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ORIGINAL RESEARCH

A Comparison of Demographics, Disease Activity, Disability, and Treatment Among Rheumatoid Arthritis Patients with and without Osteoporosis

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Introduction: Osteoporosis (OP) is one of the most common comorbidities associated with rheumatoid arthritis (RA). Literatures reported that the risk for developing OP was strongly associated with duration and severity of RA. We aim to elaborate on the consequences of OP on disease activity and management plan in patients with RA.

Patients and Methods: A retrospective cohort study recruited 408 patients, including those with RA alone and with RA plus OP. The RA disease activity in the patients was assessed using disease activity score in 28 joints (DAS28-CRP). A statistical analysis was performed to compare data between the two groups of patients and determine any significant risk factor associated with the development of OP in RA patients.

Results: Of 408 patients who were included in this study, 353 patients (86.5%) had only RA, while 55 patients (13.5%) had RA with OP and showed significant difference ($P = 0.04$) concerning age categories. Patients diagnosed with RA and OP had RA duration longer than RA-only patients (independent t-test, $P = 0.01$). The two groups had almost similar disease activity at the three clinical visits, as well, had nearly similar disability at their first visit, whereas RA with OP patients had significant greater disability at their 2nd and 3rd visits (independent t-test, $P = 0.001$). Both groups were treated with the same biologic and non-biologic medication of similar frequency, although RA patients with OP received steroid more frequently than patients had RA only (61.7% vs. 41.7%, chi square test, $P = 0.03$).

Conclusion: There was no significant difference in disease activity at both groups of patients. However, RA with OP group had longer duration of RA, were more frequently treated with steroids, and had greater disability. We recommend physicians focus on controlling RA disease activity, early screening for and treating of OP.

Keywords: rheumatoid arthritis, osteoporosis, disease activity, biologic, disease modifying antirheumatic drugs, effects, RA OP

Introduction

Generally, the rheumatic diseases are characterized by local and systemic bone loss that has multifactorial basis including direct effects of inflammatory process (disease activity), inadequate nutrition, decreased lean body mass, immobility, and the effects of therapeutic agents, namely glucocorticoids (GC).[1] Among these rheumatic diseases is rheumatoid arthritis (RA), a chronic inflammatory autoimmune disease of the joints that is associated with disabilities and multiple comorbidities including osteoporosis (OP), called secondary OP.[2] OP can be defined as a decreased bone mineral density (BMD) due to imbalance in bone remodeling

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cycle, where the rate of bone resorption exceeds bone formation, leading to microarchitectural deterioration that ultimately causes frail bones and susceptibility to fracture.[1,3] Very recently, Almutairi et al conducted a meta-analysis study based on systematic reviews to estimate the global prevalence of RA that appeared to be 0.46% with a 95% prediction interval (0.06–1.27%).[4] Multiple studies showed that OP occurred in 30–50% of RA patients,[5–7] where the risk for developing OP was strongly associated with duration and severity of the disease, in addition to the age and gender of the patients.[8,9] Therefore, pre-menopausal women with RA are two times more susceptible to have OP and bone fractures compared to age-matched healthy controls,[10] and so are male individuals with RA.[11]

In RA, the earliest radiological sign of bone destruction is the periarticular osteopenia, which is mainly associated with disease activity, and then followed by bone erosion that indicates increasing disease activity and disability of the disease.[1] Likewise periarticular bone loss, citrullinated proteins antibodies (ACPA) are associated with systemic bone loss, with a titer-dependent effect on BMD.[12] The further stage of markedly bone loss in RA is the development of OP.[1] The development of OP in patients with RA elaborates on the interplay between the cells of the immune system with those involved in the regulation of bone remodeling, in particular via receptor activator of the nuclear factor kappa-B ligand (RANKL)/osteoprotegerin (OPG) system and WNT/ß-catenin signaling pathways. RANKL is a cytokine of the tumor necrosis factor (TNF) family and, with its decoy molecule OPG, is essential for osteoclast maturation and development.[13] On the other hand, the WNT/ß-catenin signaling pathway activates the transcription of osteoblast-specific genes that enhances osteoblast differentiation and is considered as a major regulator of osteogenesis.[14]

