CLINICAL STUDY

Risk Factors of Osteoporosis in Women Over 50 years of Age: A Population Based Study in the North of Iran

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Abstract

Objective: The objective of this study was to identify the reproductive risk factors of osteoporosis in women over the age of 50 years in north of Iran. Extensive differences in the epidemiological pattern of osteoporosis on the basis of geographical and ethnic grouping have been reported. Previous studies addressing these issues in Iran are very limited.

Materials and Methods: This survey is a population-based study of the women over 50 years of age in the north of Iran in 2004. All recruited subjects were interviewed by purpose-trained interviewers using structured questionnaires including demographic variables, reproductive and medication history. Diagnosis of osteoporosis was based on ultrasonography and the positive cases were confirmed by dual X-ray absorptiometry (DEXA). Statistical analyses were performed using χ^2 test, *t*-test, and analysis of variance. The adjusted odds ratio and 95% confidence intervals (CI) were reported by multiple logistic regression analyses.

Results: Of the 796 women who participated in this study, 147 women (18.5%) were identified as having osteoporosis. Significant correlations were found between osteoporosis and parameters of age, age at menarche, parity, years of menstruation, educational level, job, physical activity, exercise, body mass index (BMI), usage of oral contraceptive pills and menopausal status. After adjusting for variables, the age of 70 years or more and the passage of more than 15 years since menopause were identified as significant risk factors for osteoporosis (OR=2.76 and 1.83, respectively). In comparison to being a 'housewife', having a job and physical activity of more than 3 hours a week and a body mass index (BMI) of more than 25 were identified as protectors against osteoporosis.

Discussion: In spite of the low incidence of smoking and alcohol intake in our population as risk factors of osteoporosis, the prevalence of this worldwide public health problem is high in the north of Iran. These findings should help to identify women at risk and to design an early strategy based on eliminating modifiable risks for prevention of osteoporosis.

Keywords: osteoporosis, quantitative ultrasound, reproductive risk factors

Özet

Elli Yaşın Üzerindeki Kadınlarda Osteoporozun Risk Etkenleri: Kuzey İran'da Topluma Dayalı Bir Çalışma

Amaç: Bu çalışmanın amacı, Kuzey İran'da 50 yaşın üzerindeki kadınlarda osteoporoz üstünde üretkenlik sistemine bağlı risk etkenlerini tanımlamak olmuştur. Daha önceki araştırmalarda, coğrafik dağılım ve etnik gruplandırılmalara göre osteoporozun epidemiyolojisinde geniş kapsamlı farklar bildirilmiştir. İran'da bu konularda önceden yapılmış araştırmalar çok kısıtlıdır.

Materyal ve Metot: Bu inceleme, 2004 yılında İran'ın kuzeyinde 50 yaşın üzerindeki kadın nüfusuna dayandırılmış bir çalışmadır. Çalışmaya katılanlara eğitilmiş görüşmeciler yardımıyla demografik değişkenler, üretkenlik ve ilaç tüketim öyküsü konularını kapsayan anket formları doldurtulmuştur. Osteoporoz tanısı, ultrasonografi ile konulmuş ve pozitif olgular DEXA (ikili X ışını soğurma) tekniği ile kesinleştirilmiştir. İstatistiksel analiz χ^2 testi, *t*-test ve varyans analizi ile yapılmıştır. Ayarlanmış olasılık oranı (OR: odds ratio) ve %95 güven aralığı (CI: confidence interval) multipl lojistik regresyon analizleri ile hesaplanmıştır.

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Sonuçlar: Bu çalışmaya katılan 796 kadından 147'sinde (%18.5) osteoporoz tanımlanmıştır. Osteoporoz ile yaş, menark yaşı, gebelik sayısı, menstrüasyon yıl süresi, eğitim düzeyi, iş, bedensel etkinlik, egzersiz, beden kütle indeksi (BMI: body mass index), oral doğum kontrolü ilaçları tüketimi ve menopoz durumu arasında önemli korelasyon görülmüştür. İstatistiksel değerlendirmelerde değişkenlerin ayarlamaları sonrasında, 70 yaş veya üstünde olmanın ve menopozdan sonra 15 ya da daha fazla yıl geçmiş olmasının osteoporoz içim önemli risk etkenlerini oluşturduğu (sırasıyla, OR=2.76 ve 1.83) ortaya çıkmıştır. Ev kadınlığı ile karşılaştırıldığında, bir işte çalışma, haftada 3 saatin üstünde bedensel etkinlik ve beden kütle indeksinin (BMI) 25 veya üstünde oluşu osteoporoza karşı koruyucu etkenler olarak tanımlanmıştır.
Tartışma: Sigara ve alkol tüketimi gibi bazı risk etkenlerinin, incelemenin yapılmış olduğu toplumda olasılığı düşük de olsa, bu dünya çapındaki sağlık probleminin kuzey İran'da yaygın olduğu görülmektedir. Buradaki bulgular, risk altındaki kadınları erken tanımlayarak osteoporozun önlenmesi için değiştirilebilir risklerin giderilmesini içeren erken strateji tasarımında yardımcı olabilir.

