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Prevalence and associated factors of osteoporosis in female patients with rheumatoid arthritis

Abstract

Background: Osteoporosis (OP) is a common complication of inflammatory arthritis such as rheumatoid arthritis (RA). In this study we evaluated Osteoporosis and its related factors in RA patients.

Methods: This cross - sectional study was carried out from 2010 to 2011 on 121 women with RA aged 45-75 years. These patients were selected and divided in two groups according to their bone mineral densitometry (BMD) status, osteoporotic and non osteoporotic. The data about OP and potential related factors were recorded. T-test for quantitative and X² for qualitative variables were used for group comparison.

Results: The mean age of the patients was 55.7±10.1 and the duration of the disease was 10.1±9.2 years. Thirty nine (32.3%) of patients had T score ≤ -2.5 [28 (23.1%) in the lumbar spine and 20 (16.5%) in the femoral neck of regions]. The age and body mass index (BMI) were the most significant factors related to OP (p=0.00, p=0.01). Surgery induced menopause was conversely related to OP in neck of femur (p=0.04). OP in femur was related to overall fracture in patients (p=0.02) and also with seropositivity for RF (p=0.04) and body mass index (p=0.01).

Conclusion: The prevalence of OP in our patients was higher than expected. Old age, menopause, low BMI and seropositivity were the main risk factors of osteoporosis.

Keywords: Osteoporosis, Rheumatoid arthritis, Bone mineral density, Risk factors

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Rheumatoid arthritis (RA) is the most prevalent inflammatory arthritis. The prevalence is estimated up to 1% (1, 2). Osteoporosis (OP) is a common complication of inflammatory arthritis such as RA. Although the mechanisms of OP in RA are not fully understood, it is thought that osteoclast and its dysfunction with cytokines which mediated them are the principal pathogenesis factors of this bone disease (3). Disease activity, aging, anti-rheumatoid agents such as corticosteroids and methotrexate, low calcium intake, vitamin D deficiency, low activity and seropositivity are some related factors that may influence on OP in RA patients (4, 5). The prevalence of OP in RA was evaluated as 2 fold more than controls (4, 6). Prevalence of OP in RA patients in different parts of the world was reported to be between 22% to 36% (3, 7-8). In one study in Iran, the prevalence of OP in post menopausal women was 8.9%, but the prevalence of OP in another study on RA patients with same mean age was 40.4% (9, 10). It may be that Iranian RA patients have some risk factors for OP that makes it more prevalent. So further studies about this potentially treatable complication in rheumatoid arthritis patients should be done. In this study, we tried to evaluate OP and some related factors in RA patients.

Methods

A cross - sectional study was carried out from 2010-2011 on 121 women with rheumatoid arthritis who had been referred to rheumatology clinic in Sari, Iran.

RA was defined according to ACR 1987 (11). Bone mineral densitometry (BMD) was done by Dual-energy X-ray absorptiometry DEXA method. Osteoporosis was defined as T-score lower than -2.5 in lumbar spine (L2-L4) or left hip (Neck of femur) (12). The patients were divided in two groups according to their bone mineral densitometry results, patients with OP (T-score \leq -2.5 in femoral neck or L2-L4 spine) and without OP. The data about OP and potential related factors such as body mass index (BMI), age, menopause, drugs use for RA or OP, history of fracture, and factors related to RA such as health assessment questioner (HAQ), disease activity score (DAS 28), use of steroids and methotrexate, drugs for OP treatment or prophylaxis, cumulative dose of glucocorticoids (dose of glucocorticoids according prednisolone \times 364 \times years /1000), duration of disease, seropositivity for RF and anti CCP, and serum levels of calcium and alkaline phosphates were noted.

The sites of fractures were also recorded. HAQ is an 8 item questionnaire evaluating the RA patients' activities last week and its reliability and validity have been shown in Iranian RA patients (13). Two groups were compared regarding RA and OP factors, and also were compared for the related factors in spine and femur OP separately. The statistical analysis was done by t-test for quantitative and

X^2 test for qualitative variables.

Results

One hundred twenty one female patients with RA were evaluated. The mean age was 55.7 \pm 10.1 and the duration of the disease was 10.1 \pm 9.2 years. Thirty - nine (32.3%) of patients had osteoporosis (T score \leq -2.5 in L2-L4 lumbar spine or femoral neck). The prevalence of L2-L4 lumbar spine or femoral neck OP was 28 (23.1%) and 20 (16.5%), respectively. Twenty-six (21.5%) of patients had fractures: 9 patients with wrist fractures, 6 patients with humerus fractures, 4 patients with leg fractures and 2 with spine and foot and finally 1 in knee (patella), femur, ankle fractures. The age and BMI were the most significant factors that were significantly different between the two groups with and without osteoporosis (p=0.00, p=0.01, respectively) (table 1). With logistic regression analysis, patients with BMI \leq 25 kg/m² are 3.9 times (95% CI: 1.3-12.4) at risk of osteoporosis and this risk is 4.1 (95% CI: 1.3-12.4) in cases age more than fifty years. One hundred-two (84.3%) of patients were current users of low dose of glucocorticoids and 78 (64.5%) were using methotrexate without any significant difference in two groups (table 1).

