Bone mass measurement using quantitative ultrasound in healthy Saudi women

A cross-sectional screening

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ABSTRACT

الأهداف: تقييم مدى انتشار نقص كثافة العظام لدى النساء السعوديات الأصحاء.

الطريقة: تم عمل مسح ميداني لنقص كثافة العظام في منطقة عظمة الكعب عن طريق استخدام جهاز الأشعة فوق الصوتية (Achilles Insight GE, USA) حيث شمل المسح 3269 أنثى في الفئة العمرية لقمة كثافة العظام (PBM) و 3131 أنثى في عمر ما بعد سن اليأس. جميع النساء اللاتي شملهم المسح هم أصحاء ويقطنون المنطقة الشرقية من المملكة العربية السعودية وتمت الدراسة في الفترة مابين يناير 2006 حتى ديسمبر 2007. تم إجراء الدراسة مستشفى جامعة الملك فهد، الخبر، المملكة العربية السعودية.

النتائج: كانت كثافة العظم لدى الفئة العمرية لقمة كثافة العظام طبيعية عند 2090 (63.9%) وأن 791 (24.2%) لديهن نقص تكلس العظام و 388(11.9%) مصابات بمرض هشاشة العظام. وكانت نسبة الإصابة بنقص تكلس العظام لدى النساء العازبات واللواتي يعشن في الحضر أكبرمنها لدى النساء المتزوجات و يعشن في الريف (p<0.01 and p<0.001). كما أن كثافة العظام كانت طبيعية لدى النساء ذوي التعليم الجامعي بنسبة أكبر منها لدى النساء الحاصلات على مستوى تعليم أقل من الثانوية (p<0.01). أما النساء في عمر مابعد سن اليأس PMA فكانت 948 (30.3%) منهن مصابات بنقص تكلس العظام و720 (23%) مصابات بمرض هشاشة العظام. وكانت نسبة الإصابة بنقص تكلس العظام أكبر لدى النساء اللواتي يعشن في الحضر مقارنة بالنساء القاطنات في الأماكن الصناعية أو الريفية (p<0.01) وأن الإصابة بمرض هشاشة العظام أكبر لدى النساء الحاصلات على مستوى تعليم أقل من الابتدائي مقارنة بالنساء الجامعيات (p<0.001).

خاتمة: كانت الإصابة بمرض هشاشة العظام PBM بنسبة 11.9% لدى النساء في سن قمة كثافة العظام PBM ونسبة 23% لدى النساء في سن مابعد اليأس. أما العوامل المؤثرة على خطر الإصابة بنقص تكلس العظام وهشاشة العظام فهي مستوى التعليم لدى الأنثى، والحالة الاجتماعية، عدد الأطفال، ومكان الإقامة.

Objectives: To study the prevalence of osteopenia and osteoporosis in healthy Saudi women, a community-based screening was carried out.

Methods: Three thousand and two hundred sixty-nine women in the young women in peak bone mass (PBM) age group and 3131 in the postmenopausal age (PMA) group were screened using Achilles Insight (GE, USA). Subjects included in the study were healthy and residents of eastern province. The screening was conducted between January 2006 and December 2007. The study took place in King Fahd University Hospital, Al-Khobar, Kingdom of Saudi Arabia.

Results: In the PBM age group, 2090 (63.9%) were normal, 791 (24.2%) were osteopenic and 388 (11.9%) were osteoporotic. Osteopenia was more common in single urban women compared to those who were married and living in rural areas (p<0.01 and p<0.001). Women with college education had significantly normal bone mass than women with less than high school education (p<0.01). In the PMA, 948 (30.3%) were osteopenic and 720 (23%) were osteoporotic. Osteopenic was more common in women in urban areas as compared to industrial and the rural areas (p<0.01). Those women whose education was less than primary had significantly more osteoporosis when compared to women with college education (p<0.001).

Conclusion: In the PBM, 11.9% were osteoporotic and in PMA group 23% were osteoporotic. Factors that influenced the risk for osteopenia and osteoporosis included level of education, number of children, and place of living.