Anahtar sözcükler: osteoporoz, nicel ultrason, üretkenlikte risk etkenleri

Introduction

Osteoporosis and the increasing risk of subsequent fracture is one of the most prevalent community health problems affecting the elderly population in developed and developing countries and its prevalence is increasing (1,2).

The prevalence of osteoporosis is difficult to determine, because many people who experience osteoporosis are not being diagnosed. Using a strict definition of osteoporosis, i.e., T-score of less than –2.5 SD (statistical difference) below the mean value for young women, the prevalence of osteoporosis has been reported to be 13 to 18% in women above 50 years of age in the USA (3).

Extensive differences of the epidemiological pattern of osteoporosis among geographic regions, ethnic groups and races have been reported. According to several epidemiological projects published over recent years, developing countries will account for over 70% of all osteoporosis fractures in the world by the year 2050 (4). In a study, Asian background was reported as a risk factor of osteoporosis (5). Prevention of osteoporosis would be better achieved by identifying particularly the patients at risk and by providing the appropriate intervention. Therefore, a population-based study is needed to determine the prevalence and identification of patients at risk within the general population of the society concerned.

In Iran, the studies that have addressed the problem of osteoporosis in the population are very few in numbers. The population investigated in one study consisted of men and women, regardless of menopausal status, while two other studies included perimenopausal women who visited primary health clinics (6-8).

Dual X-ray absorbtiometry (DEXA) is the 'gold standard' diagnostic technique for osteoporosis, but it has the disadvantage of not being portable and it is expensive. Quantitative ultrasound (QUS) is a simple, quick, portable and inexpensive technique that can be used to predict risk of osteoporotic fractures. Measurements are usually made at the heel which is a particularly useful site since it is composed primarily of cancellous bone, similar to the spine. Screening of osteoporosis by QUS has become widely available in Europe (9-11).

Several epidemiological surveys in different parts of the world have extensively analysed the potential risk factors of osteoporosis, including demographic characteristics, medical history, smoking, physical activities, but the conclusions were controversial for different ethnic groups (12,13). Therefore, extrapolation of these findings to our population and implementation in routine clinical evaluation is not necessarily valid. In particular, reproductive factors such as menstruation, obstetrics and lactation history and their long term effects on bone mineral density in the postmenopausal period have not been intensively described. This is a population based study concerned with assessing the potential risk factors associated with low bone mineral density in women over 50 years in the north of Iran with special emphasis on maternity and reproductive history.

Materials and Methods

Study design, subjects and sampling

A cross-sectional survey was conducted in the north of Iran to identify the prevalence of osteoporosis and related risk factors in 2004. All women older than 50 years and residing at urban and rural areas in north of Iran irrespective of their racial or ethnic backgrounds were included in the study. Those women that were not interested in participating or had severe illness or were too old to participate were excluded. Considering the prevalence of osteoporosis to be 15% and the precision to be 0.03; a total number of 544 subjects were taken for sample size and to deal with the effect of cluster sampling this number was multiplied by 1.5 and 816 subjects were targeted. In proportion to the urban and rural distribution of the population, 25 clusters from urban areas and 30 clusters from rural areas were selected to cover a total of 500 urban and 300 rural subjects. The subjects were then randomly selected in each cluster.

Study variables

A structured questionnaire consisting of 36 items in sections including demographics (age, job, education, and residential

place), reproductive history (number of pregnancy, menarche age, menstrual irregularity, lactation period, menopause age and duration of menopause), drug history (oral contraceptives, calcium, hormone replacement therapy, corticosteroids, thyroxin) and social history (physical activity and smoking status) was presented to all subjects on a face to face basis by a trained interviewer. Body Mass index (BMI) was calculated as 'weight (kg)/height (m^2)'. Menstrual cycle intervals of 25 to 35 days were considered as regular menstruation. Irregularity and intermittent regularity was based on the declaration of the women about their cycle intervals. Weight of women was measured in light clothes using a standard scale. The women were asked about the level of their physical activity which was categorized as 'none', less than 3 hours in a week and equal or more than 3 hours in a week. Menopause was defined as 12 months of amenorrhea.

