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Ethnic Differences in Bone Mass and Vitamin D status in Young Women Living in the UK

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ABSTRACT

The connection between bone geometry and ethnicity has yet to be fully researched, especially as it relates to 25-hydroxyvitamin D (25(OH)D. This preliminary study aimed to investigate differences in bone geometry specifically at the radius and tibia, as well as in 25(OH)D concentrations, between Saudi (S), Pakistani (P), and Caucasian (C) premenopausal women. A further aim was an examination of a possible link between 25(OH)D concentration and indices of bone geometry. Seventy-two healthy premenopausal women (22 S, 23 P, and 27 C), aged ≥18 years, were evaluated for volumetric bone mineral density and 25(OH)D concentration. At the 4% radius, Saudi women had a lower BMC, as well as a smaller total bone area and trabecular area than Caucasian women. At the 4% tibia, Saudi women had a lower total vBMD than did Pakistani women. Serum 25(OH)D levels in Saudi (36.5(22.4)) and Pakistani (31.4(16.8)) women were significantly lower than in Caucasian (81.9(20.0)) ($p<0.05$). There were no statistically significant correlations between 25(OH)D status and pQCT bone variables in any of the three ethnic groups. This study suggests a possible need for attention to bone health in premenopausal Saudi women as well as improvement in vitamin D levels in Saudi and Pakistani populations.

Key words: *Bone mineral density, 25-hydroxyvitamin D, pQCT, Ethnicity, Premenopausal women*

INTRODUCTION

The term vitamin D is a misnomer. Although widely referred to as a vitamin, it is a pro-hormone produced in the skin when exposed to the sun. Dietary intake can also provide vitamin D in lower amounts. Vitamin D plays an important role not only in metabolizing calcium and promoting healthy bones but also in immunomodulation and anti-proliferation, which affects immune and cellular health [1]. Besides its well-known association with rickets and osteomalacia, vitamin D deficiency has thus been linked to an extensive range of other health conditions [1, 2]. The prevention of vitamin D deficiency is therefore of key importance, but there is cause for alarm as low levels of vitamin D are seen across the world. While deficiencies are not surprising in extreme northern or southern regions with little sunlight for portions of the year, thereby limiting the skin's production of vitamin D, what is surprising is that these deficiencies are also found in regions with plenty of sunshine year-round [3, 4].

A good example of this mismatch between the amount of sunshine and vitamin D levels comes from the Middle East, where 25-hydroxy-vitamin D (25(OH)D) concentrations are among the lowest in the world [5, 6]. In Saudi Arabia, vitamin D deficiency has been reported in all age groups, from newborns up to the elderly, in both men and women [7]. A systematic review of 13 studies conducted in Saudi Arabia and published from 2011 to 2016 indicated a pooled prevalence of vitamin D deficiency (< 50 nmol/l) of 81.0 % (95 % CI: 68.0 %–90.0 %) [7].

Although the Arabian Gulf region is characterized by sunshine for most of the year, its residents, especially women, still have low levels of vitamin D due to reduced exposure to the sun. Decreased exposure to sunlight may be attributed to the overly hot climate and clothing covering the skin. This is compounded by a lack of food

fortification with calcium and vitamin D, and low consumption of naturally rich sources of vitamin D, such as oily fish, leading to vitamin D deficiency. There is a dearth of published data on the 25(OH)D status of Saudi women living in high latitude western countries, where latitude may be an additional factor in their already elevated risk of deficiency because of reduced skin exposure to sunlight, modest style of dress, and little dietary vitamin D intake [8].

Vitamin D deficiency is a known risk factor for poor bone health. Previous studies have confirmed that young healthy Saudi females have a low bone mineral density (BMD), likely due in part to insufficient calcium intake and insufficient sun exposure [9, 10]. In another study, Saudi women were shown to have lower BMD compared to their US counterparts, which the authors suggested was likely due to more pregnancies and longer periods of lactation alongside vitamin D deficiency [11]. In terms of other Middle Eastern countries, the spinal BMD values of Qatari women were similar to those of Saudi women but lower than those of Caucasians [12]. Another study found no differences in BMD between Kuwaiti and Caucasian women at the lumbar spine and proximal femur [13].

The prevalence of vitamin D deficiency is especially high in certain ethnic populations in western nations, such as Blacks and people of Middle Eastern and South Asian descent [14]. However, 25(OH)D status in these populations has not been investigated until recently.

