Osteoporosis and Its Relationship with Various Risk Factors in Postmenopausal Women in Denizli Province

Denizli İlindeki Postmenopozal Kadınlarda Osteoporoz Oranı ve Çeşitli Risk Faktörleriyle İlişkisi

Mustafa Gürkan TAŞKALE, MD,[a]
Yurdaer SERMEZ, MD[b]

[a]Department of Endocrinology, Bakırköy Dr. Sadi Konuk Research Hospital, İstanbul
[b]Department of Internal Medicine, Division of Endocrinology and Metabolism, Pamukkale University Medical Faculty, Denizli

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Yazışma Adresi/*Correspondence:*
Mustafa Gürkan TAŞKALE, MD
Bakırköy Dr. Sadi Konuk Research Hospital, Department of Endocrinology, Division of Endocrinology and Metabolism, İstanbul, TÜRKİYE/TURKEY
taskale@yahoo.com

ABSTRACT Objective: Osteoporosis is an important clinical condition frequently seen in postmenopausal women. It is the major cause of vertebrael and hip fractures. The incidence of osteoporotic fractures has been increasing and half of the elderly female population in most Western as well as Asian countries has been affected. The aim of this study was to determine the postmenopausal osteoporosis rate and evaluate the relationship between osteoporosis and various risk factors in postmenopausal women living in the central and rural areas of Denizli. **Material and Methods:** Subjects were selected randomly among postmenopausal women who were enrolled in Village Health Centers of Denizli Provincial Directorate of ,Health by public announcements. We evaluated 1100 postmenopausal women out of 16113 women, aged 45-80 years. The bone mineral density of the patients was measured by quantitative ultrasound of the tibia. Subjects with T scores lower than -2.5 SD were diagnosed as osteoporosis according to the World Health Organization criteria. **Results:** The rates of osteoporosis in various areas ranged between 19.8% and 53.9% (mean 36.8%). The subjects were divided into two groups as with osteoporosis and without osteoporosis. Average menarche age was greater in the osteoporotic group. The subjects who had taken hormone replacement therapy (HRT) had lower osteoporosis rate. Subjects with osteoporosis had lower exercise score and had lack of sun exposure due to covering. A positive correlation was found between osteoporosis age and the duration of menopause. **Conclusion:** We found that the incidence of osteoporosis among postmenopausal women was very high especially in rural areas of Denizli. Age, duration of menopause, age of menarche and multiparity appeared to be important risk factors in development of osteoporosis. However, HRT, physical activity and sun exposure could prevent osteoporosis. Understanding the epidemiology and fracture risk of osteoporosis may ultimately aid in reducing the public health burden of this common disorder.

Key Words: Osteoporosis; postmenopause; risk factors

ÖZET Amaç: Osteoporoz postmenopozal kadınlarda sık görülen önemli bir klinik durumdur. Vertebra ve kalça kırıklarının başlıca nedenidir. Osteoporotik kırıkların sıklığı artmaktadır ve çoğu Batı ülkesinde ve Asya ülkelerindeki yaşlı kadın nüfusunun yarısı etkilenmektedir. Bu çalışmanın amacı Denizli'nin merkezindeki ve kırsal kesimindeki postmenopozal kadınlarda postmenopozal osteoporoz oranını saptamak ve osteoporozla çeşitli risk faktörleri arasındaki ilişkiyi değerlendirmekti. **Gereç ve Yöntemler:** Olgular halka yapılan duyuruyla Denizli'deki Sağlık Bakanlığı İl Sağlık Müdürlüğü'ne bağlı sağlık ocaklarında kayıtlı postmenopozal kadınlar arasından rastgele seçildi. Yaşları 45-80 arasında olan 16113 kadından 1100 postmenopozal kadını değerlendirdik. Hastaların kemik mineral yoğunlukları tibianın kantitatif ultrasonu ile ölçüldü. Dünya Sağlık Örgütü kriterlerine gore T skoru -2.5 standart sapmanın altında olan hastalara osteoporoz tanısı konuldu. **Bulgular:** Çeşitli bölgelerde osteoporoz oranı %19.8 ile %53.9 arasında değişiyordu (ortalama %36.8). Olgular osteoporozu olanlar ve olmayanlar olmak üzere iki gruba ayrıldı. Osteoporozu olan grupta menarş yaşı daha büyüktü. Hormone replasman tedavisi (HRT) alanlarda osteoporoz oranı daha düşüktü. Osteoporozu olanların egzersiz skoru daha düşüktü ve örtünmeye bağlı olarak güneşe maruziyetleri azdı. Osteoporoz yaşı ile menopoz süresi arasında pozitif korelasyon bulundu. **Sonuç:** Özellikle Denizli'nin kırsal bölgesindeki postmenopozal kadınlarda osteoporoz sıklığının çok yüksek olduğunu bulduk. Yaş, menopoz süresi, menarş yaşı ve multipartite osteoporoz gelişiminde önemli risk faktörleri olarak görülmektedir. Fakat HRT, fiziksel aktivite ve güneşe maruz kalmak osteoporozu önleyebilir. Osteoporozun epidemiyolojisinin ve kırık riskinin anlaşılması bu yaygın hastalığın halk sağlığına getirdiği yükün azaltılmasına yardımcı olabilir.

