normative BMD values in Isfahan were ouly acquired for the young women. Therefore, for the management of patients, determining the secondary causes of osteoporosis (Z-scores<-2) it is highly recommended to establish the normal range for the entire age range of 20-80 years normal women and make further investigations to find the reason(s) for the discrepancies in the normal BMD ranges of women in Iran.

Key words: Bone mineral density, dual energy X-ray absorptiometry, osteoporosis

INTRODUCTION

Osteoporosis is a chronic disease that involves a reduction in bone strength and an increased risk of fracture. Bone Mineral Density (BMD) is highly correlated with bone strength, accounting for 75-85% of the variances in the bone tissue strength (Mazess, 1982). BMD, measured by dual energy X-ray absorptiometry (DXA), can establish the diagnosis of osteoporosis before the first fracture has occurred. BMD, a key determinant of bone strength, predicts fracture risk in a powerful manner. In age-adjusted proportioual hazard models, a Standard Deviation (SD) decrease in femoral neck BMD showed a 49% increase in fracture in white women (Cauley *et al*., 2005).

Osteoporosis is a worldwide problem among postmenopausal women (Salehi *et al*., 2008; Demir *et al*., 2008; Pongchaiyakul *et al*., 2006; Löfman *et al*., 2000). In the UK, 1/3 of women and 1/12 of men affected from osteoporosis (Byers *et al*., 2001). The investigations showed that in the next 50 years, considering the population growth in the old people in Asia, South America and Africa, it

Corresponding Author: Salamat Mohammad Reza, Department of Medical Physics,
Isfahan University of Medical Sciences, Isfahan, Iran

is expected almost 75% of these fractures occur in progressing countries (Genant *et al*., 1999). A study, that recently performed in Iran showed osteoporotic fracture data was important public health problem in Iran (Abolhasani, 2004).

Commercial DXA scanners contain sets of BMD reference data for different populations, although these databases may not be consistent due to the relatively small numbers of measurements taken on women in the young normal range (Binkley *et al*., 2005; Kiebzak *et al*., 2007). These reference data allow a patient's BMD measurement to be compared with the expected peak bone mass of a young normal of the same sex and ethnicity (referred to as T-score) and to the mean age-matched value for the normative population (called Z-score) (Kanis, 1994; Kin *et al*., 1991). The World Health Organization (WHO) has established diagnostic criteria for osteoporosis based on T-scores and not BMD values (Kanis, 1994). These criteria define osteoporosis in terms of a T-score below -2.5, i.e., BMD at a skeletal site more than 2.5 SD below the young adult mean for that population. This definition depends on having a set of BMD reference data (Mean±SD) for each skeletal site for the particular reference population. T-score can be easily adjusted upwards or downwards if an inappropriate reference population is chosen. In fact, it has been recommended that the improper use of T-scores has probably resulted in the misdiagnosis of over 1 million patients in the period 1989-1997 in USA alone (Mazess, 1997).

The aim of this study was to determine the misdiagnosis due to use of reference BMD values of the young women in the manufactures data base for the femur/spine (Salamat *et al*., 2006, 2007), underestimation/overestimation of the T-scores and compare it with the young normal sets acquired in Iran (Sayed Bonakdar *et al*., 2005; Larijani *et al*., 2005). Also to compare the BMD values acquired in this study with the other populations.

MATERIALS AND METHODS

A total of 359 healthy Isfahani women consisting of 185 premenopausal and 174 postmenopausal were measured. All referred patients fill a questioner about earlier sicknesses and drug use, gynecological history, nutritional habits, physical activity, education level and other life-style habits. The selected women had no parental history of hip fracture, were not cigarette smokers, with no body weight less than 57 kg, not used oral corticosteroids longer than 3 months, had no serious long-term conditions to increase fracture risk, such as hyperthyroidism or malabsorption and had no known history of diseases and were not on Hormone Replacement Therapy (HRT) before or after the menopause. The subjects had no osteoarthritis, scoliosis, or other bone deformities. The following groups were also excluded: (1) hysterectomized women (for whom it was not possible to define menopausal status) and bilaterally ovariectomized women, (2) women with diseases or medications known to affect bone metabolism, as described by Kröger *et al*. (1994). Postmenopausal women were defined as those who had their menstrual period at least one year before the scan date, having the clinical definition of the menopause (Hulka and Meirik, 1996).