To date, few studies have looked in detail at other aspects of bone health beyond BMD in Pakistani women, with none assessing tibial peripheral quantitative computer tomography (pQCT) in premenopausal women in this ethnic group and none assessing either radial or tibial pQCT in any age group in Saudi women. An understanding of bone geometry in Pakistani and Saudi premenopausal women is key to recognizing risk factors for fracture in these groups, as well as enhancing diagnosis and therapy for osteoporosis in later life. The present study assesses ethnic differences in pQCT-derived bone variables in Saudi (S), Pakistani (P), and European Caucasian (C) premenopausal women living in the United Kingdom (UK). It also investigates serum 25(OH)D status in these ethnicities and examines a possible link between pQCT-derived bone variables and 25(OH)D status.

The few studies that have measured bone health in South Asians living in the West have indicated that BMD disparities between Caucasian and South Asian premenopausal women could be due simply to differences in bone size [15]. However, one study, using peripheral quantitative computer tomography (pQCT) in postmenopausal women, identified poorer bone strength in those from South Asia, based on a 20% decrease in polar Strength Strain Index (SSIp) and a 40% reduction in predicted fracture load (under bending), compared to Caucasian women [16]. Similarly, another investigation using pQCT showed a greater medullary and radial cross-sectional area but lower volumetric bone mineral content (BMC), volumetric bone mineral density (vBMD), cortical thickness, and cortical area in South Asian premenopausal women than European women in the same age group [17]; these differences were not accounted for by variations in body size due to ethnicity. However, a different study comparing women of South Asian descent to their Caucasian counterparts found similar radial vBMD [18], demonstrating inconsistencies in the published literature.

MATERIALS AND METHODS

Study population

The cohort from the first D-FINES study was re-invited in the summer of 2012 to participate in further investigations, including re-assessment of 25(OH)D levels, anthropometrics, and pQCT measurement of the radius and tibia. Letters inviting all premenopausal women to participate again in the study were sent, and a total of 50 pre-menopausal healthy females were recruited to the new study (n=27 Caucasian and n=23 Pakistani).

In the summer of 2013, premenopausal Saudi women were recruited from local universities in London and elsewhere in the south of England and underwent the same measurements and tests as the Caucasian and Pakistani women had in 2012. The Saudi women had lived in the UK for at least two years before the study. Ethical approval was given by the University of Surrey Research Ethics Committee. Written, informed consent was given by all participants, and all research was conducted following the Declaration of Helsinki. A total of 22 Saudi women were included in the new study.

Study measures and methodology

Serum concentrations of 25(OH)D were measured by the SupraRegional Assay Laboratory, Manchester as previously described in detail [19].

Bone indices were measured using a Stratec Medizintechnik GmbH XCT2000L bone densitometer scanner. Radiation regulations at the local and national levels were met, and all investigators were sufficiently trained in

radiation techniques before they operated the scanner. pQCT measurements were taken at two sites of the non-dominant radius (the 4% distal radius and the 66% diaphyseal radius) and three sites of the non-dominant tibia (the 4% distal tibia, 14% diaphyseal tibia, and 38% mid-shaft tibia).
The predicted fracture load was calculated by the software using the following equation:

$$F_B = \frac{4\sigma_B \times SSI}{l} \quad (1)$$

FB= Fracture load [N]; σB= Ultimate load = 180 Mpa; l = distance between supports

The strength strain index was calculated as:

$$SSI = \sum_{i=1}^{n} \left(\left(r_i^2 \times a \times CD \right) / r_{max} \times ND \right) \quad (2)$$

CD=measured cortical density (mg/cm^2); ND=normal physiological density (1200mg/cm^3) (taken from: Stratec manual 6/11/9 Man62e.doc)
For each radial or tibial scan, the total radiation dose was under 2 microsieverts (μSv). Weekly calibration of the pQCT machine was carried out by a quality control phantom.