Anahtar Kelimeler: Osteoporoz; postmenopoz; risk faktörleri

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Osteoporosis is a common disease that may lead to serious disability, increased morbidity and mortality, and significant health-care costs.[1] It is also the major cause of vertebrael and hip fractures. The incidence of osteoporotic fractures has been increasing and half of the elderly female populations in most Western as well as Asian countries has been affected.[2] Approximately, 30-50 percent of postmenopausal women are estimated to have osteoporosis.[3,4] Dual-energy X-ray absorptiometry (DXA) is an accurate and precise method of determining bone mineral density (BMD), and has been used mainly for the diagnosis of osteopenia and osteoporosis for ascertaining fracture risk and monitoring the treatment.[5] Recently, quantitative ultrasound (QUS) has been proposed as a reliable alternative method for evaluating osteoporosis and fracture risk. It may be useful for measuring both the quality and quantity of bone and many studies demonstrated its ability to determine the fracture risk, independent of age and BMD.[6,7] This study was carried out in postmenopausal women living in the central and rural areas of Denizli province, in Western Anatolia Region of Turkey. Our aim was to determine the incidence of postmenopausal osteoporosis and evaluate its relationship with various risk factors.

MATERIAL AND METHODS

Provincial Directorate of Health (PDH) was informed about the design of this study. Because the approval of PDH was granted, we did not apply for further Research Council approval. This population-based cross-sectional study was conducted under the supervision of a researcher from Pamukkale University Medical Faculty, after the approval of PDH. Public announcements were made by PHD to collect subjects from 13 villages of Denizli. There were 16113 postmenopausal women enrolled in Village Health Centers (VHC) in as much as last census. Finally, 1100 postmenopausal women aged 45-80 years were included in the study from within the subjects who applied after the announcement and accepted to participate. All participants gave their written informed consent.

All subjects completed an interviewer-administered risk factor questionnaire, which contained sections on cigarette smoking, alcohol and caffeine consumption. Their physical activity was also evaluated by the information about the occupation, work and leisure-time activities. The history of medical problems and medications known to affect bone mineral density including diabetes mellitus, obesity, thyrotoxicosis, anorexia, connective tissue diseases, neoplasms, immobilization history (longer than two months), use of corticosteroids more than three months, thyroid hormone, phenytoine and hormone replacement therapy (HRT) for 12 months or more were excluded. Although more than 3 cm height loss is another risk factor,[8] we did not evaluate this, because heights of these subjects were not measured previously. Additionally, the cases who used antiresorptive drugs for osteoporosis and those with type 1 diabetes mellitus were excluded.

Body weight (Wt) was measured, (after removal of shoes and heavy outdoor clothings) using a balance beam scale. Height (Ht) was measured (after removal of shoes) using a Filizola stadiometer. Height and weight were used to calculate the body mass index (BMI, as kg/m^2). The age, age at menarche and menopause, years since menopause, parity condition, history of fracture and fracture history in the family were recorded. All cases were evaluated for back pain and the exposure to the sun (because women living in rural areas of Denizli generally covered due to religion and traditions). BMD measurement was carried out by means of QUS of the tibia. Speed of sound (SOS, meters per second) was determined at the right tibia using the Sound Scan 2000 (Myriad Ultrasound Systems, Israel; version 1.20 and 1.30 BETA). The standard measurement size was defined as the mid-point between the apex of the malleolus and the distal patellar apex. The probe was moved manually across the mid-tibial plane, parallel to the long axis of the tibia, searching for the site with maximal SOS reading, lasting about 5-10 minutes. The average of the five highest readings was considered as the representative result.[7,9] Data were analyzed and expressed as SOS and T score. Although there has been no consensus on the T score cut-offs and di-

agnostic categories to be used with QUS, the instrument used commonly in Turkey also accepts the World Health Organization (WHO) criteria as cut-off values. Subjects with a T score lower than-2.5 SD were diagnosed as osteoporosis.[10]

Diagnostic laboratory investigations (for hyperthyroidism, diabetes mellitus, rheumatoid arthritis or others) were not carried out in this study. Additionally, diagnostic compatibility between QUS and DXA was not investigated.