The referred subjects had BMD measurements for the lumbar spine (L2-L4) and proximal left femur, using a Norland DXA total body bone scanner (Norland XR46, Atkinson USA). The measurements were performed at Isfahan Osteoporosis Diagnosis Centre. Heights and weights were measured before the scans were taken. Body Mass Index (BMI) was calculated as kilogram per square meter. The long-term reproducibility (coefficient of variation) of the DXA scanner for BMD measurements during the study period was assessed, using the phantom provided by the manufacturer. Student t-test was used to find if the difference between the means of the spine and femoral neck BMDs for pre and postmenopausal women were significant. The present study data and the data acquired from other populations such as Caucasians (Mazess and Barden, 1999), Kuwait (Dougherty and Marzouk, 2001), Lebanon (Maalouf *et al*., 2000), Morocco (El Maghraoui *et al*., 2006), Qatar (Hammoudeh *et al*., 2005), Saudi (El Desouki, 1995) and Tehran (Larijani *et al*., 2005) were compared.

RESULTS

The mean height, weight and BMI of the premenopausal women were slightly higher than the postmenopausal women (Table 1). The mean values for the height, weight and BMI of the premenopausal women for the same age groups were slightly higher than the postmenopausal women; the BMI of both pre and postmenopausal women slightly increased with age (Table 2). BMD decrease with age for the lumbar spine and femoral neck are presented in Table 3. The spine BMD decreases with age for both pre and postmenopausal females. However, the femoral neck decreases from the 3rd age decade group to 4th age decade group and then increases to the 5th age decade group and decreases again. Independent t-test results at the 0.05 level on different sites for the pre and postmenopausal women showed that for the 5th age decade group there were significant differences between the two means of spine, troch, femur neck and total femur ($p \leq 0.02$). However, the difference for the 6th age decade group was only significant for the spine BMD ($p<0.05$).

Figure 1 shows plots of spine and femur against age for Iranian and Arab countries as a function of age. The Fig. 1 exhibits that Isfahani women had a similar trend of decrease in spine BMD with age to Tehranis and Saudis. However, the BMD of spine for Isfahanis was lower than other countries. Figure 1 demonstrates that the Lebanese had the smallest femur BMD values for all age groups. Table 4 shows BMDs and T-scores, using Norland manufacturer provided reference values i.e., Caucasian young peak BMD and Isfahani young peak BMD of the spine and femoral neck for studied subjects. Table 4 reveals that using the manufacturer's data base the spine T-score is substantially

Table 1: Characteristics of study population

Characteristics	Premenopausal women (N = 185)	Postmenopausal women (N = 174)
Age (year)	37.2±7.8	51.8±4.5
Height (cm)	157.4±5.6	156.3±5.7
Weight (kg)	70.0±11.3	65.8±5.5
BMI (kg m^{-2})*	28.4±4.4	27.0±1.8

Results are expressed as Mean±SD. BMI: Bone Mass Index

Table 2: Height, weight and body mass index in pre and postmenopausal women by age groups

Age group	Premenopausal				Postmenopausal			
(year)	N	Height (cm)	Weight (kg)	BMI (kg m^{-2})	N	Height (cm)	Weight (kg)	BMI (kg m^{-2})
20-29	9	162.5±3.3	67.4±12.7	25.5±4.4				
30-39	19	159.3±3.3	65.8±10.2	26.0±4.5				
40-49	85	157.1±5.7	71.0±10.8	28.7±4.2	53	155.8±5.7	64.9±4.9	26.7±1.8
50-60	72	155.6±4.9	70.3±11.8	29.0±4.4	121	156.1±5.8	66.2±5.7	27.2±1.8

