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Prevalence of Osteoporosis Among Patients with Rheumatoid Arthritis

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Abstract

Background and objectives: Rheumatoid arthritis is an autoimmune disease characterized by inflammation of the joints. The aim of this study was to investigate the prevalence of osteoporosis among patients with rheumatoid arthritis in Erbil city.

Methods: A cross-sectional study was conducted in Rizgary and Hawler Teaching Hospital that started from September 2022 to September 2023. A convenient sample of hundred patients was included in the study. Rheumatoid arthritis patients were assessed in a cross-sectional design by Dual Energy X-ray Absorptiometry Scan T-score. All participants registered an initial two paged questionnaire form; a verbal consent was achieved from all patients. Bone densitometry solution was used in Hawler Teaching Hospital and to be calibrated to their standards.

Results: Patients with rheumatoid arthritis in whom bone mineral density was measured, 31 patients (31 %) had osteoporosis, 33 patients (33%) had osteopenia, 36 patients (36%) had normal result. Odd ratio (OR), its 95% confidence interval was calculated for results with positive finding from baseline characteristics. For example, Patients with osteoporosis had longer disease duration (≥7 years; OR= 2.84, 95 % CI: 1.03 to 7.83, P= 0.042).

Conclusion: Osteoporosis is prevalent among rheumatoid arthritis patients in Erbil city. The prevalence was significant among lower body mass index, steroid users and old age post menopause patients.

Keywords: Body mass index, Osteoporosis, Rheumatoid arthritis, Risk factors

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Introduction

Osteoporosis is defined as low level of bone mineral density, which is caused by change in fine structures of bone. Predisposes patients to fractures by low force trauma and results in significant disability.[1] Rheumatoid arthritis is one of the most common autoimmune diseases that in the early stages of the disease begins with pain and symmetrical swelling of the small joints of the hands, feet, swelling of the soft tissue around the joints and morning stiffness and fatigue and it is characterized by persistent synovitis and progressive destruction of symmetrical multi-joints and intra-articular manifestations including subchondral lesions, decreased bone mass, and reduced generalized bone density.[2,3] Osteoporosis is one of the most known common extra-articular complications of rheumatoid arthritis and its prevalence in rheumatoid arthritis patients is almost twice that of the general population. Osteoporosis is a systemic skeletal disease characterized by decreased bone mineral density and its complication (increased fragility and fracture due to reduced resistance to torsion and compression). Bone fragility in people with rheumatoid arthritis includes a combination of systemic inflammation, circulating autoantibodies, and pro-inflammatory cytokines (IL1, IL6, TNF, etc.).[4] Chronic inflammation in people with RA affects bone metabolism and disrupts the normal resorption cycle and reduces localized and generalized bone mineral density (BMD). There are three types of bone cells: osteoblasts are responsible for bone formation, osteoclasts are responsible for bone resorption, and osteocytes are basic cellular components in bone remodeling. Under normal circumstances there is balance between the amount of bone resorption and the amount of bone formation. Pathogenesis of osteoporosis in rheumatoid arthritis is due to interaction between immune system and bone remodeling process, inflammatory pathway in RA is initiated by interleukins such as (IL-1, IL-6 and IL-8) and tumor necrosis factor-alfa (TNF-α).[5] Bone mass index is decreased by risk factors such as disease severity, gender, especially after menopause, decreased vitamin D levels, advanced age, using corticosteroids and disease-modifying anti-rheumatic drugs (DMRADs) and decreased mobility.[6] Fractures increase morbidity and mortality, reduce quality of life, reduce independent functioning of people, especially in old age, and increase economic burden. Vertebral fracture is one of the most common fractures due to decreased BMD, which causes limitation of activity, disability, kyphosis and decreased pulmonary function.[7] The diagnosis of osteoporosis is made by measuring of bone marrow density, which is assessed by dual x_ ray absorptiometry (DEXA) scan according to World Health Organization (WHO) classification T score. World Health Organization (WHO) implied criteria based on T score to diagnose osteopenia (T score between −1.0 and −2.5 SD), osteoporosis (T score at −2.5 SD and less) and normal result (T score at −1 and more). Fracture Risk Assessment (FRAX) tools scoring system is used to compute the 10 years probability of a major osteoporotic fracture (i.e., vertebral, hip and long bones).[8] The aim of this study was to investigate the prevalence of osteoporosis among patients with rheumatoid arthritis in Erbil city.