The statistical analyses were performed Statistical Package for the Social Sciences version 16 (SPSS 16, Chicago, IL, USA). The differences between both groups were analyzed by Pearson's Chi-square test and Student's t-test where appropriate and followed by multiple logistic regression models with all potential risk factors. We used one-way ANOVA test to assess differences among more than two groups. Correlations were analyzed by Pearson's correlation test. All results were expressed as the mean ± SD, and P values smaller than 0.05 were considered as statistically significant.

RESULTS

The rates of osteoporosis in the center and various rural areas of Denizli in Western Anatolia ranged between 19.8% and 53.9% (mean 36.8%, population-adjusted prevalence 33.6%) (Table 1). The rate of osteoporosis increases with age whereas SOS values decreased with age (Table 2).

TABLE 1: The frequency of osteoporosis in the center and various rural areas of Denizli (center of Denizli had lower osteoporosis rate than rural areas, p< 0.001).

Villages	Osteoporosis rate (%)
Acipayam	26.9
Akalan	30.8
Honaz	37.5
Karahayit	37.8
Serinhisar	53.9
Guney	37.5
Cardak	53.3
Buldan	36.1
Civril	27.4
Cameli	49.4
Cal	29.4
Citak	37.2
Denizli (center)	19.8

TABLE 2: The rate of osteoporosis in postmenopausal women and the SOS values according to the age groups, (p< 0.001).

Age groups	Osteoporosis rate	SOS (m/s)
45-54	7.2	3742 ± 413
55-64	39	3608 ± 359
65-74	48.1	3584 ± 308
75+	66.7	3403 ± 345

SOS: Speed of sound.

The subjects were divided into two groups as osteoporotic (group I) and non-osteoporotic (group II) groups. The clinical data of the cases are shown in Table 3.

Menopause age, fracture history, fracture history in the family, caffeine intake, adequate calcium intake, smoking, diabetes mellitus, hyperthyroidism, and drug use were not found statistically significantly different between group I and II (Table 3, and 4).

When cases were divided into two groups according to BMI, osteoporosis rate was found as 28.9% in cases with BMI >30 kg/m^2 while this rate was 30.6% in cases with BMI <30 kg/m^2; however this difference was not significant. The complaint of back pain was more frequent in group I than group II. We also evaluated various risk factors in both groups (Table 4).

A positive correlation was found between osteoporosis and age (r= 0.33, p< 0.001) and duration of menopause (r= 0.34; p< 0.001). There was a negative correlation between SOS and age (r= -0.41; p< 0.001) and duration of menopause (r= -0.44; p< 0.001). Similarly a negative correlation was found between T score and age (r= -0.35; p< 0.001), and the duration of menopause (r= -0.39; p< 0.001).

The ratios for fracture history and parents' fracture history were not significantly different between group I and II. On the other hand, the SOS values of the cases with facture history was significantly lower than the cases with no facture history (3541 ± 429 m/s vs. 3617 ± 311 m/s, p< 0.01, respectively).

TABLE 3: The clinical data in Group I and group II (ns: not significant).

Parameters	Group I (n= 349)	Group II (n= 751)	p value
Age (yrs)	61.5 ± 8.6	55.3 ± 8.1	<0.001
Weight (kg)	67.6 ± 12.5	68.6 ± 12.1	ns
BMI (kg/m^2)	28.3 ± 4.4	28.3 ± 4.5	ns
Menopause age (yrs)	44.4 ± 6	45.6 ± 6.6	ns
Duration of menopause (yrs)	16.9 ± 9.9	9.2 ± 9.7	<0.001
Age at menarche (yrs)	14.7 ± 1.8	14.3 ± 1.5	<0.01
Back pain rate (%)	73.4	55.4	<0.001

TABLE 4: Comparison of the various risk factors in groups I and II.