Table 3: BMD (g cm^{-2}) decrease with age for the lumbar spine and femoral neck

Age group	Premenopausal					Postmenopausal		
(year)	N	L2-L4	Femoral neck	Troch	Total Femur	N	L2-L4	Femoral neck
20-29	9	1.085±0.09	0.913±0.13	0.680±0.10	0.929±0.11			
30-39	19	1.059±0.14	0.869±0.14	0.683±0.10	0.914±0.11			
40-49	85	1.042±0.15	0.899±0.13	0.720±0.11	0.965±0.12	53	0.950±0.17	0.831
50-60	72	0.958±0.17	0.803±0.12	0.659±0.11	0.901±0.12	121	0.913±0.14	0.809

Table 4: BMDs and T-scores, using Norland manufacturer provided reference value i.e., [1]Caucasian young peak BMD and [2]Isfahani young peak BMD of the spine and femoral neck for pre and postmenopausal women

	Premenopausal women (N = 185)			Postmenopausal women (N = 174)			
Region	BMD (g cm^{-2})	[1]T-score	[2]T-score	BMD (g cm^{-2})	[1]T-score	[2]T-score	Δ
L2-L4	1.012±0.161	-0.551±0.99	-1.450±1.19	0.919±0.140	-1.13±0.92	-2.11±1.12	-9.2
FN	0.859±0.136	-1.090±1.17	-0.683±1.14	0.816±0.119	-1.46±1.01	-1.05±0.99	-5.0

Results are Mean±SD; Δ: Percent difference between pre and post menopause BMD; L2-L4: Lumbar spine; FN: Femoral neck

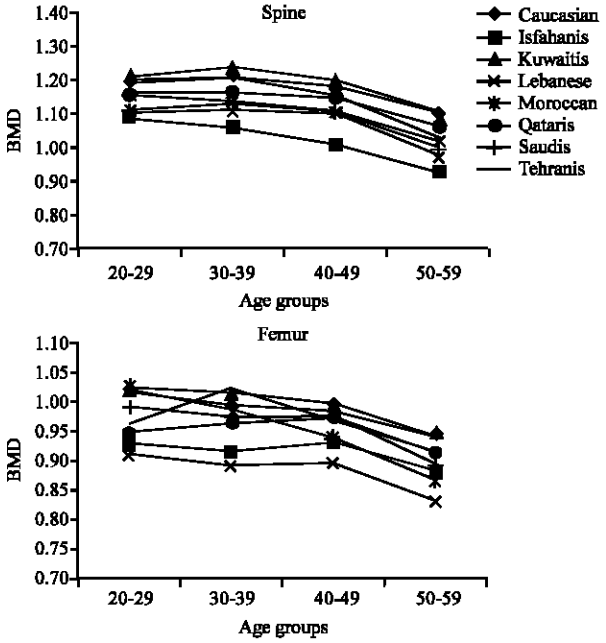

Fig. 1: BMD (g cm^{-2}) of Iranian women at the spine and femur compared with Caucasian and some Arab women

Table 5: Classification of postmenopausal women according to the WHO criteria, using the manufacturer provided reference data and Isfahani normative young peak normal

	Manufacturer provided reference data, N (%)						Isfahani normative young peak normal, N (%)					
	Normal		Osteopenic		Osteoporotic		Normal		Osteopenic		Osteoporotic	
Region	N	%	N	%	N	%	N	%	N	%	N	%
L2-L4	78	44.8	87	50.0	9	5.2	52	29.9	97	55.7	25	14.4
FN	26	14.9	79	45.4	69	39.7	73	41.9	96	55.2	5	2.9

Columns show the number and percent of women for each classification, respectively

higher than the Isfahan normative reference data. However, the case for the femoral neck is totally different, i.e., using the manufacturer data base showed substantially lower femoral neck T-score. This overestimation/underestimation was found for both groups of subjects. The difference between the BMD of spine and femoral neck for the pre and postmenopausal subjects were -9.2 and -5.0%, respectively. Table 5 classifies postmenopausal women according to the WHO criteria using the manufacturer provided reference data and Isfahan normative young peak normal (Sayed Bonakdar *et al*., 2005). Table 5 shows that using the manufacturer reference data overestimates the normal subjects for the spine and underestimates the normal subjects for the femoral neck.