Diagnosis of osteoporosis was carried out using quantitative ultrasound technique with UBIS-5000 device (DMS, France). This instrument automatically identified an area in the heel bone that has the least bone density and gave the T-score, Z-score, and BUA as variables relevant to Asian populations. A T-score of less than –2.5 SD of reference value for young adult female population was considered to reflect osteoporosis. All positive cases were confirmed by DEXA.

Statistical analyses

The variables were described by the 'mean±SD' or 'frequency' (percent), as appropriate. For continuous normally distributed variables, *t*-tests and analyses of variance (ANOVA) were employed. Categorical variables were analyzed using χ^2. The correlation between continuous variables and bone stiffness were assessed by Pearson correlation coefficient. To determine the variables independently associated with osteoporosis, multiple logistic regressions were conducted. Odds ratios (OR) and 95% confidence intervals (CI) were calculated. Forward elimination of variables was used to remove those variables not significantly predictive of outcome, as indicated by the Wald χ^2. All statistical analyses were performed using SPSS for windows version 13.0 (SPSS Inc, Chicago).

Results

Among the 796 women over the age of 50 years enrolled in this study the response rate was 98% and eight subjects were excluded because of incomplete data. The mean age of the 788 women who underwent quantitative ultrasound was 63.36 years, ranging between 50 and 92. Of the participants 95.7% were menopausal, with an average age of 48.3 years (range, 30 to 64) at the cessation of menstruation. Twenty nine subjects (3.9%) were reported to be current or past smokers; 95 subjects (11.9%) were reported to have used corticosteroids orally or by injection within the last six months; 45 women (5.7%) were reported to have used thyroxin and 9 women (1.1%) were reported to have used estrogens. None of the participants had a history of alcohol intake. Of the participants 291 (36.6%) resided in rural and 504 (63.3%) in urban areas; 83% of all the subjects were illiterate or had only completed primary school and the majority (74.9%) of them were housewives. There was a history of hormone replacement therapy and calcium supplement utilization in 1/1% and 18.9%, respectively.

A significant relationship was observed between physical activity and osteoporosis ($p<0.001$). Table 1 and 2 show the characteristics of the investigated population with respect to osteoporosis and the *p*-values.

On the basis of ultrasonography and the T-score criteria, 147 women (18.5%) had osteoporosis and 645 women (81%) were normal. The prevalence of osteoporosis increased significantly with age before (11.4%) and after (45.2%) 70 years of age ($p<0.001$). Similarly, a statistically significant difference was seen in the mean age for the two groups (Table 1). The mean age at menarche in women with osteoporosis was also significantly higher than in the normal group ($p<0.01$), but this was not observed for the age at menopause.

The prevalence of osteoporosis in rural areas was higher than in urban areas (22.1% versus 16.6%; $p<0.05$). Housewives were more likely to develop osteoporosis (89.1%) as compared to working women (10.9%) ($p<0.001$). Similarly, prevalence of osteoporosis among illiterate women was significantly higher (21.5%) than among educated women (4.4%). The prevalence of osteoporosis in women with BMI less than 25 was higher than in women with BMI of over 25, ($p<0.0001$). In postmenopausal women there was high prevalence of osteoporosis as compared to the premenopausal women ($p<0.01$). The mean years of menstruation in normal women was significantly higher than in women with osteoporosis ($p<0.001$), but there was no statistically significant difference for the duration of lactation, oophorectomy and corticosteroid use in the two groups. The mean number of pregnancies also showed a significantly positive correlation with osteoporosis.

In this study only 9 women had used estrogen as hormone replacement therapy and none of them showed osteoporosis.

Multiple logistic regression results

The OR and 95% confidence interval values measured for those variables that had statistically significant relationship in bivariate analysis with osteoporosis (defined as T-score of less than –2.5 SD) are presented in Table 3. Age, independently of all other variables, was significantly associated with increased risk of osteoporosis. The odds of osteoporosis in women over 70 years of age was 3.6 times (95% CI=2.14-6.09) higher than in women below 70 years. The OR for 'having a job' (working women) was lower (0.49) as compared to that (1.00) for the unemployed 'housewives'.

