Bone Mineral Density and Some Physiological Changes in Rheumatoid Arthritis Patients

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Abstract

Rheumatoid arthritis (RA),was relatively common disease with many extra articular manifestations; one of these manifestations was osteoporosis which is well-known complication of rheumatoid arthritis ,related to disease activity, that may occur by RA itself or as a side effect to pharmacological treatment.The study was designated to estimatedifference in bone mineral density results between patients with RA and control group.The cross-sectional/control study was conducted in rheumatology unit in Marjan teaching hospital in AL-Hilla city/Babylon /Iraq from 12th / November/2012 to 31th / May / 2013. The total number of subjects involved in this study was 184 (120 patients and 64 apparently healthy persons as control). Bone mineral density results were significantly lower in RA patients than in control group. The study revealed that osteoporosis was common in RA patientsandbone loss in RA was an ongoing phenomenon which continues despite anti-inflammatory treatment with DMARD.

الخلاصة

التهاب المفاصل الروماتيزمي هو مرض شائع نسبيا مع كثير من الاعراض الغير مفصليه ، واحدة من هذه الاعراض هو مرض هشاشة العظام الذي هومن المضاعفات المشهورة لمرض التهاب المفاصل الروماتيزمي (RA) و المتعلقة بنشاط المرض. وصممت الدراسة لتقدير الاختلاف في كثافة المعادن في العظام بين مرضى التهاب المفاصل الروماتيزمي ومجموعة المقارنة.

تمت هذه الدراسة المقطعية/المقارنة (Cross–sectional/control study) في وحدة أمراض الروماتيزم في مستشفى مرجان التعليمي في مدينة الحلة من ١٢تشرين الثاني ٢٠١٢إلى ٣١ ايار 2013. وكان العدد الكلي للأشخاص المشتركين في هذه الدراسة ١٨٤ شخص (١٢٠ مريضا و ٦٤ مقارن).وكانت نتائج كثافة المعادن في العظام لدى مرضى التهاب المفاصل الروماتيزمي اقل بكثير من مجموعة المقارنة.

استنتجت الدراسة أن فقدان العظام لدى مرضى التهاب المفاصل الروماتيزمي ظاهرة مستمرة التي لا تزال على الرغم من العلاجات المضادة للالتهابات (DMARD).

Introduction

Rheumatoid arthritis (RA) is a chronic inflammatory autoimmune disease that causes chronic inflammation of the synovium with subsequent destruction and deformity of the joints [1].

Rheumatoid arthritis affects approximately 0.5%-1% of adults all over the world. Individuals are usually diagnosed between the fourth and sixth decades of life.Women are 2 to 3 times more likely to be diagnosed than men [2,3].

Rheumatoid arthritis associated with a high risk for morbidity and premature death secondary to the earlier development of cardiovascular disease ,lung diseases and malignancy [4].

Bone and cartilage erosion occur during the natural progression of RA as a result of subtle underlying abnormalities in immune regulation and function. Accumulation and persistence of the lymphocyte infiltrate in the rheumatoid synovium are characteristic features of the disease [5].

Extra-articular manifestations of rheumatoid arthritis occur in about 40% of patients, either in the beginning or during the course of their disease [6].

Systemic features in RA are frequent, mostly related to vasculitis, and often a reflection of longstanding inflammation, most organs can be involved. These manifestations occur as frequent in men as in women and may appear at any age [7].

Bone destruction is a central feature of rheumatoid arthritis. Increased osteoclast activity contributes to local and systemic abnormalities of bone remodeling, including bone erosions and focal and systemic osteoporosis [8]. So, the risk of fracture resulting from bone fragility is the most important clinical aspect of the disease [9].

Osteoporosis (OP) is more frequent in patients with RA than in the general population due to active systemic inflammation characterized by low bone mass, and micro architectural deterioration of bony tissue, with a consequent increase in bone fragility and susceptibility to fractures [10].

The incidence of osteoporosis amongpatients with rheumatoid arthritis is 15-20% at the hip and spine [11].

Aim of The Study

The aim of the study involved:

1-The evaluation of changes in bone mineral density in rheumatoidarthritis patients by examining the bone mineral density in symptomatic and asymptomatic osteoporotic patients.

2-The determination of the effect of drug used in treatment on bone density.

3- Determine whether lower bone mineral density is associated withhigh erosion scores among patients with RA.

4- Elucidate the relation between severity of disease , duration of rheumatoid arthritis, duration of treatment and changes in bone mineral density.

Materials and Methods

This study was approved by the local research ethics committee.The study was conducted in Merjan Teaching Hospital from November /2012 to May/2013to identify the prevalence of osteoporosis in RA patients .In this study120 patients (91 female and 29 male) who had RA were included. All the patients diagnosed with rheumatoid arthritis according to ACR revised criteria 1987 and clinically assessed by rheumatologist. All patients was free from any endocrine orchronic digestive tract conditions,spontaneous vertebral fracture, kyphosis or scoliosis, smokers, pregnant women,history of cancer ,secondary myositis or any inflammatory myopathy or connective tissue disease combined with RA, and patients on antiresorptive treatment which may interfere with the results of bone mineral density.