DISCUSSION

The purpose of bone density measurement is to identify patients suffering from osteoporosis, to predict the risk of fracture, detect small changes in bone density and monitor treatment. The achievements of these aims require the bone densitometry system to be accurate and precise and the BMD of a suitable reference range is used. Normal reference range has a crucial role since the determination of T-score is based on it, diagnosing a person as a normal, osteopenic or osteoporotic.

Age related bone loss follows a different trend depending upon a particular site and gender. In this study, we found for the femur a slight bone loss for the age group 20-29 to 30-39 years, a slight gain from the age group 30-39 to 40-49 years. This latter could be probably due to osteoarthritis, aorta calcification and degenerative facet sclerosis often existing at this age. Then after the age 50 years a sharp decline in BMD. Present results are consistent with the findings of Lebanese and Saudis (Maalouf *et al*., 2000; El Desouki, 1995). The femur BMD of Lebanese women was the lowest, compared to the Iranian women or other Arab nations. However, the spine BMD of the Isfahanis women had the lowest BMD values, with a negative slope in the entire BMD v age graph.

Results of DXA scanners are expressed in terms of BMD, T- and Z-scores. Ideally a person scanned with different DXA systems should have similar BMD and uniquely classified as normal, osteopenic or osteoporotic. However, this is not true. The differences in various system calibration and image analysis algorithms have been solved either using equations converting BMD of one equipment to another or using a similar phantom and expressing BMD in standardized values (sBMD) (Genant *et al*., 1994; Dequeker *et al*., 1995; Tothill *et al*., 1995). However, the problem of using different normal ranges still exists. Some publications have proposed the use of local data, while others found that those provided by the manufactures are well suited with their national data (Ryan *et al*., 1993; Simmons *et al*., 1995; Lehman *et al*., 1995). The differences among different normal ranges can be attributed to both real deviations from the peak bone mass due to life styles and genetic characteristics as well as to the method of normal subject selection (Lunt *et al*., 1997; Yu *et al*., 1999). Therefore, subjects of such studies should randomly be selected so that best represent a population, should be free of any illness or taking any medication affecting bone metabolism, cosseting a large population. In this study, women were randomly selected from all social classes from all women referred, having no risk factor for osteoporosis.

Comparing our own normal female range (Sayed Bonakdar *et al*., 2005) with the manufactures data base normal range made a substantial difference in the estimation of subjects classified as normal, osteopenic or osteoporotic according to WHO classification (Kanis *et al*., 1994). This proved the impact on diagnosis of using various normal ranges for comparison. In fact using the manufacture provided reference data for the femoral neck diagnosed 85.1% of the subjects as osteopenic or osteoporotic, while using the Isfahan normative data ouly 58.1% of the subjects were diagnosed as osteopenic or osteoporotic. For the spine the diagnosis was reversed, i.e., using the manufacturer provided reference data 45% of the subjects were found as normal, while using present normative data 30% of subjects were found normal. The Lebanese normal range is closer to present data and can be used as diagnosis based on at least T-score is concerned; however, there is a small difference in Z-scores which influences patient's management.

The normative peak BMD values acquired for Iranian women in Isfahan (Sayed Bonakdar *et al*., 2005) and Tehran (Larijani *et al*., 2005) were different, in particular for the spine. Isfahani women had significantly lower BMD at the spine (10.4%) and femur (3.6%) at the age of 20 years. The difference increased as the age increased, which might be due to the difference in life style, level of physical activities, coffee and tea consumption, use of inadequate vitamins in particular vitamin D and nutritional habits. The normative BMD values in Isfahan were only acquired for the young women. Therefore, for the management of patients, determining the secondary causes of osteoporosis (Z-scores<-2) it is strongly recommended to make further investigations to find the reason(s) for the discrepancies in the normal BMD ranges.

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