Statistical analysis
All statistical analyses were carried out using SPSS 23 (SPSS Inc., Chicago, US). Ethnic variations in pQCT bone indices and serum 25(OH)D status was evaluated using One-Way Analysis of Variance (ANOVA). Any pQCT variable which showed statistically significant ethnic differences during ANOVA testing underwent further analysis of covariance (ANCOVA) to control for the possible confounding effects of age, BMI, and height. This was done as two ANCOVA models, the first for age and BMI, and the second for age and height. BMI and height were not put in the same model due to the known strong correlation between these two variables. Associations between 25(OH)D and pQCT bone variables were calculated using Spearman's Rho correlation due to the abnormal distribution of 25(OH)D. Partial correlations, controlling for key confounders, were not undertaken as no results from the Spearman's Rho analyses were statistically significant. Bonferroni correction was used to adjust the initial P value cut-off (P≤0.05) to account for multiple testing.

RESULTS AND DISCUSSION

Participant baseline characteristics
Seventy-two women (n=22 S, n=23 P, and n=27 C) took part in the study. All results are presented as mean (SD) unless stated otherwise. The Saudi women were significantly younger (by 11–15 years) than the Pakistani and Caucasian women (S: 26(5); P: 41(8), and C: 37(5); p<0.001). Caucasian women were significantly taller (by 7 cm) than women in the other two groups (C: 166(6) cm; S: 160(6) cm and P: 160(5) cm; p<0.001). However, weight and BMI did not differ significantly among the ethnic groups **(Table 1)**, although the Saudi and Pakistani groups were classified as overweight on average (BMI 26–29 kg/m^2), with the mean BMI in the Caucasian group being at the top of the normal range (18–25 kg/m^2).

Table 1. Demographic, anthropometric & functional measurements among the ethnic groups

	S (n=22)	P (n=23)	C (n= 27)	*P*
Age (years)≠	25.88[4.80]^a	41.22[8.38]^b	36.55[4.68]^b	<0.001
Weight (kg)≠	68.53[27.36]	71.67[13.93]	67.59[10.59]	0.767
Height (cm)≠	159.47[6.25]^b	159.50[4.78]^b	166.41[5.93]^a	<0.001
BMI (kg/m2)≠	27.45[13.73]	28.20[5.53]	24.46[3.90]	0.337
Normal n(%)	11(64.7)	7(38.9)	12(54.5)	-
Overweight n(%)	2(11.8)	4(22.2)	8(36.4)	-
Obese n(%)	2(11.8)	5(27.8)	1(4.5)	-

Mean [SD]; ≠One-way ANOVA (Tukey test, subset for alpha=0.05). S=Saudi, P=Pakistani, C=Caucasian. Like superscripts indicate statistically significant differences.

Differences in pQCT bone indices between ethnic women groups
Table 2 shows the results for pQCT bone indices and ANOVA results at the 4% and 66% radius among the three ethnic groups. After Bonferroni adjustment for multiple testing, using a revised cut-off for P of ≤0.002 (21 tests

for radius), only ethnic differences in BMC, total area and trabecular area at the 4% radius remained statistically significant. The Caucasians had higher BMC, total area, and trabecular area in comparison with Saudi and Pakistani women, but Tukey's post-hoc tests established that the only statistically significant differences were between Saudi and Caucasian women. There were no statistically significant ethnic differences for any variables at the 66% radius. Following age and BMI adjustments, ANCOVA showed that the ethnic difference for 4% radius BMC (P=0.001), total area (P=0.001), and trabecular area (P=0.001) maintained its statistical significance. Similarly, following adjustment for age and height, the ethnic difference for 4% radius total area (P=0.001) and trabecular area (P=0.001) remained statistically significant, but the difference for BMC (P=0.004) did not.

Table 2. pQCT bone indices at the radius among Saudis, Pakistanis, and Caucasians