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Osteoporosis is a disease in which the net loss of bone exceeds bone formation and it occurs in women after estrogen loss in postmenopausal age (PMA).[1-3] Postmenopausal osteoporosis (PMO) is a major public health epidemic worldwide. Osteoporosis has been labeled as a silent epidemic, which can be prevented if early interventions are made. Most women with PMO present with a fracture as the first indication of the disease.[4] Careful preventive measures, such as identifying risk factors, early diagnosis by screening methods, and proper management strategies are crucial.[5,6] With better economic conditions and improvement in the health care delivery of Saudi Arabia, the citizens are living longer, which has put them at greatly increased risk of osteoporosis.[7,8] The prevalence of PMO and its related complications in Saudi Arabia is not well established and few structured, studies about PMO in Saudi Arabian women have been reported.[9-12] Based on the reports from previous small studies, we hypothesized that the prevalence of osteoporosis in Saudi females is higher than the other parts of the world.[9,11,12] Studies have demonstrated that quantitative ultrasound (QUS), measurements can discriminate normal subjects from osteoporotic patients and it has ability to predict osteoporotic fracture risk and can be used to identify subjects with a high risk of bone fragility.[13] The present study is undertaken to evaluate the true prevalence of osteopenia and osteoporosis in healthy Saudi Arabian females at peak bone mass (PBM) age and postmenopausal age group from all areas of Eastern Province using quantitative ultrasound of the Calcaneum (Os Calcis).

Methods. The study was based on the measurement of stiffness index (SI) and T-scores for the diagnosis of osteopenia and osteoporosis using QUS, Achilles Insight (GE, USA), which provides images of the calcaneum and measures broadband ultrasound attenuation (BUA) and speed of sound (SOS) values in a circular region. Physicians and nurses were selected and trained for the screening techniques. The screeners were stationed at shopping Malls, health centers in the cities of Dammam, Al-Khobar, Thoqba, Qatif, Saihat and in the Al-Hassa region, and outpatient department of King Fahd Hospital of the University, Al-Khobar, King Fahd Hospital, Al-Hofuf, and Qatif Central Hospital. Women in the PBM age group were also screened at the College of Girls, Dammam and King Faisal University, Dammam and Al-Hassa. Screening was carried out in the period between January 2006 and December 2007. Convenient available sample without randomization was used in this community based cross-sectional survey. The benefits of the screening were explained to the participants and a verbal consent was obtained. The inclusion criteria in the screening program were Saudi women in the age group of 25-35 years (young age; peak bone mass age group) or ≥50 years of age and being postmenopausal, not on medications which affect the bone mass such as steroids or hormonal therapy, having no known diseases, non smokers and resident of eastern province. Women who were already diagnosed to have osteopenia or osteoporosis by WHO criteria and were on therapy were excluded from the study. After the verbal consent, the questionnaire was filled by the screener, which included a brief medical history was obtained, data about marital status, number of children, and abortions, place of birth and place of living, and level of education was obtained and documented. Weight and height were then measured using SECA Model 220, (Germany) and the body mass index (BMI) was calculated. Achilles express calculates SI of the Os calcis using BUA and SOS. The assessment was carried out at the right foot. If the subject had history of fracture or any bony disorder of the right foot then the left foot was used for the study. The QUS devise was calibrated on a daily bases and the measurement was performed in a temperature controlled environment (room temperature) using gel-coupled QUS system. The precision of the instrument was 97% at the time of measurement of the SI and T-scores. Three thousand and two hundred sixty-nine women in the peak bone mass (PBM) age group and 3131 in the postmenopausal age group were screened. The data was entered into the database and analyzed. Women were classified according to the T score, normal if T score is ≥1.0, osteopenic if T score between -1.0 and -1.8, and osteoporotic if T score ≤1.8. The data was calculated for the means and standard deviation to summarize quantitative variables and the percentage for categorical variables. Ordinal logistic regression was employed to determine whether the BMI, marital status, number of pregnancies, level of education and area of residency have an effect on the prevalence of the osteopenia or osteoporosis. The data was analyzed using SPSS (Statistical Package for the Social Sciences),[14] version 14.0, Chicago, Illinois. Statistical significance was taken as p value of <0.05 with confidence interval of 95%. The study was approved by the Research and Ethical Committee of College of Medicine, King Faisal University, Dammam and was funded by King AbdulAziz City for Science and Technology, Riyadh.