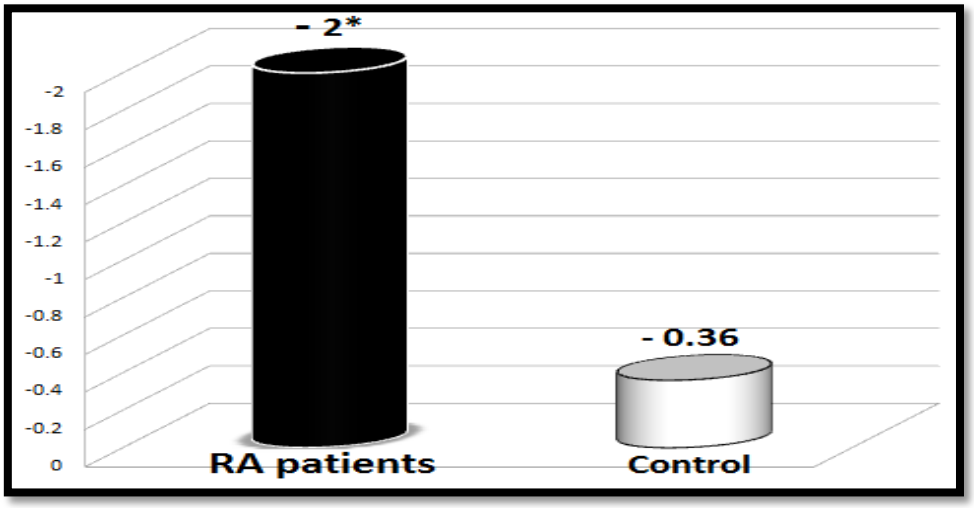
Sixty four apparently healthy persons were chosen as control group , they were similar to patients in age, sex, occupation and residence with the same exclusion criteria of the patients.

Bone mineral density at the lumbar spine were measured using dual energy x-ray absorptiometry (DXA).Based onbaseline T scores, patients were categorized into three groups:

osteopenia(-1> T-score> -2.5), osteoporosis (T-score ≤ -2.5)or normal (T-score ≥ -1).

Results

Bone mineral density was significantly lower (p<0.05) in RA patients than in control group (Figure.1).



P<0.05

Figure 1 Bone mineral density(BMD) in rheumatoid arthritis patients and control group.

Osteopenia was found in 18.7 % of RA patients and osteoporosis in 38.8% of RA patients. While, normal bone mineral density was 42.5%,of RA patients.

In regard to rheumatoid arthritis profile table.(1) show bone mineral density changes in relation to rheumatoid arthritis profile.

Table 1 Bone mineral density changes in relation to rheumatoid arthritis profile

Variable		Bone mineral density		
		Osteopenia %	**Osteoporosis %**	**Normal %**
Duration of RA P < 0.05	<1year	25	12.5	62.5
	1-9 years	24.7	23.2	52.1
	10-19 years	25	41.7	33.3
	>20years	26.7	**73.3***	0.00
Treatment P > 0.05	With DMARD	28.9	29.9	41.2
	Without DMARD	30.5	21.7	47.8
Steroidtreatment P>0.05	With Steroid	30	37	33
	Without Steroid	15.2	22.8	62
DAS28 P<0.05	Mild	0.0	0.0	**100***
	Moderate	26.1	17.4	56.5
	Sever	30	38.6	31.4

DAS 28: disease activity score.

In regard to morning stiffness andrheumatoid nodule normal bone mineral density results was significant (p<0.05) in percentage76.5%,75% in patients with negative morning stiffness and without rheumatoid nodule respectively.

While, no significant difference (p>0.05) in bone mineral density

results between patients with positive rheumatoid factor as compare with negative rheumatoid factor.

Osteoporosis was significant ($p<0.05$) in patients with present bone erosion in percentage 80.4% in rheumatoid arthritis patients.

Body mass index(BMI) was taken to all patients ,in RA patients with morbid obesity normal bone mineral density results was highly significant ($p< 0.01$) in percentage 54.9%.While,In RA patients with typical BMI osteopenia was found in 3% and 45% had osteoporosis.

Also ,patients was divided into two groups according to physical activity: sedentary and non-sedentary life style the results was in RA patients with non-sedentary physical activity, normal bone mineral density results was significant ($p<0.05$) in percentage 69.4%.

