

Is grand multiparity a risk factor for osteoporosis in postmenopausal women of lower socioeconomic status?

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Abstract. – OBJECTIVE: We aimed to determine whether grand multiparity is a risk factor for osteoporosis among postmenopausal women of lower socioeconomic status.

PATIENTS AND METHODS: We conducted a single center study between February 2012 and February 2013 on 50-60 year old postmenopausal women of lower socioeconomic status without a history of medical disease. Women with a body mass index (BMI) between 20 and 25 were included in the study. The grand multiparous group (group A) consisted of 38 women with 10 or more deliveries. Women with a history of three or fewer deliveries composed the control group (group B). Dual-energy x-ray absorptiometry was used to measure the bone mineral density (BMD) of the proximal femur neck and lumbar spine (L1-L4).

RESULTS: The mean ages of groups A and B were found to be 54.3 ± 2.5 and 53.1 ± 2.7 years, respectively. Average parity in groups A and B was 11.1 ± 1.7 and 2.4 ± 0.7 , respectively. Time since the onset of menopause was 3.6 ± 2.7 years in group A and 6.0 ± 2.9 in group B. The prevalence of osteoporosis was similar in both groups (71.1%-81.4%, $p = 0.273$). We found that grand multiparity was an ineffective indicator of either femoral or lumbar osteoporosis ($p = 0.87$ and $p = 0.26$), but osteoporosis five years after the onset of menopause was found to be significantly higher ($p = 0.02$).

CONCLUSIONS: The duration of menopause is an independent risk factor of osteoporosis. However, the number of pregnancies is neither a determinant nor a protective factor for osteoporosis in postmenopausal women coming from a low socioeconomic background.

Key Words:

Grand multiparity, Osteoporosis, Postmenopause.

Introduction

Osteoporosis is the most common metabolic bone disorder. It results in bones becoming fragile and fracturing easily in the absence of or with minimal trauma¹. It is a major public health problem and particularly dangerous for the elderly population. Fractures lead to increased mortality and morbidity and impair quality of life. In some women, the onset of the disease appears to be related to pregnancy and lactation. Both pregnancy and breast-feeding are argued to be associated with changes in maternal calcium homeostasis, resulting in decreased bone mineral density (BMD)².

Calcium requirements are substantially increased in pregnant and breastfeeding women in order to meet the calcium needs of the growing fetus and nursing infant for bone mineralization and growth³. It is generally accepted that the mother's body adapts to these increased calcium needs via enhanced intestinal absorption of calcium, without the need for increased dietary calcium⁴. The greatest transfer from pregnant woman to the fetus takes place during the second and third trimesters, when fetal bone development peaks, and again during lactation. The main mechanism for calcium loss is skeletal resorption due to the increased levels of parathyroid hormone related peptide released from the breast⁵. Although it is difficult to explain the apparent association between pregnancy and osteoporosis, this phenomenon may be related to changes in hormonal activity during pregnancy.

In post-menopausal women, there is a reduction in serum estrogen levels, leading to bone loss. Estrogen plays an important role in skeletal maintenance due to its osteo-protective action⁶. In this context, post-menopausal status is a major risk factor for osteoporosis⁷. Few epidemiological studies among post-menopausal women with osteoporosis have failed to demonstrate a clear relation between parity and BMD^{8,9}.

There has been an ongoing debate on routine universal calcium and vitamin D supplementation during pregnancy. In this study, we contribute to this debate by investigating the effects of grand multiparity on osteoporosis. We hypothesized that a subgroup of grand multiparous women (with low socio-economic status) may be more susceptible to lower bone mineral density. Therefore, calcium supplementation in this subgroup during pregnancy may have clinical value in the primary prevention of osteoporosis. In this manner, we aimed to investigate the bone mineral densities of post-menopausal grand multiparous women coming from a low socioeconomic background and to compare these results with age and BMI matched controls.