		S (n=22)	P (n=23)[b]	C (n=27)	*P* value≠
4% radius	**BMC (g/cm)**	1.0(0.2)[a]	1.1(0.2)	1.17(0.1)[a]	0.001
	Total Area (mm^2)	320.9(47.8)[a]	344.5(34.5)	374.8 (43.3)[a]	0.001
	Total vBMD (mg/cm^3)	303.1(48.8)	312.7(46.9)	315.7(45.4)	0.70
	Trabecular density (mg/cm^3)	171.5(30.7)	175.8(38.2)	179.0(35.5)	0.81
	Trabecular Area (mm^2)	144.3(21.5)[a]	154.9(15.5)	168.5(19.5)[a]	0.001
	Trabecular Area as % of Total Area	53.4	51.0	47.7	-
66% radius	**BMC (g/cm)**	1.0(0.1)	1.0(0.2)	1.2(0.5)	0.10
	SSIPOL (mm^3)	192.7(50.5)	218.4(69.1)	357.6(339.5)	0.04
	Total Area (mm^2)	136.0(17.8)	131.5(22.9)	165.3(88.2)	0.135
	Total vBMD (mg/cm^3)	710.8(63.5)	771.1(87.8)	746.6(86.3)	0.10
	Cortical Area (mm^2)	65.0(11.9)[a]	73.2(17.2)	83.4(29.4)[a]	0.04
	Cortical density (mg/cm^3)	1114.1(46.6)	1124.9(43.3)	1134.8(38.5)	0.33
	Cortical Thickness (mm)	1.8(0.3)[ab]	2.2(0.5)[a]	2.2(0.3)[b]	0.009
	Fracture Load X (N)	407.6(121.7)	436.3(145.1)	773.5(922.9)	0.10
	Fracture Load Y (N)	463.5(96.5)	521.5(169.9)	772.2(663.8)	0.06
	PERI C (mm)	41.2(2.7)	40.5(3.5)	44.5(9.8)	0.13
	Cortical Area as a % of Total Area	47.8	55.7	50.6	-

≠One-way ANOVA (Tukey test, subset for alpha=0.05). Data expressed as the mean (SD); Abbreviations: BMC, Volumetric Bone Mineral content) SSIPOL=Polar strength-strain index, PERI C, periosteal circumference. ENDO C, endosteal circumference, S=Saudi, P=Pakistani, C=Caucasian. pQCT=Peripheral quantitative computed tomography. N=newtons. Like superscripts indicate statistically significant differences.

Table 3 illustrates results for the tibial pQCT bone indices (4%, 14%, and 38% sites) and ANOVA results among the three ethnic groups. After Bonferroni adjustment for multiple testing, using a revised cut-off for P of ≤0.002 (25 tests for tibia), only ethnic differences in total vBMD at the 4% tibia remained statistically significant, with Tukey's post-hoc tests showing a statistically significant difference in total vBMD between the Saudi and Pakistani women only (S had only 82% of the total vBMD of SA). ANCOVA confirmed that the ethnic difference in total vBMD remained statistically significant after controlling for BMI and age (P=0.001, n=20 S, n=19 SA, n=26 C) as well as for height and age (P=0.002, n=20 S, n=19 SA, n=26 C).

Table 3. pQCT bone indices at the Tibia site among Saudis, Pakistanis, and Caucasians

		S (n=22)	P (n=23)	C (n=27)	*P* value≠
pQCT 4% tibia	**BMC (g/cm)**	2.7(0.5)[a]	3.3(0.6)[b]	3.2(0.5)[b]	0.003
	Total Area (mm^2)	958.1(140.1)	970.0(157.6)	1071.2(140.7)	0.045
	Total vBMD (mg/cm^3)	281.0(32.6)[b]	345.9(55.0)[a]	303.3(31.8)[b]	<0.001
	Trabecular Area (mm^2)	431.0(63.0)	436.4(71.0)	481.9(63.3)	0.045
	Trabecular density (mg/cm^3)	206.6(36.4)[b]	275.9(68.4)[a]	228.7(29.2)[b]	0.001
	Trabecular Area as a % of Total Area	45.0	45.0	45.0	-