Discussion

Osteoporosis is more common in patients with RA than in the general population .In the current study bone mineral density results show significant decrease ($p<0.05$) in RA patients as compare to predictive value in control group.The same findings are reported byother studies of Dolan,*et al.*,(2002); Van Staa, *et al.*,(2006); Hafez,*et al.*, (2011); Heidari,*et al.*, (2012), [12-15]. This difference between RA patients and control group is due to direct effect of RA on bone density by the fact that chronic synovial inflammation in RA leading to overexpression of tumour necrosis factor (TNF) that can promote osteoclastogenesis leading directly to both focal and generalized bone loss and increased risk of fractures.

In addition, many indirect factors associated with inflammatory arthritis contribute to the risk of osteoporosis, These includes: immobility; weight loss; low calcium diet and use of medications known to promote bone loss such as glucocorticoid.

In the current study osteoporosis was significantly higher (73.3%) in long duration of disease (more than twenty years).This result agrees withSarkis,*et al.*,(2009); Gu¨ler-Yu¨ksel, *et al.*, (2009), [11,16]. This fact may be due to high disease activity ;delay diagnosis of disease; with poor compliance to treatment.

There was no significant difference in bone mineral density results between patients with treatment and without treatment this result goes with Heidari,*et al.*,(2012); Hafström,*et al.*, (2009); Di Munno,*et al.*,(2005), [15,17,18] The findings of the present study indicate that bone loss in RA is an ongoing phenomenon which continues despite the anti-inflammatory effect of DMARD that will reduce inflammation in several joints like hip joints and exert beneficial effect in preserving further BMD. While the lumbar spine region is less affected by inflammatory process in RA, and therefore, no beneficial effect of anti-inflammatory treatment is expected to be gained.

In the present study bone mineral density was affected by glucocorticoid treatment but not statistically significant. This result matches with the results obtained by Van Staa, *et al.*,(2006);Wijbrandts, *et al.*,(2009); Kim,*et al.*, (2010), [13,19,20].The findings of the current study may have been due to the low dose of corticosteroid administered and low dose glucocorticoid may reduce markers of bone formation leading to generalized osteoporosis, but they also counteract RA-associated inflamm-ation and slow the rate of bone loss proximal to sites of active disease.

In the present study patients with mild disease activity were significantly normal bone mineral density than moderate and sever DAS and patients

with severe DAS have the highest percentage of osteoporosis this finding agrees with studies of Heidari, *et al.*,(2012); Myo,*et al.*, (2011),[15, 21].This may be related to the effects of pro-inflammatory cytokines on bone cells ,that patients with active RA are at increased risk of developing osteoporosis.

Morning stiffness and Rheumatoid nodule both show significant relation to bone mineral density changes as highest percent of patients with no morning stiffness and/or no Rheumatoid nodule having normal bone mineral density results.

This may be explained by that both morning stiffness and Rheumatoid nodule occur more in severe form of RA. So, when they are absent indicates less severe form of RA leading to little involvement of bone mineral density as changes in bone density occur more in sever RA.

There was no significant difference ($p>0.05$) in bone mineral density results in relation to presence of rheumatoid factor .This results agrees with the studies ofHafez,*et al.*,(2011); Mobini,*et al.*,(2012), [14,22].

Normal bone mineral density results was significant ($p<0.05$)in patients with absent bone erosion this consistent with Gu¨ler-Yu¨ksel,*et al.*,(2009); Zhang,*et al.*,(2010); Desai, *et al.*, (2010), [16,23,24]. The association between progressive erosive disease and generalized BMD loss indicates common pathophysio-logical mechanisms, that osteoclasts mediate focal bone erosions in RA and the extent of focal bone erosions generally correlates with the severity of RA and progresses throughout the course of disease.

Normal bone mineral density results was highly significant ($p<0.01$) in patients with morbid obesity,this result goes with the studySarkis,*et al.*,(2009); Finkelstein, *et al.*,(2008); Short,*et al.*,(2011),[11,25,26]. This may be due toa larger body mass imposes a greater mechanical strain on bone, however, osteocytes are thought to sense mechanical loading of the skeleton and in response to that it will sent a signals to other bone cells that either reduce osteoclastic bone resorption or increase osteoblastic bone formation resulting in an attenuation of bone loss in heavier women and in response, bone mass may increase to accommodate the greater load.

Non-sedentary level of physical activity was highly significant (69.4%) in patients with normal bone mineral density results this agrees withBilberg,*et al.*,(2005); Lemmey,*et al.*,(2009); Thompson,(2009),[27-29]. This result may be related to the effect of physical activity in improving muscle strength and preventing falls(in postmenopausal women and old male) which is important because most fragility fractures are related to falls. While, in children ,adolescents and young adult physical activity may increase peak bone mass.

In conclusion, the findings of this study indicate that bone loss in RA is an ongoing phenomenon which continues despite anti-inflammatory treatment with DMARD. Preservation of bone mass in RA requires additional treatment program for osteoporosis. So early interventional therapy and screening are required to prevent development of destructive RA and its sequel.

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