Risk factors	Group I	Group II	p value
Parity condition	4.6 ± 2.8	4.1 ± 2.3	<0.05
Fracture history (%)	4.6	3.8	ns
Fracture history in family (%)	10	11	ns
HRT (%)	2.9	7.3	<0.05
Caffeine intake	4.5	3.6	ns
Adequate calcium intake (%)	85.5	90.1	ns
Smoking (%)	2.6	1.8	ns
Diabetes mellitus (%)	10.4	13.1	ns
Hyperthyroidism (%)	1.7	3	ns
Drug usage (%)	2.6	2.1	ns
Adequate activity (%)	35.3	59.8	<0.001
Adequate sun exposure (%)	4.6	21.9	<0.001

The SOS values (r= 0.32; p< 0.001) and T score (r= 0.30; p< 0.001) were positively correlated with physical activity. A strong relationship was found between osteoporosis and lower levels of physical activity (χ^2= 25.327; SD= 1; p< 0.001) and HRT (χ^2= 40.91; SD= 1; p< 0.005). Additionally, multiparity was negatively correlated with T score (r= -0.20; p< 0.001) and SOS values (r= -0.18; p< 0.001). There was no correlation between osteoporosis and BMI. Moreover, in multiple logistic regression analysis, a high activity level, sun exposure and HRT were found as significant factors that prevent osteoporosis (Table 5).

DISCUSSION

According to WHO 30% of postmenopausal white women could be affected by osteoporosis.[10] In the present study, the proportion of osteoporosis in postmenopausal women ranged between 19.8% and 53.9% (mean 36.8%).

The QUS may be used for first-line public osteoporosis screening and it may be accepted as a valid and practical method.[11,12]

Fracture risk not only depends-on BMD, but also other factors such as bone turnover rate, bone architecture and geometry etc.[13,14] Therefore, WHO developed a fracture risk assessment tool (FRAX®) recently. It is a computer-based algorithm that provides models for the assessment of fracture risk in men and women to estimatea 10-year-fracture probability. The data used to estimate fracture risk in this tool are age, sex, weight, height, previous fracture, parents' hip fracture history, smoking, use of corticosteroids, presence of rheumatoid arthritis, secondary osteoporosis (type 1 diabetes, hyperthyroidism, hypogonadism, malnutrition or malabsorption and chronic liver disease), alcohol consumption and BMD.[15] The FRAX tool Turkey results may be incorrect probably due to insufficient data.[13] In this paper, we also evaluated other risk factors such as menarche age, daily activity status, sunlight exposure, suffering from back-pain, and type 2 diabetes mellitus.

It is not surprising that there is no uniform entity as diabetic osteopathy due to the different pathogenesis of diabetes mellitus type 1 and type 2.[16] Type 1 diabetes mellitus is characterized with absolute insulin deficiency and was previously called as insulin dependent diabetes mellitus, and insulin has anabolic effect on the tissues. Type 1 diabetes is a disease of youngsters and occasionally occurrs after 2nd decade of life [which called latent autoimmune diabetes of adults (LADA)]. We excluded patients with type 1 diabetes due to presence of chronic end-organ complications and a small number of cases. Patients with type 2 diabetes mellitus display an increased fracture risk despite a higher BMD which is mainly attributable to the increased risk of falling.[17] In our study, type 2 diabetes ratio among cases with osteoporosis was not statistically different when compared to the cases without osteoporosis.

TABLE 5: Independent variables related to osteoporosis as in logistic regression model.

							95% confidence interval (CI) for Exp (B)	
	B	Standard Error (SE)	Wald	df	p	Exp (B)	Lower	upper
Sun exposure	1.5059	0.2796	29.0057	1	<0.001	4.5083	2.6062	7.7986
Activity	0.8598	0.1406	37.3751	1	<0.001	2.3627	1.7935	3.1127
HRT	0.8680	0.3673	5.5851	1	0.018	2.3821	1.1597	4.8930
Back pain	-0.4868	0.1537	10.0329	1	0.002	0.6146	0.4547	0.8306
Constant	-3.2082	0.4426	52.5329	1	<0.001			

-2 log likelihood ratio: 1246,100.

Previous studies showed that age and menopausal status were important risk factors for osteoporosis, and were strongly associated with fracture risk in older women.[18-20] Our findings are in accordance with the age and menopausal status of previous studies. In the present study, osteoporosis rate increases with age, and there is a strong correlation between osteoporosis and the duration of menopause.

The majority of the cross-sectional studies on age at menarche and premenopausal bone health suggest an inverse relationship between two. Some of the studies demonstrated a relationship between spinal bone density and age of menarche, and women with normal bone mineral density (BMD) had experienced menarche significantly earlier than women with lower mineral density.[21,22] In contrast, some studies found no significant relationship between menarche age and bone mass.[23-26] In our study, age of menarche was significantly older in osteoporotic group. These different results may be explained with different criteria used for case selection (e.g. age ranges of cases that affect menopausal status and rate of osteoporosis were not equal among different studies) as a result of different study designs and including more subjects into the study when compared to other studies.