Patients and Methods

The study was conducted between February 2012 and February 2013 at a state hospital. Post-menopausal women (50-60 years old) without a history of medical disease (e.g., hyperthyroidism, hyperparathyroidism, Cushing's syndrome, bowel and renal diseases, breast cancer) were recruited into the study. The women were matched for BMI and age. They were all from a rural area. Thyroid stimulating hormone (TSH), parathyroid hormone (PTH), and renal function were analyzed to exclude undiagnosed renal, thyroid, or parathyroid diseases. Women who had taken medications such as bisphosphonates, hormone replacement therapy (HRT), oral corticosteroids, thyroxin, vitamin D preparations, calcium, and thiazide diuretics were also excluded. Height and weight were recorded for every woman meeting the inclusion criteria. Each patient's BMI was calculated, and patients with a BMI between 20-25 kg/m² composed the study group. Patients with a BMI above 25 were excluded. Therefore, we excluded any possible confounding effect of weight on osteoporosis. Overall, 81 women were eligible for the study, and these women were administered a validated questionnaire regarding

medical history, education and reproductive history, number of pregnancies, and age of menopause.

The women were divided into two groups. The grand multiparous group (group A) consisted of 38 women with a history of 10 or more deliveries. Women with a history of three or fewer deliveries composed the control group (group B, n = 43). Dual-energy x-ray absorptiometry (DEXA) (Norland Eclipse XR, Norland Corp., Ford Atkinson, WI, USA) was used to measure the BMD of the left proximal femur and lumbar spine (L1-L4). Osteoporosis was defined as bone density T scores higher than -2.5 standard deviations (SD). We decided to evaluate lumbar and femoral T scores because femoral neck T-Score is considered as a gold standard for risk assessment of vertebral fracture. Nevertheless, lumbar L1-L4 T-score measurement with DEXA is widely accepted tool for clinical practice and for defining patients with an increased fracture risk¹⁰. All women were of low socioeconomic status. Overall, their literacy rate was very low; no patients had finished secondary school, and the socioeconomic levels of the participants were comparable between the study groups. All of the women participating in the study were from the same religious and regional background.

Statistical Analysis

Data were represented as mean $\pm$ SD, range, and percentage as appropriate. Pearson's chi-squared test and Student's *t*-test were used for the statistical analysis of qualitative and quantitative parameters, respectively. A *p*-value of 0.05 was set to test statistical significance. Analysis was done using SPSS 16.0 (SPSS Inc., Chicago, IL, USA) statistical software package.

Results

Evaluation of the general characteristics of the women who had 10 or more births revealed that the mean ages of groups A and B were found to be 54.3 ± 2.5 and 53.1 ± 2.7 years, respectively. Average parity in groups A and B was 11.1 ± 1.7 and 2.4 ± 0.7 , respectively. Time since the onset of menopause was 3.6 ± 2.7 years in group A and 6.0 ± 2.9 in group B (Table I). In group A, 35 women had 10-14 deliveries and 3 women had 15 or more deliveries. In group B, 43 women had 1-3 deliveries.

Table I. Descriptive values of age, parity, duration of menopause, densitometry of femur and lumbar bone between groups.

	Women had 10 or more deliveries (group A)		Women had 3 or fewer deliveries (group B)	
	Mean	Min-max	Mean	Min-max
Age (year)	54.3 ± 2.5	50-59	53.1 ± 2.7	50-59
Parity	11.1 ± 1.7	10-17	2.4 ± 0.7	1-3
Duration of menopause (year)	6.04 ± 2.9	1-12	3.6 ± 2.7	0-10
Lumbar T score (SD)	-1.3 ± 1.4	-4.2-2.3	-1.1 ± 1.1	-3.0-1.1
Femoral T score (SD)	-0.49 ± 1.16	-3.0-2.1	-0.48 ± 1.13	-2.7-2.9

Min-max: minimum-maximum.

We analysed calcium and phosphor levels with respect to the study groups and observed that there was no statistically significant difference among groups (mean calcium level in group A and B were 9.4 and 9.5 respectively, mean phosphor level in group A and B were 3.6 and 3.8 respectively).