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Results. In the PBM age group, 3269 women were screened out of which 2090 (63.9%) were normal, 791 (24.2%) were having osteopenia and 388 (11.9%) were having osteoporosis (**Table 1**). The SI in the normal group was 104.4 versus 79.3 in osteopenic and 64.5 in the osteoporotic women (p<0.001). The average age was 29.2±3.3 years in the normal subjects, 29.5±3.3 years in the osteopenic women, and it was 29.3 years in the osteopenic women. The BMI in the osteopenic females was lower as compared to the normal group (p<0.001). Out of 1123 single women in PBM group, 761 (36%) were normal compared to 64% (1329 out of 2146) who were married. Osteopenia was more common in single women compared to those who are married (p<0.01). The prevalence of osteoporosis in the single and married females in the PBM group was similar. Comparing the place of living between rural, urban, and industrial areas, women who were living in the urban areas had higher prevalence of osteopenia (p<0.001). The prevalence of osteopenia was 19.7% (in the rural population and 24.5% in the urban population. The analysis showed that women with college education had normal bone mass when compared to those with secondary education and primary education (p=0.035). When comparison was made between the groups for osteoporosis; women with college education were less osteoporotic than women with primary or secondary education (p=0.003) (**Table 2**). In the PMA group, 3131 patients were screened.

One thousand and four hundred sixty-three (46.7%) were normal, 948 (30.3%) were osteopenic and 720 (23%) were osteoporotic. The demographic data is given in **Table 3**. The average age of the screened women was 54.16±6.33. Women with osteoporosis were older than those with normal bone mass (56.2 versus 52.8 years) with a p<0.05. There were more osteopenic women in the urban areas as compared to the industrial and the rural areas (p<0.03) (**Table 4**). **Table 5** shows the differences in 3 groups in terms of education. Women with an education of less than primary school had

Table 1 - Demographic data of women in peak bone mass age group (N=3269).

Parameter	Group A normal (n=2090)	Group B osteopenia (n=791)	Group C osteoporosis (n=388)	*P*-value between A and B	*P*-value between A and C
Age (years)	29.2 ± 3.3	29.5 ± 3.3	29.3 ± 3.3	NS	NS
BMI (kg/m^2)	26.9 ± 6.41	25.9 ± 5.61	26.4 ± 6.91	0.002	NS
Stiffness index	104.4 ± 12.8	79.3 ± 4.2	64.5 ± 9.2	0.001	0.001
T- Score	0.1 ± 0.79	≤1.3 ± 0.23	≤2.3 ± 0.59		
Z-Score	0.1 ± 0.82	≤1.3 ± 0.27	≤2.2 ± 0.64		

Data re expressed as mean ± standard deviation. NS - not significant

Table 2 - Osteopenia and osteoporosis related to level of education in peak bone mass age group.

Bone mass	Primary school (n=871)	Secondary school (n=608)	College education (n=1790)	*P*-value
Normal	546	367	1177	0.035
Osteopenia	209	151	431	0.91
Osteoporosis	116	90	182	0.003

Table 3 - Demographic data of women in postmenopausal age group (N=3131).

Parameter	Normal (n=1463)	Osteopenia (n=948)	Osteoporosis (n=720)	*P*-value between A and B	*P*-value between A and C
Age (Years)	52.8 ± 5.2	53.5 ± 5.7	56.2 ± 8.1	0.001	0.001
BMI (kg/M^2)	31.1 ± 6.34	30.2 ± 6.41	30.0 ± 7.07	0.3	0.1
Stiffness Index	99.6 ± 8	79.3 ± 5.7	62 ± 13.8	0.01	0.001
T- Score	0.0 ± 0.72	≤1.3 ± 0.23	≤2.5 ± 0.73		
Z-Score	0.7 ± 0.83	-0.6 ± 0.5	≤1.6 ± 0.89		

Data are expressed as means ± standard deviation.

Table 4 - Osteopenia and osteoporosis related to place of living in postmenopausal age group.

Bone mass	Group A industrial (n=122)	Group B rural (n=752)	Group C urban (n=2257)	*P*-value
Normal (n=1463)	62	363	1038	0.36
Osteopenia (n=948)	34	201	713	0.03
Osteoporosis (n=720)	26	188	506	0.3

Table 5 - Osteopenia and osteoporosis related to level of education in postmenopausal age group.

Bone mass	Primary school (n=2373)	Secondary school (n=158)	College education (n=600)	*P*-value
Normal	1071	86	306	0.004
Osteopenia	711	46	191	0.68
Osteoporosis	591	26	103	0.004

significantly more osteoporosis when compared to those with college education ($p<0.004$).