Patients and methods

All 100 patients of rheumatoid arthritis (RA) in this research registered an initial two paged questionnaire form, a verbal consent was achieved from all patients, demographic picture and medical history were obtained. Patients were assessed in a cross-sectional design and divided into three groups according to their Bone Mineral Densitometry (BMD) status (i.e., osteoporotic, osteopenic and normal

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group).A total of 100 patients with RA were recognized initially from September 2022, patients who visited the Rheumatology Consultation and medical ward at the Rizgary Teaching Hospital, all participants have been diagnosed as RA according to the American College of Rheumatology/European League against Rheumatism (ACR/EULAR) 2010 classification criteria, which at least 6 scores are needed for the definite diagnosis of (RA), which is based on number and types of Joints involved, serology, acute phase reactants, duration of the disease. The inclusion criteria included aged over 18 years and having RA. Medical information of the participants was collected including demographics, clinical, laboratory, and treatment data. Lifestyle habits (e. cigarette smoking, heavy alcohol intake), medical background (i.e., BMI, comorbidities such as hypertension (HTN), diabetes mellitus, thyroid disease, chronic kidney disease (CKD), liver disease, cardiovascular disorders (CVD), respiratory disorders and osteoarthritis (OA)), and previous histories (i.e., COVID-19 infection, osteoporosis and fractures) were notified. Rheumatoid arthritis related medications including dose and duration of oral glucocorticoids and use of either conventional synthetic DMARDs (i.e., Methotrexate, Leflunomide, Hydroxychloroquine and Sulfasalazine Azathioprine) or biological synthetic DMARDs (i.e., Infliximab, Rituximab, Adalimumab and Etanercept) was reported. All participants in this research registered an initial two paged questionnaire form, a verbal consent was achieved from all patients, demographic picture and medical history were obtained. Joint swelling and tenderness were assessed for Disease activity, these evaluations together with laboratory results, medication information (current and cumulative glucocorticoids doses), history of previous fracture, osteoporosis, smoking, and alcohol intake were all entered into the database. Laboratory data to identify the seropositive status of RA by anti-CCP and RF. Disease activity was monitored using ESR and Disease Activity Score-28 (DAS28-ESR). The DAS28-ESR calculator data inputs are number of tender and swollen joints, global health and acute phase reactant (ESR). A DAS28 of greater than 5.1 means the disease is highly active, between 3.2 and 5.1 implies moderate disease activity, between 2.6 to 3.2 the diseases activity is low, and less than 2.6 indicates remission. Only patients with BMD data obtained three months from the time of enrollment were included in this study. Bone mineral densitometry (BMD) was assessed by Dual Energy X-ray absorptiometry (DEXA) scan. Diagnoses of osteopenia and osteoporosis were made based on the (WHO) T-score criteria (-1.0 to -2.5 SD and ≤ -2.5 SD) respectively. osteoporosis was identified at the lowest T-score at either the three sites (total hip, femoral neck or lumbar spine) according to the recommendation from the (ISCD). For those reasons, population in our study has been classified into three groups (osteoporotic, osteopenic and normal) based on the T-score. This research is submitted to the Ethics and Scientific committees of the Kurdistan Higher Council of Medical Specialties for scientific and ethical approval. The purpose of this study is explained for each patient and a written consent is obtained from each patient. Baseline characteristics were compared between three groups (osteoporosis, osteopenia and normal), all groups were defined by bone mineral density results measured by DEXA scan T-score, mean and standard deviation were calculated.