The prevalence of osteoporosis was similar in both groups (71.1%-81.4%, $p = 0.273$) (Table II). The average L1-L4 score in group B was -1.1 ± 1.1 , and their femoral score was -0.4 ± 1.1 ; similarly these scores were -1.3 ± 1.4 and -0.4 ± 1.1 , respectively, for group A (Table III). These results indicated that grand multiparity was not an effective risk factor for either the femoral or lumbar bone regions ($p = 0.875$ for L1-L4, $p = 0.268$ for the femur).

Table II. Comparison groups in terms of osteoporosis.

	Women had 10 or more deliveries (group A)	Women had 3 or fewer deliveries (group B)
Osteoporosis	11 (57.9%)	8 (42.1%)
Normal	27 (43.5%)	35 (56.5%)

Pearson chi-square p value: 0.273.

We also performed an overall analysis without splitting the patients into groups. This analysis revealed that the duration of menopause is an independent risk factor of osteoporosis ($p = 0.022$). This interpretation was also the same when we evaluated the two study groups individually (Table IV) (Figure 1).

Discussion

Osteoporosis is the most common metabolic bone disorder, and it is associated with multiple risk factors. Menstrual factors such as late age of menarche, early menopause, and amenorrhea have been shown to be risk factors of osteoporosis in previous studies^{11,12}. Many factors influence the severity of bone mass loss that occurs during the post-menopausal period. Only a few studies have reported the effects of parity on BMD using a population of post-menopausal women with high parity. There are many case reports on pregnancy associated osteoporosis that examined patients during pregnancy. In contrast, our study investigated the long term effect of grand multiparity on the bones. In this study, we aimed to investigate the effect of grand-multipar-

Table III. Comparison groups in terms of femoral and lumbar osteoporosis respectively.

	Osteoporosis n (%)	Normal n (%)
Femoral T score		
Women had 10 or more deliveries (Group A)	3 (7.9%)	35 (92.1%)
Women had 3 or fewer deliveries (Group B)	3 (7.0%)	40 (93%)
Lumbar (L1-L4) T score		
Women had 10 or more deliveries (Group A)	10 (26.3%)	28 (73.7%)
Women had 3 or fewer deliveries (Group B)	7 (16.3%)	36 (83.7%)

Pearson chi-square p value for femur and lumbar T score: 0.875 and 0.268.

Table IV. Comparison of patients according to the years of menopause, in terms of osteoporosis.

	< 5 year menopause	> 5 year menopause
Osteoporosis	8 (15.4%)	11 (37.9%)
Normal	44 (84.6%)	18 (62.1%)

Pearson chi-square *p* value: 0.022.

ity on bone mineral densities of post-menopausal women with lower socioeconomic status. In our study, we demonstrated that grand multiparity is not associated with osteoporosis in our study population.

Two studies^{13,14} on Turkish postmenopausal women revealed low spinal BMD in women who had born more than five children and asserted high parity as a risk factor for low spinal BMD and osteoporosis. Oktay et al¹⁵ reported that an extended breast-feeding period (> 1 year per child) is the highest risk factor for osteoporosis, independent of age at first breast-feeding. However, high parity also has been claimed to have a protective effect on osteoporosis. Although several authors^{16,17} have reported that women with multiple pregnancies have a lower fracture risk

than nulliparous women, there has been an ongoing debate about the long term clinical relevance of low BMD with multiparity. Michaelsson et al¹⁸ found that the risk of fracture is reduced with each child delivered. In contrast, Keramat et al¹⁹ reported that multiparity greater than three was a risk factor for osteoporosis in both Iran and India. Parazzini et al²⁰ reported that there was no relationship between pregnancy and osteoporosis. Interestingly, Turan et al²¹ highlighted that grand multiparity does not appear to play a role in increasing the risk of osteoporosis at a more advanced age. The study included women with a history of more than 10 deliveries. Previous studies had chosen different cut-off values for the number of deliveries; therefore, we speculate that this discrepancy may have influenced these controversial results. In order to minimize such a bias for defining multiparity, we used different selection criteria that included both women with fewer than three and women with more than 10 deliveries. Afterwards, we compared these two groups with each other. We hypothesized that this kind of comparison would be more effective in documenting a significant difference if there is a real independent effect of multiparity on bone mineral density.