Discussion. Osteoporosis is a silent disease leading to a major morbidity and mortality in the aging population around the world. In the past, it was believed that osteoporosis is a disease of the Caucasian race and the eastern men and women are protected from this debilitating condition but this has been proven to be far from the truth. Previous studies from different parts of the Kingdom found the prevalence of osteoporosis in the PMA group to be in the range of 35-45%. Those studies were of small sample size and mostly used hospital based population and sometimes without any consideration for the associated diseases that may influence the incidence of osteopenia and osteoporosis.[9-12,15-17] Findings from above studies showed that the prevalence of osteopenia and osteoporosis in Saudi population is comparatively higher than what is reported from the western countries using QUS. To prove this, a more structured and large population based study such as the present one was needed. Dual energy x-ray absorptiometry (DXA) is still the gold standard test for the diagnosis of low bone mass (osteopenia and osteoporosis). Dual energy x-ray absorptiometry has low precision error of 1-2% versus 3-4% for the ultrasonography;[18] however, access to axial DXA may be limited or costly. Also, it will be difficult to use DXA machine for a community-based screening program. On the other hand, several studies did confirm that calcaneal ultrasound can predict fracture risk with an accuracy rate similar to that of DXA machine.[19-21] One issue which is still unsettled is the diagnosis of low bone mass by QUS utilizing the same WHO threshold of T-Score used for the DXA machines. This may not be appropriate when screening for osteoporosis by QUS.[21-23] Frost et al,[24] studied 420 healthy women aged 20-79 years with no known risk factors for osteoporosis and 97 postmenopausal women with vertebral fractures. They compared DXA measurement of the hip and spine with the QUS measurement on 3 calcaneal ultrasound devices and they concluded that for the 3 QUS devices used in the study, a T score of -1.8 would result in the same percentage of postmenopausal women classified as osteoporotic as the WHO threshold for BMD measurement by DXA (T score -2.5). On the other hand, Turk et al[25] compared DXA with the QUS in patients with inflammatory bowel disease and found that, when patients with a T score of ≤1.0 scanned by DXA were classified as having bone disease. Quantitative ultrasound was sensitive to identify bone disease in 93% of patients with a specificity of 63% if patients with a T score of ≤1.0 scanned by DXA were classified as bone disease. The sensitivity of the QUS to detect osteopenia and osteoporosis was 84% and 72%. Alternatively, lower negative QUS T score cutoff of ≤1.8 identified 83% of osteoporosis at lumbar spine and 100% at hip. In our analysis, we used a cutoff value of ≤1.8 as the threshold for the diagnosis of osteoporosis. Hien et al[26] used the same cutoff value in the analysis of the result of their population-based, cross-sectional survey. Ardawi et al[27] screened 1980 (1065 females and 915 males) randomly selected Saudis from Jeddah area with an age range of 20-79 years by DEXA and they found that 43.4% of the female patients (50-79 years) were osteopenic and 28.2% were osteoporotic using a Saudi reference value. This findings support the fact that using a threshold of T score of ≤1.8 for the Achilles QUS measurement is valid for the diagnosis of osteoporosis as compared to DEXA. The results of this study showed that 30.4% of women in the PMA group were osteopenic and 23% were osteoporotic, even though the majority of our patients were in the early postmenopausal age group. This study further suggests that using a threshold of T score of ≤1.8 for the Achilles QUS measurement is valid for the diagnosis of osteoporosis as compared to DEXA. Sosa et al[28] after screening of 1451 females from Spain using QUS, found that 21.9% of patients aged 51-70 years were osteoporotic if a T score cutoff value of ≤1.8 for the diagnosis of osteoporosis is used. Kim et al[29] found the prevalence of osteoporosis among 552 Korean women above the age of 50 years to be 11.8% using QUS with a T score cutoff value of ≤2.5. Also, Sharma et al[30] used a T score cutoff value of ≤2.5 using QUS and found the incidence of osteoporosis to be 20.25% among 158 women from India. The result of this community based study showed that the prevalence of osteoporosis in Saudi females at PMA group is similar to what was reported from the other parts of the world.