Results

All 100 participants were fulfilling the 2010 ACR/EULAR criteria for diagnosis of rheumatoid arthritis and provided the required information on time, demographic and clinical characteristics were assessed and they have been divided into three groups:

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osteoporosis, osteopenia and normal result. A pie chart shown in Figure (1). represents the differences of the DEXA scan between female and male participants, in which osteopenia account for the majority of the results among male participants.

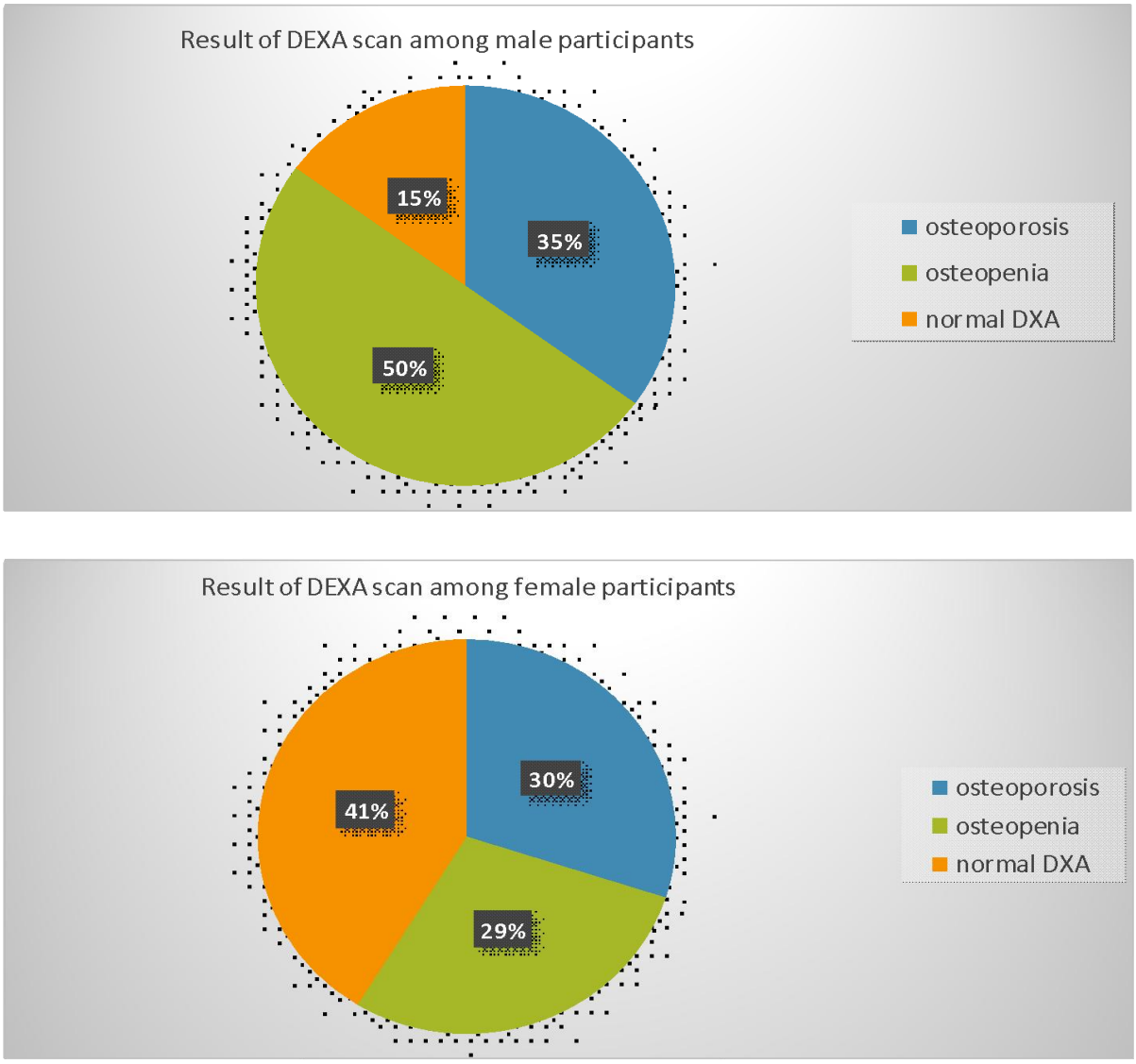

Figure (1): Difference between result of Dual-Energy X-Ray Absorptiometry (DEXA) scan, among male and female participant illustrated in a pie chart.