Table 1. Quantitative variables and their correlation with osteoporosis

Variables	Normal mean ±SD	Osteoporosis mean ±SD	*p*
Age (years)	61.8±0.3	69.8±0.6	0.001
Age at menarche (years)	13.38±1.74	13.88±1.96	0.003
Duration of lactation (month)	82.98±66.08	88.25±69.68	0.39
No. of pregnancy	5.76±2.91	6.62±3.27	0.002
Years of menstruation	35.41±5.44	33.70±6.38	0.001
Age at menopause (year)	48.83±5.31	47.83±6.62	0.09
Weight (kg)	67.7±12.29	55.99±14.10	0.001
Height (cm)	151.27±6.55	146.91±6.32	0.001

Table 2. Quantitative variables and their correlation with osteoporosis

Variables	Normal n (%)	Osteoporosis n (%)	*p*
Menstrual pattern			
Irregular	74 (11.7)	12 (8.6)	0.57
Sometimes regular	76 (12.0)	18 (12.9)	
Regular	485 (76.4)	110 (78.6)	
Menopause			
No	33 (97.1)	1 (2.9)	
Yes	612 (80.7)	146 (19.3)	0.02
Employment			
Housewife	462 (77.9)	131 (22.1)	0.001
Working	181 (91.9)	16 (8.1)	
Education			
Illiterate	516 (78.5)	141 (21.5)	0.001
Educated	129 (95.6)	6 (4.4)	
Place of living			
Rural	226 (77.9)	64 (22.1)	0.05
Urban	418 (83.4)	83 (16.6)	
Oral Contraception			
No	301 (76.4)	93 (23.6)	0.001
Yes	344 (86.4)	54 (13.6)	
Oophorectomy			
No	535 (80.1)	93 (87.5)	0.129
Yes	133 (19.9)	9 (12.5)	
Exercise			
None	493 (78.8)	133 (21.2)	0.001
<3 hours	35 (81.4)	8 (18.6)	
≥3 hours	117 (95.1)	6 (4.6)	
Cortisone (oral & injection)			
No	572 (82.1)	125 (17.9)	0.22
Yes	73 (76.8)	22 (23.3)	
BMI (kg/m2)			
<25	119 (62.3)	72 (37.7)	0.001
>25	524 (87.8)	73 (12.2)	

Interestingly, women who exercised for up to 3 hours in a week had higher odds of developing osteoporosis compared to inactive women. In contrast, the odds of osteoporosis in women who exercise more than 3 hours a week was significantly lower than the reference group (OR=0.34, 95% CI=0.13-0.86). BMI of over 25 (kg/m^2) gave the odds of osteoporosis as 0.29, lower than that for BMI under 25. To explore the effect of menstruation characteristics on osteoporosis including the age at menarche, menstruation years and age at menopause, we defined these predictors

Table 3. Predictors of osteoporosis (T-score<-2.5) obtained by multiple logistic regression analysis

Variables	OR	95% CI	*p*
Age			
<70	1		
>70	2.76	1.54-4.94	0.001
Age at menarche			
11-15	1		
7-11	1.09	0.38-3.13	NS
>15	1.48	0.73-2.99	
No. of pregnancies	1.05	0.97-1.13	NS
Years of menstruation			
<40 years	1		
>40 years	0.41	0.13-1.31	NS
Age at menopause			
45-55	1		
30-45	1.41	0.81-2.46	NS
>55	2.56	0.72-9.08	
Years since menopause			
<15 years	1	0.99-3.39	0.053
>15 years	1.83		
Employment			
Housewife	1		
Working	0.49	0.24-0.99	0.03
Education			
Illiterate	1		
Educated	1.02	0.37-2.82	NS
Oral contraceptive use			
No	1		
Yes	1.11	0.67-1.83	NS
Exercise (hours in a week)			
None	1		
<3 hours	2.88	1.16-7.18	0.02
≥3 hours	0.34	0.13-0.86	
Weight (kg)	0.98	0.95-1.006	NS
Height (cm)	0.91	0.87-0.96	0.001
BMI (kg/m2)			
<25	1		
>25	0.29	0.15-0.61	0.001

again as dummy variables. Age at menarche was classified to three groups as lower than 11 years, over 15 years and 11 to 15 years, taken as the normal age range of menarche. Either early or late of menarche appeared to increase the odds of developing osteoporosis by 1.22 and 1.5 times, respectively, but the values were not statistically significant. Duration of menstruation was classified as over or below 40 years and, as expected, the odds of developing osteoporosis was lower (0.39) for menstruation for over 40 years although this was not statistically significant. The age at menopause was also classified to three groups; 45 to 55 years, as the normal age range for menopause, 30-45 years and over 55 years; and, in spite of increasing odds for both the lower and the higher age groups compared to the 45 to 55 year range, the values were not statistically significant.