pQCT 14% tibia	**BMC (g/cm)**	1.9(0.5)[a]	2.2(0.4)	2.3(0.4)[b]	0.014
	SSIPOL (mm^3)	1031.1(415.1)[a]	1273.2(308.0)	1330.4(328.6)[b]	0.046
	Total Area (mm^2)	368.6(122.0)[a]	469.7(84.5)[b]	421.9(92.6)	0.037
	Total vBMD (mg/cm^3)	549.5(127.1)	495.1(95.8)	571.6(117.4)	0.179
	Cortical Area (mm^2)	126.5(33.2)[a]	139.9(36.4)	156.5(29.0)[b]	0.029
	Cortical density (mg/cm^3)	1142.4(18.9)[b]	1092.1(67.3)[a]	1135.6(24.5)[b]	0.003
	Cortical thickness (mm)	2.1(0.2)[b]	2.0(0.6)[b]	2.5(0.4)[a]	0.013
	PERI C (mm)	66.6(14.1)	76.5(7.1)	72.1(9.9)	0.063
	Cortical Area as a % of Total Area	34.3	29.8	37.1	-
pQCT 38% tibia	**BMC (g/cm)**	2.7(0.8)[a]	3.0(0.5)	3.3(0.7)[b]	0.042
	SSIPOL (mm^3)	1095.0(402.3)[a]	1193.5(325.3)	1402.5(362.6)[b]	0.046
	Total Area (mm^2)	9408.0(1607.9)	9659.3(1890.3)	9981.2(1529.6)	0.132
	Total vBMD (mg/cm^3)	859.2(64.9)	860.3(87.6)	903.5(76.9)	0.150
	Cortical Area (mm^2)	206.0(62.2)[a]	238.4(49.9)	255.7(54.0)[b]	0.038
	Cortical density (mg/cm^3)	1188.0(26.1)	1158.0(54.4)	1179.8(19.4)	0.064
	Cortical thickness (mm)	4.1(0.9)[b]	4.5(0.8)	4.9(0.8)[a]	0.030
	Fracture Load X (N)	2477.1(908.1)	2861.8(845.7)	3135.8(786.6)	0.079
	Fracture Load Y (N)	2276.6(908.9)	2463.7(663.4)	2798.1(780.6)	0.148
	PERI C (mm)	61.8(10.7)	67.1(7.5)	67.3(8.3)	0.166
	Cortical Area as a % of Total Area	2.2	2.5	2.6	-

≠One-way ANOVA for posthoc (Tukey test, subset for alpha=0.05). Data expressed as the mean (SD); Abbreviations: BMC Volumetric Bone Mineral Content, SSIPOL=Polar strength-strain index, PERI C, periosteal circumference. S=Saudi, P=Pakistani, C=Caucasian. pQCT=Peripheral quantitative computed tomography. N=newtons. Like superscripts indicate statistically significant differences.

25(OH)D concentration

Differences in the participants' 25(OH)D levels could be grouped according to three cut-off points. At the lowest level, with 25(OH)D<25nmol/L, were 33% of Saudis, 29% of Pakistanis, and 0% of Caucasians. In the next cut-off group, with 25(OH)D<50nmol/L, were 73% of S, 88% of SA, and 0% of C. Finally, 93% of Saudis, 94% of Pakistanis, and 42% of Caucasians had a 25(OH)D status of <75nmol/L, with 4.5% of Saudis, 4.6% of Pakistanis, and 58.0% of Caucasians showing 25(OH)D levels of ≥75nmol/L. On average, Pakistani women had the lowest level of 25(OH)D (31.4 (16.8) nmol/L, n=23) followed by Saudi women (36.5 (22.4) nmol/L, n=22), with both groups being classified on average as insufficient (<50nmol/L). The highest 25(OH)D concentrations were recorded in the Caucasian women, who were classified as sufficient (≥ 50nmol/L) on average (mean 25(OH)D 81.9 (20.0) nmol/L, n=27). One-way ANOVA showed a statistically significant difference in 25(OH)D between the three groups (P<0.001). Tukey's post-hoc tests confirmed that Caucasian women had significantly greater 25(OH)D concentrations than their peers in both Saudi and Pakistani ethnic groups (P<0.05) by 45.4nmol/L and 50.5nmol/L respectively, but there were no other group differences that reached statistical significance.

Association between pQCT indices and 25(OH)D within ethnic women groups

Table 4 shows the full details of Spearman's Rho correlations between all pQCT indices and 25(OH)D status in each ethnicity. After Bonferroni adjustment for multiple testing, using a revised cut-off for P of ≤0.0005 (108 tests), no statistically significant correlations were found between 25(OH)D level and any bone parameter at either the radius or tibia, within any ethnic group.