The results of studies that investigated the effect of parity on osteoporosis in both pre- and postmenopausal women are also inconsistent. Recent hip fracture studies found that multiparous (more than four children) women were at a higher risk than women with one or two children.[27,28] Our findings indicate that multiparous women are at higher risk for osteoporosis. This may be explained by the inadequate calcium intake during pregnancy and breastfeeding.[29]

Weight is consistently associated with positive measurements of BMD in normal premenopausal and obese women.[30,31] BMI has been studied less, however it also demonstrates a consistent positive relationship with bone mineral measurement.[32,33] In two prospective studies of obese and pre- and postmenopausal women, BMD decreased dramatically with weight loss and was regained with subsequent weight gain.[34-36] In our study, osteoporosis rate was found to lower in obese individuals, however the difference with the nonobese cases was not statistically significant. Some cross-sectional studies reported that physical activity was positively related with BMD,[35-37] but other studies did not confirm this finding.[38-40] Walking and aerobic exercise were associated with high BMD when compared to sedentary controls.[41] Our cases had no regular exercise, however regular physical activity was lower in osteoporotic group than in non-osteoporotic group.

Caffeine intake increases urinary calcium excretion for at least three hours after consumption and it has been associated with some evidence of altered bone remodeling process.[42,43] In an observational study, daily consumption of caffeine equivalent to 2-3 cups of coffee was associated with accelerated bone mineral loss from the spine and total body in postmenopausal women who consumed less than 744 mg calcium/day.[44] Another study reported a small but significant negative relationship between caffeine intake and calcium balance that was no longer significant after adjusting for calcium intake.[45] We found that caffeine intake

was similar in both groups. Women living in rural areas do frequently consume coffee in our country as a tradition.

Smoking has an increasing cumulative negative effect on BMD. BMD decreases approximately 2% per decade after menopause in female smokers.[46] Because Turkish women living in rural areas generally do not smoke, the rate of smoking was very low in our cases.

Reports concerning the effects of alcohol on BMD yielded conflicting results. Although some studies found no association between alcohol consumption and BMD,[47] some others observed a significant inverse association.[48] Excess alcohol intake appears to have a modest adverse effect on the preservation of bone mass, mainly by suppressing bone formation.[49] However none of the cases in this study consumed alcohol. For that reason, we could not evaluate the relationship between osteoporosis and alcohol consumption.

To our knowledge, it is known that hormone replacement therapy (HRT) prevents the reduction of bone density related to the postmenopausal hypoestrogenism. It was recently reported that low-dose oral contraceptive administration was able to prevent perimenopausal decrease in radial and vertebral BMD.[50-52] Similarly, we found that subjects who were on HRT had lower osteoporosis rate regardless of oral or transdermal use.

The lack of calcium intake is one of the important risk factors for osteoporosis. Conversely, an increase in calcium intake decreases the activation frequency of osteoclasts.[53] Intervention studies indicated that calcium supplementation of approximately 1000 mg/day can prevent premenopausal bone mineral loss at all clinically relevant skeletal sites.[54,55] Recent reviews also concluded that adequate or supplemental calcium intake reduced bone mineral loss in premenopausal women.[56,57] In our cases, calcium intake was similar in both groups. Therefore, there may be other factors that affect the absorption and excretion of calcium such as dietary fiber, protein and sodium intake, irregular and insufficient calcium intake or vitamin D insufficiency.[58] In fact, our cases were not administered vitamin D in addition to calcium, and they had lack of sun exposure due to traditional and religious covering.

Although the SOS values of the cases with fracture history were lower than the ones without fracture history, significant difference was not found between group I and II. This may be explained by the other fracture risks as bone geometry, etc., apart from low bone mineral density.

The difference of osteoporosis rate between central and rural areas may be explained with genetic predisposition as a result of frequent consanguineous marriages, less medical care, low income and education levels, however, this issue is open to discussion because we did not evaluated these data.

CONCLUSION

In accordance with the literature, our study indicates that the incidence of osteoporosis is very high in postmenopausal population especially in the rural areas of Denizli. It must be emphasized that age, duration of menopause, age of menarche, and multiparity appear as important risk factors in development of osteoporosis. In contrast, HRT, physical activity and sun exposure are able to prevent osteoporosis. QUS is a reliable and easy alternative method for screening of osteoporosis. In addition, another main advantage of QUS examination is alosence of any radiation exposure and the low cost of the equipment. Understanding the epidemiology and fracture risk of osteoporosis may ultimately aid in reducing the public health burden of this common disease. Additionally, fracture a risk assessment tool (FRAX®) for Turkish people may be developed after new comprehensive studies.

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