The previously reported higher prevalence is most likely related to the small size of the studies and the fact that it was hospital based. Few studies, used QUS to assess the prevalence of low bone mass at the PBM age group. The prevalence of osteoporosis was only 0.8% in the age group of 20-29 years and 2.1% in the age group of 30-39 years in the study carried out by Hien et al.[26] This study indicates that the prevalence of osteoporosis in Saudi females at PBM age is higher than what was reported from the other parts of the world. Possible explanations for the above finding include low exercise activity in these females due to social factors and the high prevalence of vitamin D deficiency in this part of the world.[31] Both lack of physical activity and low vitamin D level hinders the attainment of PBM. It was shown that low socioeconomic status and educational levels influence the prevalence of chronic diseases in many of the developed and developing countries.[32,33] Little data is available regarding the influence of the level of education on osteopenia and osteoporosis.[34,35] Varenna et al[36] found a higher prevalence of osteoporosis in postmenopausal women having low level of education. In this study, the prevalence of osteoporosis in PBM group was 10.1% in women with college education versus 13.3 in women having less than a primary school education ($p<0.01$). Likewise in the PMA group, the level of education had a significant bearing on the prevalence of osteopenia and osteoporosis. Comparing women who had less than a primary school education versus college educated women, the prevalence of osteoporosis was 24.9% versus 17.2% ($p<0.01$). This finding has a great implication when it comes to targeting the groups of population for the prevention of osteopenia and osteoporosis. The role of pregnancy on the development of osteoporosis has being discussed for a long time. Effects of pregnancy on the maternal bony skeleton are still evolving and many researchers have reported conflicting results regarding the immediate effect of pregnancy on bone mass.[37-39] Bone remodeling during and after pregnancy was shown to have a positive correlation between parity and bone mineral density.[15,40-41] In this study, comparing women with ≥6 children versus women who had <6 children, did not show any significant differences between the 2 groups. It is well established that the incidence of various diseases differ between the urban and rural population.[42,43] Sadat-Ali et al[12] found that the prevalence of osteoporosis in rural population was less than the urban population, based on the BMD analysis. Similarly, Pongchaiyakul et al[44] found the hip BMD to be higher in the rural population compared to the urban population. The above findings were also confirmed by other reports.[45] In this study, the prevalence of osteopenia in the urban areas was higher as compared to the industrial and the rural areas. This indicates that women in the urban areas need special attention when it comes to prevention of osteopenia and osteoporosis.

The present study has few limitations. Even though, several QUS devices such as the one we used are now in the clinical use for diagnosis of osteopenia and osteoporosis but standardization of instruments is one of the major limitations. The second factor was the software which is in use classify osteopenia and osteoporosis uses different ethnic reference values which may be different from Saudi population. Lastly, to compare the QUS values with DXA was beyond the scope of this study, hence was not undertaken.

In conclusion, the present study was able to highlight important facts about the prevalence of osteopenia and osteoporosis in the eastern province of Saudi Arabia. The prevalence of low bone mass in the PMA group is similar to what was reported from the other part of the world. While the prevalence of osteopenia and osteoporosis is high at the PBM age group, which may indicate that, the development of low bone mass starts at an early age. Educated women and women with higher parity were less osteoporotic and women living in the rural areas were less osteopenic and osteoporotic than the city dwellers. The above findings can help in the planning of prevention programs for the low bone mass. Furthermore, similar studies needs to be carried out at the other regions of Saudi Arabia as part of a population-based survey.

References

1. Rosen CJ. Restoring aging bones. ***Sci Am*** 2003; 288: 70-77.
2. Marcus R. Postmenopausal osteoporosis. ***Best Prac Res Clin Obstet Gynaecol*** 2002; 16: 309-327.
3. Fleisch H. Pathophysiology of osteoporosis. ***Bone Mineral*** 1993; 22 (Suppl) 1993; S3-S36.
4. Nichols KJ. Evaluation of osteoporosis. ***J Am Osteopath Assoc*** 2000; 100 (1 Suppl): S4-S7.
5. Chopra A. Osteoporosis: a new understanding of its impact and pathogenesis. ***J Am Osteopath Assoc*** 2000; 100 (1 Suppl): S1-S4.
6. Iqbal MM. Osteoporosis: epidemiology, diagnosis, and treatment. ***South Med J*** 2000; 93: 2-18.
7. Cassel CK. Successful aging. How increased life expectancy and medical advances are changing geriatric care. Geriatrics 2001; 56: 35-39.
8. Mann E, Icks A, Haastert B, Meyer G. Hip fracture incidence in the elderly in Austria: an epidemiological study covering the years 1994 to 2006. ***BMC Geriatr*** 2008; 8: 35.
9. Sadat-Ali M, El-Hassan AY, Ibrahim EM, Al-Frehi H, Al-Muhanna F. Postmenopausal osteoporosis in Saudi women: A pilot screening. ***Ann Saudi Med*** 1993; 13: 272-274.
10. Al-Nuaim AA, Gremli M, Al-Nuaim M, Saud-Kagi A. Magnitude of osteoporosis related fractures in Saudi Arabia. Presented at the symposium on osteoporosis. 1993 December 14-15. Dammam, Kingdom of Saudi Arabia. Dammam (KSA): King Faisal University Press; 1993