Table 4. Spearman's Rho correlations for the relationship between 25(OH)D and bone indices

	S (n=22)		**P (n=23)**		**C (n=27)**	
Parameter	**r**	**p**	**r**	**p**	**r**	**p**
4% Radius						
BMC (g/cm)	-0.273	0.324	-0.096	0.715	-0.142	0.563
Total Area (mm^2)	0.104	0.713	-0.21	0.418	-0.116	0.637
Total vBMD (mg/cm^3)	-0.421	0.118	0.001	0.996	-0.235	0.333
Trabecular Area (mm^2)	-0.218	0.435	0.206	0.428	-0.272	0.260
Trabecular density (mg/cm^3)	0.104	0.713	-0.21	0.418	-0.106	0.665
66% Radius						

BMC (g/cm)	-0.279	0.315	-0.288	0.280	0.319	0.183
SSIPOL (mm^3)	-0.264	0.341	-0.226	0.384	0.293	0.223
Total Area (mm^2)	-0.172	0.541	-0.560	0.019	0.104	0.673
Total vBMD (mg/cm^3)	-0.282	0.308	0.097	0.711	0.168	0.491
Cortical Area (mm^2)	-0.166	0.554	-0.219	0.397	0.16	0.514
Cortical density (mg/cm^3)	-0.221	0.428	-0.005	0.985	0.179	0.464
Cortical thickness (mm)	-0.182	0.516	-0.071	0.786	0.086	0.726
PERI C (mm)	-0.271	0.328	-0.25	0.333	-0.147	0.547
BMC (g/cm)	0.061	0.830	-0.28	0.277	0.344	0.149
SSIPOL (mm^3)	-0.172	0.541	-0.560	0.019	0.104	0.673
4% Tibia						
BMC (g/cm)	-0.566	0.044	-0.074	0.820	0.23	0.358
Total Area (mm^2)	-0.286	0.344	-0.504	0.094	0.063	0.804
Total vBMD (mg/cm^3)	-0.357	0.231	0.434	0.158	-0.104	0.681
Trabecular Area (mm^2)	-0.286	0.344	-0.504	0.094	0.064	0.801
Trabecular density (mg/cm^3)	-0.445	0.128	0.329	0.296	-0.092	0.717
14% Tibia						
BMC (g/cm)	-0.256	0.399	-0.13	0.688	0.128	0.612
SSIPOL (mm^3)	-0.225	0.459	-0.14	0.664	0.115	0.651
Total Area (mm^2)	-0.011	0.972	0.357	0.254	0.117	0.645
Total vBMD (mg/cm^3)	-0.692	0.009	-0.343	0.275	0.015	0.951
Cortical Area (mm^2)	-0.349	0.242	-0.266	0.403	0.175	0.488
Cortical density (mg/cm^3)	-0.302	0.316	-0.203	0.527	0.106	0.675
Cortical thickness (mm)	-0.571	0.041	-0.291	0.359	0.247	0.324
PERI C (mm)	-0.011	0.972	0.357	0.254	0.117	0.645
38% Tibia						
BMC (g/cm)	-0.187	0.541	-0.305	0.336	0.02	0.938
SSIPOL (mm^3)	0.022	0.943	-0.238	0.456	0.22	0.381
Total Area (mm^2)	-0.429	0.144	-0.196	0.541	0.003	0.990
Total vBMD (mg/cm^3)	-0.049	0.873	-0.112	0.729	0.061	0.810
Cortical Area (mm^2)	-0.148	0.629	-0.312	0.324	0.154	0.542
Cortical density (mg/cm^3)	0.187	0.541	0.224	0.484	-0.428	0.076
Cortical thickness (mm)	-0.088	0.775	-0.161	0.617	0.053	0.836
PERI C (mm)	-0.429	0.144	-0.196	0.541	0.003	0.990

S=Saudi, P=Pakistani, C=Caucasian. Abbreviations: BMC Bone Mineral Content, SSIPOL=Polar strength-strain index, PERI C=periosteal circumference

To summarize, the present study found that Saudi women had a smaller BMC, total area, and trabecular area, compared with Caucasian women at the 4% radius, as well as a lower total vBMD than Pakistani women at the 4% tibia. There were no ethnic differences in any of the bone indices at the 14% or 38% tibia sites or the 66% radius site. Saudi and Pakistani women had low 25(OH)D levels compared to their Caucasian peers, with Caucasians having 45–50 nmol/L higher 25(OH)D levels, 2.3 to 2.6 times or 29–33% greater than Saudi and Pakistani women that were vitamin D deficient (25(OH)D <25nmol/L). There was no relationship in this study between 25(OH)D and bone indices, for any bone parameter, in any of the ethnic groups.

