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ORIGINAL ARTICLE

Serum leptin and osteoporosis in postmenopausal women with primary knee osteoarthritis



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KEYWORDS

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Abstract *Aim of the work:* The purpose of this study was to evaluate the relationship of serum leptin level and osteoporosis in postmenopausal women with knee osteoarthritis (KOA).

Patients and methods: The study included 40 postmenopausal women with primary KOA and 37 age-matched postmenopausal healthy controls. Plain X-ray knees were performed and assessed using the Kellgren–Lawrence (KL) grading scale. Bone mineral density (BMD) was assessed using dual-energy X-ray absorptiometry (DXA) in lumbar spine, hip and forearm regions. As a bone turn-over marker serum osteocalcin was measured. Serum leptin level was assessed in patients and control.

Results: The mean age of the KOA patients was 58.05 ± 5.7 years. Osteoporosis was detected among 15% of the KOA patients and 35.1% of the control. The BMD was significantly increased at the spine and wrist in the patients than in the control ($p = 0.011$ and $p = 0.015$ respectively). The serum osteocalcin was comparable between patients (19.74 ± 8.05 ng/ml) and control (21.2 ± 8.36 ng/ml) ($p = 0.5$). Serum leptin was significantly higher in the patient (58.7 ± 27.17 ng/ml) compared to the control (48.75 ± 13.19 ng/ml) ($p = 0.048$), and significantly correlated with the degree of KOA ($p = 0.017$). No significant correlation was found between serum osteocalcin level or the BMD and the degree of KOA. There was a significant negative correlation between serum osteocalcin level and forearm BMD in KOA patients ($r = -0.33$, $p = 0.038$).

Conclusions: Although postmenopausal women with KOA had significantly higher BMD, both diseases can coexist. It seemed that osteoarthritis does not prevent the occurrence of osteoporosis. Our study suggested a promising role of leptin as a biomarker of KOA.

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1. Introduction

Osteoarthritis (OA) and osteoporosis (OP) are extremely frequent among elderly people and their impact on life quality makes them of high socio health relevance. While OA is a joint disease characterized by degeneration of articular cartilage and bone remodeling that may affect different sites and involve peripheral or axial joints [1], OP is characterized by low bone mass, and microarchitectural deterioration of bony tissue, with a consequent increase in bone fragility and susceptibility to fractures. According to the WHO criteria, osteoporosis can also be defined as a value of bone mineral density (BMD) more than 2.5 standard deviations below the young normal mean [2].

It would be anticipated that osteoporosis and osteoarthritis frequently coexist due to their high prevalence in elderly women but the association between these conditions is still controversial [3,4] even after years of research since the first results indicate an apparent inverse relationship [5,6]. Indeed, many studies have shown an association between high bone mineral density at the spine and hip and OA of the hips, knees or hands [7–10]. However, other studies failed to show an inverse relationship between OA and OP and reported impaired bone quality and increased risk of fracture in patients with OA [11–14].

Leptin is a protein hormone that plays a key role in regulating energy intake and expenditure [15]. High leptin levels were associated with obesity, which is a risk factor for OA [16]. Findings on effects of leptin on bone metabolism are partly contradictory. There are studies where a positive association has been found between leptin and BMD [17,18], while there are also studies reporting no significant association [19,20] or a negative association [21,22].

We undertook this study to determine the association between radiographic features of knee osteoarthritis (KOA), and BMD at different measured sites, as well as to investigate the underlying mechanism at the tissue level through assessment of osteocalcin as a biochemical marker of bone turnover. We also evaluated the relationship of serum leptin level, osteoporosis and KOA in postmenopausal women.

2. Patients and methods

The study involved 40 postmenopausal women with KOA according to ACR clinical classification criteria for

osteoarthritis of the knee and 37 age-matched postmenopausal women asymptomatic for KOA were included as a control group.

The study was explained to the participants and an informed consent was given by each, after approval from the local ethics committee of the Faculty of Medicine, Alexandria University. The exclusion criteria were (1) clinical and radiological signs of secondary OA such as, post traumatic, metabolic, and other rheumatological diseases. (2) Using drugs known to influence bone metabolism in the past two years, such as corticosteroids, bisphosphonates, sodium fluoride, raloxifene, strontium ranelate, teriparatide and hormone replacement therapy. (3) Thyroid, parathyroid, adrenal, hepatic, or renal disease; (4) malignancy; (5) hysterectomy; (6) smoking; and (7) alcohol intake.

Each participant completed a questionnaire on demographic parameters and personal history such as age of menopause, coffee intake, calcium and vitamin D supplement, and history of fragility fracture. The body mass index (BMI) was calculated. Plain X-ray knees (antero-posterior and lateral views) were performed while standing. The radiographs were subsequently evaluated by a single observer. The disease severity was assessed using the Kellgren–Lawrence (KL) grading scale [23]. Radiological KOA was defined as \geq grade 2 on KLG scale.

Lumbar spine, femoral neck and forearm bone mineral density (BMD) were measured by dual-energy X-ray absorptiometry (DXA) with a lunar prodigy densitometer. T score was obtained.

Morning fasting blood was collected from every subject for the measurement of serum osteocalcin (OCN) level. Electrochemiluminescence immunoassay of N-MID OCN was done using Elecsys 2010 immunoassay analyzer. Serum leptin concentrations were determined in all participants using an enzyme linked immunosorbent assay (ELISA) technique.

Statistical analysis: Data were analyzed using IBM SPSS software package version 20.0. Descriptive data were expressed as mean and standard deviation. Univariate analyses including t-test and Mann–Whitney test were used to test the significance of the results of quantitative variables. Moreover, Fisher's exact test was used to test for significance among qualitative variables. Linear correlations were conducted to show the relationship between BMD of the lumbar spine, hip and forearm, OA severity and other studied parameters. The significance of the results was at the 5% level of significance.

Table 1 Demographic features, bone mineral density, serum leptin and osteocalcin in postmenopausal patients with knee osteoarthritis and in control.

Characteristics mean \pm SD or median (range)	Postmenopausal women ($n = 77$)			
	KOA patient ($n = 40$)	Control ($n = 37$)	p value	
Age (years)	58.05 \pm 5.7	57.27 \pm 5.6	0.55	
Age of menopause (years)	51(45–55)	50 (42–56)	0.21	
BMI	36.03 \pm 5.9	33.7 \pm 4.9	0.07	
BMD	Lumbar spine	1.13 \pm 0.17	1.03 \pm 0.16	0.01*
	Femoral neck	0.99 \pm 0.13	0.94 \pm 0.14	0.053
	Forearm	0.71 \pm 0.08	0.65 \pm 0.07	0.018*
Serum leptin level (ng/ml)	58.7 \pm 27.17	48.75 \pm 13.19	0.048*	
Serum osteocalcin level (ng/ml)	19.74 \pm 8.05	21.2 \pm 8.36	0.5	

KOA: knee osteoarthritis, BMD: bone mineral density, BMI: body mass index.

* Significant at $p < 0.05$.

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