The underlying pathology for developing the active disease in RA can be explained by the imbalance in the immune system (including the inflammatory cells and the released cytokines) that alter bone remodeling via inhibition of osteoblast differentiation, and induction of osteoclast differentiation and hence the net result is bone resorption leading to secondary OP. Accordingly, during disease activity, Th1 and Th17 cells produce the pro-inflammatory cytokines that have a significant role in the inflammatory and bone destruction processes. Of these cytokines, TNF-α, IL-1b, IL-6, IL-11, and IL-17 have stimulatory effects either directly on osteoclast differentiation and activation, or indirectly by enhancing cell surface expression of RANKL that stimulate osteoclastogenesis.[15] Moreover, TNF-α can induce the Wnt-signaling inhibitors, sclerostin and Dickkopf-related protein-1 (Dkk-1), leading to inhibition of osteoblastic differentiation.[16] In the contrary, the inhibitory cytokines including interferon (IFN)-γ, IL-4, and transforming growth factor-β (TGF-β) inhibit the expression of OPG on osteoblast.[14] Dkk-1 is a key regulator of joint remodeling in RA[17] that was found to be significantly elevated in RA patients in a 2018 meta-analysis on 1305 patients and 504 controls.[18] It has been reported that the OPG/RANKL ratio was lower in patients with active RA than in healthy controls, while Dkk-1 was higher in those patients.[19] However, following the treatment with anti-IL-6, the OPG/RANKL ratio started to increase, while Dkk-1 decreased.[19] Therefore, OP is an inevitable complication of RA, and despite the alarming data of the prevalence of OP among patients with RA, only about 45% of RA patients are receiving calcium and vitamin D supplements,[20] while only 5.4% of RA patients who are not taking glucocorticoids (GCs) are using bisphosphonates.[21] Adding to that, due to the subsequent negative impacts of OP on the quality of life of patients with RA, early prevention, diagnosis, and further proper treatment of OP is mandatory, as well as, controlling RA disease activity is important as this treatment can have anti-osteoporotic effects.

Clearly, OP can develop in RA patients through different mechanisms including RA itself as briefly explained, the use of GCs and simply as a post-menopausal state due to estrogen deficiency. In the current study, we proposed that OP in patients with RA has a negative consequence on disease activity and thus may worsen the prognosis of RA. Therefore, a statistical comparison was conducted on a retrospective cohort of two groups of patients, the RA-only (RA without OP) patients and the RA-OP (RA with OP) patients to elaborate on the effects of OP on disease activity, patients' outcomes, and management plan.

Patients and Methods

This retrospective cohort study was conducted at Doctor Soliman Fakeeh Hospital (DSFH), a private, tertiary hospital in Saudi Arabia's western region. DSFH employs one full- and two half-time rheumatology consultants to evaluate and treat patients. Medical records of 408 patients with RA following up in the clinics from May 2018 to August 2020 were reviewed from the Saudi registry of the

Rheumatoid Arthritis Saudi Database (RASD). The inclusion criteria of the study defined as adult patients (≥ 18 years) with the diagnosis of RA-only and RA plus OP (RA-OP). The diagnosis of OP was confirmed in the patients by scoring the BMD that was measured by dual-energy X-ray absorptiometry (DEXA) scan and the request based on the treating physician clinical judgement. According to the WHO criteria.[22] BMD showing T-score < −2.5 confirms the diagnosis of OP. However, glucocorticoid-induced OP (GIOP) was confirmed in patients receiving GCs by having BMD of T-score < −1.5 and required therapeutic intervention,[23] as recommended by the American College of Rheumatology (ACR) criteria.[24]

This study was carried out longitudinally and all patients had three clinical visits for follow up with at least one clinical visit a year. The disease activity of RA in the patients was assessed using Disease Activity Score in 28 joints (DAS28) with C-reactive protein (CRP).[25] Patients who did not complete DAS28-CRP full assessment, were lost to follow-up, or had missing data were excluded. The full description of inclusion criteria and follow up visit protocols were reported in detail in a previous RASD publication.[26] All patients had signed individual consent forms before including their data in RASD. An ethical approval was obtained from the DSFH-IRB. Our study is in full compliance with Declaration of Helsinki.