The mean age of participants was 49.46±11.50 years (mean ± SD), 80% of participants were females, 20% were males. Male to female ratio was 1 to 4. 1:1 ratio maintained between pre-menopausal and post-menopausal females, disease duration was about 10.72±9.36 years (mean ± SD), mean BMI was about 27.81±5.81 kg/m² (mean ± SD). The RA patients with OP had longer disease duration, lower BMI, a statistically significant difference was observed between three groups, with a lower BMI in osteoporotic (25.45±2.77) compared to osteopenic (27.47±6.31) and normal group (30.35±6.48) (mean ±SD). In this study the mean DAS28-ESR was about (4.76±0.96)

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(mean ±SD).), It was noted that mean ESR result among OP group was higher than normal but lower than osteopenic group with significant P value (P= 0.021), Table (1).

Table (1): Demographic and clinical characteristics of the study population

Variables	Total N= (100) 95 % CI ±SD	Osteoporotic group N= (31) 31 %	Osteopenia group N= (33) 33%	Normal group N= (36) 36 %	P value
Age (mean) ±SD	49.46±11.50	53.62±8.86	48.39±12.61	46.58±11.75	0.035
Gender Female Male (Male to female ratio 1 to 4)	 N= (80) 80 % N= (20) 20%	 24 24.80% 7 6.20%	 23 26.40% 10 6.60%	 33 28.80% 3 7.20%	0.067
Pre-menopausal female Post-menopausal Female In a ratio 1 to 1	N= (40) 40% N= (40) 40%	7 12.00% 17 12.00%	14 11.50% 9 11.50%	19 16.50% 14 16.50%	0.049
Duration of disease	10.72±9.36	15.75 ±10.45	9.52±8.37	7.19±7.16	<0.001
BMI kg/m*	27.81±5.81	25.45±2.77	27.47±6.31	30.35±6.48	0.002
DAS 28 ESR	4.76±0.96	4.65±0.51	4.94±1.24	4.70±0.97	0.438
T score	-1.66 ±1.42	-3.08 ±0.40	-1.94 ±0.36	-0.05 ±1.04	< 0.000

Fifty four percent of patients were on prednisolone or its equivalent glucocorticoid. Dose of steroid was not statistically different between groups, while cumulative steroid was. Higher cumulative glucocorticoid used among OP group than the patients in the other groups (p = 0.035). DMARDs were independent risk factors among OP group (p =0.021), Table (2).

Table (2): Treatment data

Variables	Total N= (100)95 % CI ±SD	Osteoporotic group N= (31) 31 %	Osteopenia group N= (33) 33%	Normal group N= (36) 36 %	p value
Dose of steroid	5.74±2.97	5.5±1.53	6.25±4.23	5±0	0.492
Cumulative dose of steroid	10.57±13.7	16.43±18.37	8.23±8.56	4.48±7.26	0.036
Treatment (1 to 1 ratio maintained) Non-biological DMARDs	 N= (50) 50%	 12 15.5%	 23 16.5%	 15 18%	0.021
Biological DMARDs	N= (50) 50%	19 15.5%	10 16.5%	21 18%	

The higher frequency of previous fractures was noted in OP patients than the patients in the other groups, especially fractures of the digits and wrist (p = 0.046). Osteopenia is slightly more in smokers than alcohol drinkers (p = 0.367). all three groups that they had history of COVID-19 were not significantly different (p =0.018), Table (3).