Discussion

In this population-based study of female osteoporosis in the north of Iran, the overall rate of osteoporosis was 18.6% in women over 50 years of age. This study investigated the prevalence of osteoporosis by quantitative ultrasound and the prevalence of the related risk factors in a low-income and low-literacy population from both rural and urban areas. There are some reports from other countries on the prevalence of osteoporosis. For example, in the USA, a recent study using ultrasound on the heel reported an osteoporosis incidence rate of 7% among the postmenopausal women (8). The incidence of osteoporosis in China was 6.6% (in 1997), 19.8% in Thai women, 29.6% in Jordanian women (in 2003), and 15.8% among women aged 40-60 in Tehran (14-16). In a Japanese study, the prevalence of osteoporosis was 11.6%

at the femoral neck in 50-79 year-old women (17). Corresponding rates obtained from previous works in Iran ranged between 18.5-32.4% (6,7). Our estimations are in agreement with other studies (18,19). However, differences in the reports throughout the world are greatly affected by the diagnostic techniques used.

This study has confirmed that age over 70 years and years that have elapsed since menopause are still the most important risk factors for predicting osteoporosis even after adjusting for other variables. The increased risk of osteoporosis was evident after 15 years of entering menopause. The accelerated phase of bone loss that begins with irregular menstruation in the premenopausal phase continues for 4-5 years and up to 10 years after menopause. The multiple logistic regression analysis provided strong evidence for independent negative influence of age (OR=2.76) and the years sinc menopause (OR=1.83) on osteoporosis.

There was also an association between having a job, exercising, height and BMI with osteoporosis after adjusting for all other variables. Housewives were more likely to develop osteoporosis but this relationship could be confounded by age. Older people fall into lower income groups, may have had less education and tend not to be employed.

Most research in postmenopausal women suggest that strength-training exercises attenuate the progressive loss of bone in postmenopausal women but do not increase bone mass (20). In our study the effect of physical activity was defined in three categories as 'none' (reference group), less than 3 hours and more than 3 hours exercise in a week. The odds of osteoporosis was increased in the second group to 2.88 times but decreased in the third group. Some studies have reported that low-intensity exercise such as walking is ineffective for stimulating bone mineralisation (21). Physical activity transmits loads to the bone through muscle pull and gravitational force during weight-bearing activity. Because of the increase in gravitational force upon bone in a weight-bearing position, strength-training exercises performed on foot are considered to be more effective at stimulating bone formation than machine-based exercises performed in the seated position. Our findings agree with the inference that severe activity may decrease the risk of osteoporosis.

We have also confirmed that women with BMI of more than 25 were less likely to develop osteoporosis (OR=0.29). The reasons for the protective effect of higher BMI and the link between obesity and lowered osteoporosis risk are not fully understood. Some experts have postulated that estrogen produced or stored in fat tissue might attenuate bone loss.

In this study, an association was apparent between the number of pregnancies and osteoporosis which was shown to have no significance after adjusting for all other variables. Bone loss can be seen during pregnancy. Calcium needed for fetal skeletal growth during pregnancy is gained from maternal skeleton. The relationship between parity and bone mass has yielded mostly negative results (22,23), with two exceptions showing a protective effect, which is in agreement with our study (21,24). However, it is possible that the nulliparous state may reflect a hormone environment of both sterility and osteoporosis. Therefore, despite the continuous reduction of bone mineral density with frequent pregnancies, it was not likely to be a risk factor for osteoporosis in our multiparous population.

Our results have demonstrated that the duration of lactation has no association with osteoporosis. In some studies lactation for more than six months was associated with increased risk of osteoporosis (18). In other studies lactation was associated with bone loss of 1.5 to 4.0% (25) but the lost bone was regained after lactation ceased (26,27). These findings have led to the speculation that frequent breastfeeding is essential for remodeling of bone by increasing resorption and subsequent formation during lactation.

However, higher BMI might override the negative influence of hypoestrogenic state on bone mineral density. Our data could be related to high BMI noted among women in our study.

There was no association between use of oral contraceptive pills and osteoporosis. Oral contraceptive pills usage may have a beneficial effect on bone mineral density, but this has not been established in controlled trials (28). In one study, oral contraceptive pills were not found sufficient to improve bone density in anorexia nervosa (29). In another study with pre- and postmenopausal women, higher bone mineral density was found in oral contraceptive pill users than in the non-users (30).

In spite of the low prevalence of some risk factors of osteoporosis such as smoking and alcohol intake in the present study, the prevalence of this worldwide public health problem was found to be high in north of Iran where the significant predictors of osteoporosis were age, years since menopause, body mass index, working at a job and exercise.

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