At the 4% radius, this finding in Saudi women of a lower BMC, total area, and trabecular area, compared with Caucasian women, is novel as, based on the author's knowledge, there has been no published pQCT data for Saudi women of any age. Total and trabecular areas, as well as BMC, were 85% of that of Caucasian women. These ethnic differences remained after controlling for BMI, height, and age, suggesting that these potential confounders did not explain these results. The one exception was when controlling for age and height, the ethnic difference in BMC was no longer statistically significant, suggesting differences in skeletal size explain the lower radial BMC

in Saudi women. Particularly, there are no differences in density that would render the Saudi women at increased fracture risk, although a smaller skeletal size will in itself reduce bone strength and may increase fracture risk.

No ethnic differences in total radial bone density were observed between any of the three groups, which concurs with the results of Ward *et al*., who found no difference in this parameter between South Asian and Caucasian pre-menopausal women [17]. However, contrary to the previous study, the current study did not find a higher trabecular density in Pakistani than in their Caucasian counterparts [17]. This may be because the previous study had a larger sample size, and their finding was reached only after controlling for a variety of factors including 25(OH)D status, something this study did not do. The present findings are also not in line with those by Zengin *et al*. [20], who studied Black, and South Asian. and Caucasian males, who found smaller radial bone size at the 4% radius, as well as lower cortical thickness and cortical area at the 50% radius in South Asian men compared to Caucasian men. It could be that some ethnic differences are gender specific, but the differences between studies may also be due to the older age (around 60 years) of the men [20]. Finally, the current findings concur with that of the DXA study [11], in that a smaller bone size was found in Saudi women in comparison with Caucasian women.

At the 4% tibia, the present findings were biologically meaningful, with Saudi women having a lower total vBMD than Pakistani women (Saudi values were 82% of those of South Asians). This result is not likely to be due to any differences in BMI, height (skeletal size), or age as these variables were controlled for in a subsequent ANCOVA analysis, and the result remained statistically significant. With no statistically significant vBMD difference found between Saudi and Caucasian women, the present study contradicts the results of a previous study by Ghannam *et al*. [11]. The discrepancy between our two studies could be due to differing methodologies. The current study measured vBMD, which is an indicator of bone density that is independent of bone size, whereas the Ghannam *et al*. [11] study measured aBMD, which appears lower if the skeletal size is smaller, suggesting that their findings may be a function of the smaller bone size of Saudi women compared with Caucasian women. However, these differences could also reflect the difference in sample size between the two studies.

In terms of explaining the reduced tibial vBMD in Saudi women compared with their Pakistani peers, lifestyle could be a contributing factor, particularly since Saudi women in the current study were international university students, whereas the Pakistani women were not. Many of the Pakistani participants were second-generation immigrants to the UK, and so their childhood diet and activity levels are likely to differ from those who were born and raised in Saudi Arabia.

The finding of a lower tibial vBMD in Saudi women is important, since if it is also lower at clinically relevant sites (e.g., hip and spine) then this may raise the risk of osteoporotic fracture in Saudi women relative to Pakistani women. A high-resolution pQCT (HR-pQCT) study found that Caucasian postmenopausal women with a previous fragility fracture had a 3% lower distal tibial vBMD than those without such a fracture [20]. Although the data are not directly comparable, this does suggest that the present finding of a 7% lower vBMD in Saudi than in Pakistani women may be clinically relevant, in that Saudi women may be at higher risk of fragility fractures than Pakistani women in later life.

The present results showing a higher 25(OH)D status in Caucasian women, in comparison with their counterparts of Pakistani and Saudi descent, agree with previous studies that have found that western dwelling Pakistanis are a group at high risk of vitamin deficiency and that their vitamin D status is significantly lower than European Caucasians [16]. The low 25(OH)D levels seen in the Saudi women in this study support other work showing lower 25(OH)D in Arab women in the US [8]. Equally, these findings concur with work showing that young Saudi females are more vitamin D deficient than non-Saudi groups [21].

One major explanation for the lower 25(OH)D levels seen in Pakistani and Saudi women is the lack of sunlight exposure, which stems from traditional norms and beliefs. They may worry about getting tan or having skin damage from the effect of sunlight. Additionally, for reasons of modesty tied to culture and religion, both Saudi and Pakistani women cover most of their skin when they go out of the house, which will limit the endogenous production of vitamin D in the skin. Indeed, previous work found increased UVB exposure in Caucasians compared with South Asian premenopausal women [16], and deliberate avoidance of sun exposure is known amongst South Asian women living in western countries [22]. Another explanation is that Saudi and Pakistani cultures are limited in terms of vitamin D content in traditional foods. There is a lack of research comparing dietary variances in Saudi, South Asian, and Caucasian women, but it is reasonable to speculate that Caucasian women may be more apt to eat vitamin D-rich sources of food (e.g. oily fish, eggs) than South Asian women (who do not traditionally consume a lot of fish) and Saudi women (who also do not eat a diet high in oily fish and eggs).