Table 1. Related factors in osteoporosis in rheumatoid arthritis patients

| | Patients with OP (n=39) | Patients without OP (n=82) | P value |
|---|----------------------------|-------------------------------|---------|
| Age (mean \pm SD) | 63.2 \pm 9.9 | 52.0 \pm 8.0 | 0.00 |
| Duration of RA (mean \pm SD), years | 10.5 \pm 9.4 | 9.9 \pm 9.1 | 0.76 |
| HAQ score (mean \pm SD) | 3.1 \pm 3.1 | 2.7 \pm 2.9 | 0.48 |
| DAS 28 (mean \pm SD) | 3.35 \pm 1.27 | 3.20 \pm 1.19 | 0.6 |
| Cumulative dose of glucocorticoids (gr) | 15.2 \pm 15.2 | 18.7 \pm 18.9 | 0.3 |
| Usage of methotrexate (%) | 72.7% | 76.9% | 0.6 |
| Menarche age (mean \pm SD), years | 13.4 \pm 1.5 | 13.6 \pm 1.7 | 0.73 |
| Menopause age (mean \pm SD), years | 47.7 \pm 4.7 | 46.1 \pm 6.8 | 0.28 |
| Serum calcium (mean \pm SD), mg/dl | 9.3 \pm .58 | 9.2 \pm .49 | 0.56 |
| Serum ALK (mean \pm SD), mg/dl | 172.3 \pm 55.9 | 168.2 \pm 48.7 | 0.73 |
| Urine 24 hours calcium (mean \pm SD), mg/24 h | 181.7 \pm 87.5 | 194.0 \pm 72.7 | 0.56 |
| BMI (mean \pm SD), Kg/m ² | 28.0 \pm 7.2 | 30.85 \pm 4.3 | 0.01 |
| History of fracture, (N, percent) | 12 (30.8%) | 14 (17.1%) | 0.08 |
| Use of calcium, (N, percent) | 31 (79.5%) | 68 (82.9%) | 0.65 |
| Doing exercise, (N, percent) | 12 (9.9%) | 36 (29.8%) | 0.16 |
| OP treatment, (N, percent) | 21 (53.8%) | 53 (64.6%) | 0.25 |
| RF positive (N, percent) | 17 (58.6%) | 32 (45.1%) | 0.21 |
| Anti CCP positive (N, percent) | 15 (71.4%) | 25 (50.0%) | 0.09 |

Cumulative doses of glucocorticoid in OP and non-OP patients were 15.2 ± 15.2 and 18.7 ± 18.9 , respectively ($p=0.3$). Seventy-nine (65.3%) patients were menopausal, 28 (35.4%) in patients with OP and 51 (64.6%) in patients without OP, and in 21.4% of osteoporotics and in 78.6% non-osteoporotics, menopause occurred after hysterectomy and oophorectomy ($p=0.05$). Thyroid replacement therapy for hypothyroidism was used for 13.8% and 20.3% in two groups, respectively ($p=0.44$). The patients were compared for related factors in spine and femur OP separately. Surgery induced menopause was conversely related to OP in neck of femur ($p=0.04$) but not in spine. OP in femur was related to overall fracture in patients ($p=0.02$) and seropositivity for RF ($p=0.04$) (table 1).

Discussion

In this study, we found that the prevalence of OP in RA patients was 32.3% that is about one third of the patients. This is more prevalent in comparison to some other studies which was reported 22-24% (3, 7, 8) and fewer than the other Iranian RA population with 40.4% (10). Only age and BMI were significant factors related to OP. The patients with history of hysterectomy had lower risk of OP especially in femoral neck; this may be related to more attention given after surgery for taking OP prophylaxis. OP in femur was correlated with fracture and also the patients with femur osteoporosis were more RF seropositive. We showed that OP is more prevalent in lumbar spine than femoral neck. In Sugiguchi study on 105 female patients with well controlled RA, there was a greater decrease in BMD in femoral neck than the lumbar spine (5).

It may be due to the activity of the disease. In another study by Haugeberg on 394 patients with RA, femoral neck BMD was significantly reduced by 4.2% in the age group 50-59 years, and by 5.0% in 60-70 years. In this study, predictors of reduced BMD at the femoral neck were older age, low body weight, current use of corticosteroids, greater physical disability, and presence of rheumatoid factor; and in lumbar spine, the predictors were older age, low weight, and current use of corticosteroids (4). In Güler-Yüksel study done on 381 recently diagnosed RA patients who were never treated by the disease modifying arthritis drugs (DMARDs) or glucocorticoids, osteoporosis and reduced BMD were found in the spine and/or the hip in 11% and 25%, respectively in the patients. Longer symptom duration and

the presence of RF were the only RA-specific markers for osteoporosis and reduced BMD (14). In one study on 373 RA patients, the factors such as low body mass index and higher age were more predicted factors for OP. The use of corticosteroid was not independently associated with OP (15).

The prevalence of OP in our patients was higher than the other countries and fewer than other Iranian studies. It may be because of the difference of our patients especially in age, and other factors such as genetics, geography, behavior, economy, and probably some unknown factors that may be discovered later. A high percentage of patients used glucocorticoids and methotrexate but it was not different in the two groups. It may be because of the population size but it should be considered that the effects of disability and disease activity are more prominent in OP. We could not estimate the effects of cumulative dosage of glucocorticoids, because our patients were managed by other centers and we did not have their exact information. Thus, it is recommended that more attention is needed to be given to RA patients about OP especially premenopausal, and older patients with low BMI and seropositives.

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