Firstly, our study investigated the long term effect of grand multiparity on the bones. Another important comparison that should be emphasized in this study is that a subgroup analysis (patients with a postmenopausal period of more than 5 years vs. patients with a fewer period) revealed that length of the menopausal period is an independent predictor of osteoporosis. Similar to our results, several reports^{22,23} have indicated that the time elapsed after the onset of menopause is an important determinant in bone loss. Genetic factors such as race, as well as eating habits during childhood and adolescence (dietary calcium and vitamin D), exposure to sunlight, and lifestyle play significant roles in achieving the maximum level of bone mass. In our study, patients using HRT were excluded to avoid misinterpretation of the data, as it can have positive effects on bone density. BMI standardization and exclusion of HRT usage are strengths of our work since we are, thus, excluding other diseases that affect the bone. At the same time, the women who were included reflect a specific ethnic and working group which is largely homogeneous. Since calcium and phosphor levels among two groups were comparable, we sensibly do not expect any bias related with calcium or phosphor deficiency.

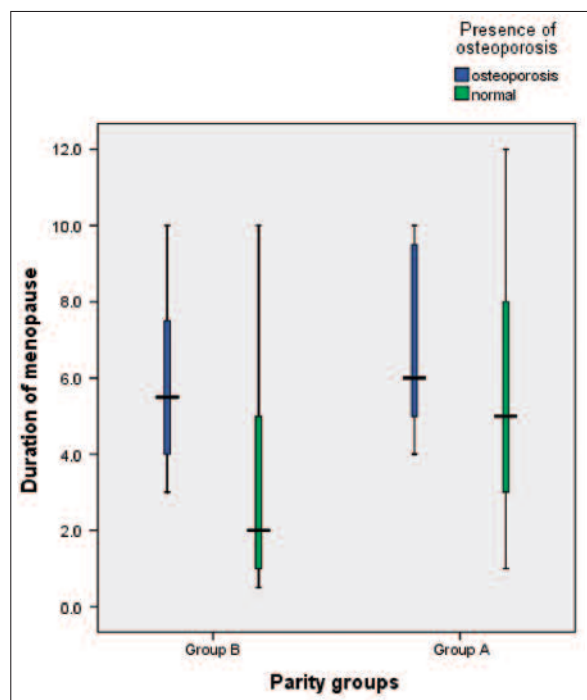


Figure 1. Distribution of osteoporosis frequency of groups according to duration of menopause.

One important strength of this study is the selection of a homogenous group of women from the same geographical region and similar socioeconomic status. Therefore, this selection is assumed to minimize the confounding effects of many other unpredicted factors (e.g., sun exposure, eating habits, Vitamin D or calcium supplementation) and focus only on the possible effects of grand multiparity on bone mineral density, if any. We also hypothesized that analysis of this group of grand multiparous women, who have never taken Vitamin D or calcium supplementation, may lead to future benefits of such supplementation. However, in this study we were unable to document a significant effect of grand multiparity on osteoporosis and we speculate that this group of postmenopausal women with high parity have a similar risk of osteoporosis compared to women with lower parity. Therefore, we suggest that parity should not be considered a risk factor of bone loss. Hence, other documented risk factors should be kept in mind for every woman in the prevention and treatment of osteoporosis, without taking the number of deliveries into account.

Conclusions

Duration of menopause is an independent risk factor of osteoporosis. Moreover, the number of pregnancies is neither a determinant nor a protective factor for osteoporosis in postmenopausal women coming from a low socioeconomic background.

Conflict of Interest

The Authors declare that there are no conflicts of interest.

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