The primary objective of the study was to evaluate the impact of OP on RA disease activity in patients with RA using DAS28-CRP score.[25] Remission was diagnosed in patients with a DAS28-CRP score < 2.6, Low disease activity in patients with a DAS28-CRP score ≥2.6 and ≤3.2, Moderate disease activity with DAS28-CRP score >3.2 and ≤5.1 and High disease activity in patients with a DAS28-CRP score >5.1. The secondary objective was to identify the significant association of various risk factors linked to the occurrence of OP among RA patients using a multivariable logistic regression analysis. The demographic and clinical variables referred in (Table 1) were investigated as risk factors for OP in RA patients

Table 1 Multivariable Logistic Regression Analysis of RA-Only Patients and RA-OP Patients Based on Demographics, Clinical Characteristics, and Treatment.

Variable	Odds Ratio	Sig.	95% Confidence Interval of Odds Ratio	
			Lower	Upper
Age (years)	0.952	0.036	0.909	0.997
Gender (Male)	3.191	0.076	0.886	11.488
Gender (Female)	Reference group			
Nationality (Saudi)	1.949	0.181	0.733	5.181
Nationality (non-Saudi)	Reference group			
Comorbidities* (yes)	1.029	0.923	0.538	1.754
Comorbidities (No)	Reference group			
DAS28 score 1st visit	0.795	0.290	0.519	1.216
DAS28 score 2nd visit	1.940	0.058	0.978	3.849
DAS28 score 3rd visit	0.784	0.550	0.354	1.739
On biological DMARDs (Yes)	2.450	0.071	0.927	6.474
On biological DMARDs (No)	Reference group			
On non-biological DMARDs (Yes)	2.039	0.266	0.582	7.151
On non-biological DMARDs (No)	Reference group			
Use of Steroid (Yes) ng/mL	1.891	0.167	0.765	4.674
Vitamin D level (ng/mL)	1.003	0.721	0.987	1.020
BMI	0.987	0.741	0.915	1.065
RF positivity (YES)	0.927	0.884	0.337	2.548
RF positivity (No)	Reference group			
ACPA positivity (YES)	0.510	0.194	0.185	1.409
ACPA positivity (No)	Reference group			
CRP	1.007	0.770	0.961	1.055

Notes: The RA-only patients' group is the reference group. The control group is RA and OP. *Comorbidities include: Diabetes mellitus, Hypertension, and Chronic kidney disease.
Abbreviations: DAS28-CRP, disease activity score in 28 joints; DMARDs, disease modifying anti-rheumatic drugs; BMI, body mass index; RF, rheumatoid factor; ACPA, anti-citrullinated peptide antibody; CRP, C-reactive protein.

and included age, gender, nationality, BMI, presence of comorbidity (namely diabetes mellitus, hypertension, or chronic kidney disease), DAS28-CRP score at each of three consecutive visits, biologic or non-biologic disease modifying antirheumatic drugs [DMARDs], steroid use, and laboratory investigations (vitamin D level, CRP, rheumatoid factor [RF] positivity, and anti-citrullinated peptide antibodies [ACPA] positivity). DAS-28-CRP was calculated at each of the first 3 consecutive visits during the study period. Disability was measured by Health Assessment Questionnaire-Disability Index (HAQ-DI)[27] at each of the first 3 consecutive visits during the study period. The HAQ-DI was scored as 0 = without any difficulty, 1 = with some difficulty, 2 = much difficulty, and 3 = unable to do.

Statistical Analyses

All data was analyzed by using the Statistical Package for Social science (IBM SPSS version 25) software program. Categorical variables were presented as the total and percentage, and continuous variables as the mean and standard deviation (SD). The chi-square test and Fisher's exact test for categorical variables and independent *t*-test for continuous variables were conducted to determine any associations between baseline characteristics, DAS28-CRP score (remission and low disease groups vs. moderate and high disease groups), and RA only versus RA with OP groups.

Logistic regression analysis with odds ratio was conducted to assess any significant associations between the explanatory variables (as the risk factors) and the dichotomous outcome of RA patients who were defined as the dependent variable whether they had OP or not. A *P*-value less than 0.05 was considered statistically significant for all tests.

Results

A total of 408 patients met the study criteria and were evaluated. Among them, 353 (86.5%) patients had only RA, whereas 55 patients (13.5%) had RA with OP (Table 2). There were no significant differences in both groups regarding the following demographics including gender, nationality, and body mass index (BMI), as well as the vitamin D status and the presence of comorbidities (DM, HTN, CKD). However, there is a significant difference (P = 0.04) at the age categories between the two groups of patients, where patients with RA plus OP showed older age than those with RA without OP (RA patients 46.3 ± 10.3 vs. RA patients with OP 64.8 ± 10.8) (Table 2). In addition, compared to RA-only patients, RA-OP patients had a longer RA duration that showed significant difference (79.5 ± 52.5 months vs. 106.6 ± 62.6 months respectively, independent *t*-test, P = 0.01). Unexpectedly, RA patients with OP reported a smoking status less than patients with RA only (9.1% vs. 22.9%, Chi square test, P = 0.01) (Table 2).