In the present study, no correlation of any statistical significance was found between any bone parameter and 25(OH)D status, at either the radius or the tibia, in any of the ethnic groups, even those groups with some level of vitamin D deficiency (Saudis and Pakistanis). This lack of correlation between 25(OH)D and total bone density seen in Saudi women agrees with the outcomes of research by Alkhenizan *et al*. [23], on Saudi women living in Riyadh, where no significant correlations between spine or total femoral BMD and serum 25(OH)D were found. It also agrees with the lack of a correlation between 25(OH)D status and spine or hip aBMD, as reported by Ghannam *et al*. [11]. However, the current results do not agree with findings of a weak association between some HR-pQCT variables and 25(OH)D in a Caucasian population [24], or between 25(OH)D status and hip aBMD in South Asians living in South Africa [25]. The results are very inconsistent in the literature, and the link between 25(OH)D and bone indices may vary by a wide range of factors. Alkhenizan *et al*. [23] suggest differences between such studies could be due to geographic differences in climate, environment, and local customs, but more research is needed.

Overall, premenopausal Saudi women may be at higher fragility fracture risk in later life, with some indicators of poorer bone health at the 4% radius and tibia sites, compared to other ethnic groups. Further research is now required into the bone health of Saudi women living in western countries, including the UK, using bigger sample size and a more representative Saudi population. Many Pakistani and Saudi women were deficient in 25(OH)D, and there is a clear need for strategies to improve 25(OH)D status in these groups in the UK. Strategies to increase access to vitamin D food sources could include food fortification, especially if applied to commonly consumed items such as rice and bread. The promotion of vitamin D supplements could also be considered, and where cultural and religious requirements permit, increased consumption of naturally vitamin D-rich foods (e.g., oily fish and eggs).

In terms of strengths and limitations, the present study is the first to examine differences in pQCT assessed bone variables among Saudi premenopausal women and the first to assess pQCT tibia data for Pakistani premenopausal women. Although the sample sizes are relatively small, the number of women was similar across the three groups. The inclusion criteria for the Pakistani and Saudi groups were individuals who had been living in the UK for more than two years, so they had recently been exposed to the same environmental factors (e.g., sunlight availability) as the Caucasian women; however, it should be mentioned that the Saudi women had not lived in the UK longer than four years (the time duration of their university course) and being international university students, they probably came from a more affluent background than their Pakistani and Caucasian counterparts. The Pakistani women were first- and second-generation immigrants, so they may not be representative of other South Asian cultural backgrounds. Most of the Pakistani participants spoke fluent English and lived in areas with a low to moderate index of multiple deprivations, so they may not be characteristic of the entire UK Pakistani female population. Similarly, Saudi women are not likely to be representative of all Saudi women living in the UK, having only lived in the UK for a few years, being of a specific age range, of affluent status, and being able to speak English fluently. More research is needed into the bone health of the more general UK Saudi female population.

Another limitation of this study is that the data were collected in summer, so the measured 25(OH)D status may underrepresent the full degree of vitamin D deficiency seen in the Saudi and Pakistani groups, which likely would be even more severe in winter and spring.

CONCLUSION

Saudi women had lower BMC and smaller total area and trabecular area than Caucasian women at the 4% radius. They also had a lower total vBMD than Pakistani women at 4% tibia, which may be detrimental to bone strength. Pakistani and Saudi women had lower 25(OH)D concentrations than the Caucasian group, with a third of the non-Caucasians being deficient (<25nmol/L). There was no correlation found between 25(OH)D levels and bone indices. The findings regarding lower tibial vBMD in Saudi women suggest a detriment to bone health and call for additional research with a larger study population and within a more representative group of Western-dwelling Saudi women. The low 25(OH)D status in Pakistani and Saudi women is a particular cause of public health concern, and measures are urgently needed to address this issue.

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