11. El-Desouki M. Bone mineral density of the spine and femur in the normal Saudi population. ***Saudi Med J*** 1995; 16: 30-35.
12. Sadat-Ali M, Al-Habdan I, Marwah S. Bone mineral density measurements of distal radius in Saudi Arabian females. ***Annals Saudi Med*** 1996; 16: 414-416.
13. Malavolta N, Mule R, Frigato M. Quantitative ultrasound assessment of bone. ***Aging Clin Exp Res*** 2004; 16 Suppl (3): 23-28.
14. SPSS Statistical Software Package, Version 14.0. Chicago, Illinois: SPSS Inc; 2007.
15. Sadat-Ali M, Al-Habdan I, Al-Mulhim FA, El-Hassan AY. Effect of parity on bone mineral density among postmenopausal Saudi Arabian women. ***Saudi Med J*** 2005; 26: 1588-1590.
16. Sadat-Ali M, Al-Habdan I, Al-Mulhim FA, El-Hassan AY. Bone mineral density among postmenopausal Saudi women. ***Saudi Med J*** 2004; 25: 1623-1625.
17. El-Desouki M. Osteoporosis in postmenopausal Saudi women using dual X-ray bone densitometry. ***Saudi Med J*** 2003; 24: 953-956.
18. Cummings SR, Bates D, Black DM. Clinical use of bone densitometry. ***JAMA*** 2002; 15: 1889-1897.
19. Bauer DC, Gluer CC, Cauley JA, Vogt TM, Ensrud KE, Genant HK, et al. Broadband ultrasound attenuation predicts fractures strongly and independently of densitometry in older women. A prospective study of osteoporotic fractures research group. ***Arch Intern Med*** 1997; 157: 629-634.
20. Pluijm SM, Graafmans WC, Bouter LM, Lips P. Ultrasound measurements for the prediction of osteoporotic fractures in elderly people. ***Osteoporosis Int*** 1999; 9: 550-556.
21. Khaw KT, Reeve J, Luben R, Bingham S, Welch A, Wareham N et al. Prediction of total hip fracture risk in men and women by quantitative ultrasound of the calcaneus: EPIC-Norfolk prospective population study. ***Lancet*** 2004; 363: 197-202.
22. Boyanov M. Diagnostic discrepancies between two closely related forearm bone density measurement sites. ***J Clin Densitom*** 2001; 4: 63-71.
23. Knapp KM, Blake GM, Spector TD, Fogelman I. Can the WHO definition of osteoporosis be applied to multi-site axial transmission quantitative ultrasound? ***Osteoporos Int*** 2004; 15: 367-374.
24. Frost ML, Blake GM, Fogelman I. Can the WHO criteria for diagnosing osteoporosis be applied to calcaneal quantitative ultrasound? ***Osteoporosis Int*** 2000; 11: 321-330.
25. Turk N, Kastelan D, Cucovic-Cavka S, Kraljevic I, Korsic M, Vucelic B. Discriminatory ability of the calcanial quantitative ultrasound in the assessment of bone status in patients with inflammatory bowel disease. ***Ultrasound Med Bio*** 2007; 33: 863-869.
26. Hien VTT, Khan NC, Lam NT, Mai, LB, Le DN, Nhung BT et al. Determining the prevalence of osteoporosis and related factors using quantitative ultrasound in Vietnamese adult women. ***Am J Epidemiol*** 2005; 161: 824-830.
27. Ardawi MS, Maimany AA, Bahksh TM, Nasrat HA, Milaat WA, Al-Raddadi RM. Bone mineral density of the spine and femur in healthy Saudis. ***Osteoporos Int*** 2005; 16: 43-55.
28. Sosa Henríquez M, Saavedra Santana P, Alegre López J, Gómez Alonso C, González Macías J, Guañabens Gay N, et al. [Calcaneous ultrasonography as measurement of osteoporosis prevalence in the general population in relation to the diagnostic criterion utilized. Data of the study GIUMO]. ***Rev Clin Esp*** 2003; 203: 329-333.