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Table (3): History of fracture and smoking, alcohol, COVID 19 histories

Variables	Total N= (51) 95 % CI ±SD	Osteoporotic group N= (24) 24%	Osteopenia group N= (11) 11%	Normal group N= (14) 14 %	p value
History of fracture	N= (14) 14%	9 9%	2 2%	3 3%	0.046
History of smoking	N= (12) 12%	4 4%	6 6%	2 2%	0.367
History alcohol	N= (2) males 2%		2 2%		
History of COVID-19	23 23%	11 11%	1 1%	9 9%	0.018

Discussion

In this study, we found that the prevalence of OP in RA patients was 31%. This result is considered to be compatible to other studies in different parts of the world. According to the results, the prevalence of OP varies in different countries and continents, which can be attributed to the population density and different time of studies, age, economic situation and lack of government attention to the issue. In addition, difference in the quality of providing medical services, access to osteoporosis screening methods, and controlling the risk factors related to it and also preventing the disease play an important role. The results of our study and other studies have shown that the prevalence of OP in people with RA is higher than the general population. Various factors play a role in increasing the prevalence of OP in patients with rheumatoid arthritis, the most important of which are continuous inflammation, glucocorticoid use, reduced physical activity due to old age and disability, and the use of DMARDs.[9-11] A systematic review conducted by Salari study to estimate the prevalence of OP in the general population. After review of 86 included studies, the worldwide prevalence of OP is estimated as 18.3% and in Asia, Europe, the Americas and Africa it was estimated as 16.7, 18.6, 12.4, and 39.5%, respectively. According to their study, the estimated prevalence was lower compared to our study, the reason is that people with RA have a higher risk of developing OP than the general population. In this study, the prevalence was lower in the Americas and higher in Africa followed by Asian and European countries.[12] In South Korea, study done by Kim D et al. in this study they investigated the results of 227,812 cases of RA with 64,290 cases of OP and it should be highlighted that 142,955 of these cases (63%) are related to the study conducted, and the prevalence of OP reported as 33.8% in their study.[13] In Corrado study, immunosuppressive drugs such as glucocorticoids and DMARDs are used to treat RA. Glucocorticoids with their anti-inflammatory effects can prevent local and systemic decrease in BMD. Furthermore, DMARDs are used to achieve remission, and evidence suggests that DMARDs prevent structural damage to cartilage and bone.[14] In Rotta study, the incidence of OP is caused by several factors among RA patients. In the pathogenesis of inflammation and reduction of BMD, various factors in immune system, are involved such as hyper-expression and the effect of autoantibodies against citrullinated proteins, pro-inflammatory cytokine secretion, and receptor activator of NF-kappa B ligand derived from T-cell.[15] The highest pooled prevalence (28.1%, 95% CI 24.4–31.8%) was obtained by omitting the study of Innala et al. and the lowest pooled

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prevalence (27.0%, 95% CI 23.3–30.7%) was obtained by omitting the study of Hu et al. The highest prevalence was found in studies conducted during 2011–2015 (36.2%), followed by 2016–2021 (27.1%).[16,17] In a meta-analysis, Ramírez et al. Reviewed the results of 45 articles and found that the prevalence of OP in patients with axial spondylarthritis varies from 11.7 to 34.4%.[18] In another meta-analysis study conducted on the general Chinese population, Chen et al. revealed that the prevalence of OP ranged from 1 to 85%.[19] Decreased vitamin D intake is associated with an increased risk of RA, and also vitamin D deficiency is associated with disease activity in patients with RA.[20] Therefore, vitamin D deficiency can be one of the common causes of RA and OP. The results of a meta-analysis study showed that vitamin D deficiency in RA patients is significantly higher than healthy individuals and serum vitamin D levels are inversely related with disease activity.[21]

Conclusion

Despite advances in the identification of the destructive mechanism and pharmacological treatment of rheumatoid arthritis, the complications associated with this disease are still common. So, screening and assessing the prevalence of osteoporosis and proper management, especially in relation to timely identification, is essential to prevent fractures. For this reason, in this study, we systematically reviewed the international databases and the results of related papers were pooled regarding the prevalence of osteoporosis.

Disclosure

The authors assert that they have no conflicts of interest.

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