29. Kim CH, Kim YI, Choi CS, Park JY, Lee MS, Lee SI, et al . Prevalence and risk factors of low quantitative ultrasound values of calcaneus in Korean elderly women. ***Ultrasound Med Biol*** 2000; 26: 35-40.
30. Sharma S, Tandon VR, Mahajan A, Kour A, Kumar D. Preliminary screening of osteoporosis and osteopenia in urban women from Jammu using calcaneal QUS. ***Indian J Med Sci*** 2006; 60: 183-189.
31. Siddiqui AM, Kamfar HZ. Prevalence of vitamin D deficiency rickets in adolescent school girls in western region, Saudi Arabia. ***Saudi Med J*** 2007; 28: 441-444.
32. Donnelly TT, McKellin W, Hislop G, Long B. Socioeconomic Influences on Vietnamese-Canadian Women's Breast and Cervical Cancer Prevention Practices: A Social Determinant's Perspective. ***Soc Work Public Health*** 2009; 24: 454-476.
33. Szanton SL, Seplaki CL, Thorpe RJ 3rd, Allen JK, Fried LP. Socioeconomic Status is associated with Frailty: the Women's Health and Aging Studies. J Epidemiol Community Health. 2009; 19 [Epub ahead of print].
34. Gemalmaz A, Oge A. Knowledge and awareness about osteoporosis and its related factors among rural Turkish women. ***Clin Rheumatol*** 2008; 27: 723-728.
35. Elliot JR, Gilchrist NL, Wells JE. The effect of socioeconomic status on bone density in a male Caucasian population. ***Bone*** 1996; 18: 371-373.
36. Varenna M, Binelli L, Zucchi F, Ghiringhelli D, Gallazzi M, Sinigaglia L. Prevalence of osteoporosis ny educational level in a cohort of postemenopausal women. ***Osteoporosis Int*** 1999; 9: 236-241.
37. Ulrich U, Miller PB, Eyre DR, Chesnut CH, Schlebusch H, Soules MR. Bone remodeling and bone mineral density during pregnancy. ***Arch Gynecol Obstet*** 2003; 268: 309-316.
38. Black AJ, Topping J, Durham B, Farquharson RG, Fraser WD. A detail assessment of alterations in bone turnover, calcium homeostasis, and bone density in normal preganancy. ***J Bone Miner Res*** 2000; 15: 557-563.
39. Naylor NE, Iqbal P, Fledelius C, Frazer RB, Eastell R. The effect of pregnancy on bone density and bone turnover. ***Bone Miner Res*** 2000; 15: 129-137.
40. Cure-Cure C, Cure-Ramirez, Teran E, Lopez-Jaramillo P. Bone-mass peak in multiparity and reduced risk of bone fractures in menopause. ***Int J Gynaecol Obstet*** 2002; 76: 285-291.
41. Forsmo S, Schei B, Langhammer A, Forsen I. How do reproductive and lifestyle factors influence bone density in distal and ultra-distal radius of early postmenopausal women? The Nord-Trondelag Health Survey, Norway. ***Osteoporosis Int*** 2001; 12: 222-229.
42. Schootman M, Fuortes L. Breast and cervical carcinoma: the correlation of activity limitations and rurality with screening, disease incidence and mortality. ***Cancer*** 1999; 86: 1087-1094.
43. Auger N, Zang G, Daniel M. Community-level income inequality and mortality in Québec, Canada. ***Public Health*** 2009; 123: 438-443.
44. Pongchaiyakul C, Nguyen TV, Kosulwat V, Rojroongwasinkul N, Charoenkiatkul S, Rajatanavin R. Effect of urbanization in bone mineral density: A Thai epidemiological study. ***BMC Musculo Dis*** 2005; 6: 1-7.
45. Sanders KM, Nicholson GC, Ugoni AM, Seeman E, Pasco JA, Kotowicz. Fracture rates lower in rural than urban communities: the Geelong Osteoporosis study. ***J Epidemol Commu Health*** 2002; 56: 466-470.