On the other hand, the two clinical groups (RA-only and RA-OP patients) revealed similar disease activity at their all three clinical visits, based on DAS28-CRP score (Tables 2 and 3). Both groups of patients as well at the first clinical visit had similar disability that is measured by HAQ-DI. However, at the second and the third clinical visits, RA patients with OP had greater disability than RA patients without OP (Independent *t*-test, P = 0.001 for both visit).

Multivariable logistic regression analyses were performed to identify potential risk factors associated with the occurrence of OP in RA patients (Table 1). These factors included gender, nationality, presence of comorbidities, DAS28-CRP score, types of DMARDs (biologics or non-biologics), use of steroid, vitamin D level, BMI measurement, positive RF and ACPA, and CRP level. Apparently, there were no significant differences in these risk factors between the two groups of patients.

In addition, the differences in therapeutic management of RA between RA-only patients and RA-OP patients were evaluated in term the type of biologic and non-biologic DMARDs and their frequency (Table 4). The results of descriptive analysis showed that both RA-only patients and RA-OP patients had received biologics with no significant differences between both groups (55.2% vs. 43.6% respectively), and so did they with non-biologics DMARDs (85.6% vs. 85.5% respectively) (Table 4). The various biologic therapies that were prescribed including anti-TNF-alpha drugs (Adalimumab, Etanercept, Certolizumab), Janus kinase inhibitors drugs (Baricitinib and Tofacitinib), IL-6 receptor agonist (Tocilizumab), and anti-B cells therapy (Rituximab). The most type of biologics that had been used by RA-only patients was the anti-TNF-alpha drugs (54.5%) compared to (18.2%) of RA-OP patients used anti-TNF-alpha therapy. On the other hand, the RA-OP patients received Janus kinase inhibitors drugs more frequently (29.6%) than other biologic therapies. With regards the non-biologic DMARDs, the most frequent drugs used by both RA patients with and without OP was methotrexate (33.1% vs. 46.8%) and showed no significant difference.

Table 2 Demographic Characteristics of Study Patients

Characteristics		All Patients N= 408 (100%)	RA** N= 353 (86.5%)	RA and OP** N=55 (13.5%)	P value*
Age (years)			46.3 ± 10.3	64.8 ± 10.8	0.04
RA duration			79.5 ± 52.5	106.6 ± 62.6	0.01
OP duration			–	82.0 ± 47.9	–
Gender	Male Female	92 (22.5) 316 (77.5)	83 (23.5) 270 (76.5)	9 (16.4) 46 (83.6)	0.23
Nationality	Saudi Non-Saudi	255 (62.7) 152 (37.3)	217 (61.6) 135 (38.4)	38 (69.1) 17 (30.9)	0.28
Smoking status	Smoker Non-Smoker	86 (21.1) 322 (78.9)	81 (22.9) 272 (77.1)	5 (9.1) 50 (90.9)	0.01
Comorbidities***	Yes No	262 (64.2) 146 (35.8)	227 (64.3) 126(35.7)	35 (63.6) 20 (36.4)	0.92
BMI	Underweight Normal Weight Overweight Obese	3 (0.7) 85 (20.9) 108 (26.6) 210 (51.7)	1 (0.3) 74 (21.1) 94 (26.8) 182 (51.9)	2 (3.6) 11 (20.0) 14 (25.5) 28 (50.9)	0.20
Vitamin D level (ng/mL)			58.2 ± 27.1	55.8 ± 26.0	0.23
DAS28 score		1st visit 2nd visit 3rd visit	3.00 ± 0.98 1.90 ± 0.60 1.68 ± 0.51	3.1 ± 1.0 2.13 ± 0.56 1.74 ± 0.33	0.52 0.40 0.42
HAQ- DI score		1st visit 2nd visit 3rd visit	0.64 ± 0.42 0.28 ± 0.25 0.14 ± 0.18	0.79 ± 0.41 0.51 ± 0.33 0.39 ± 0.30	0.68 0.001 0.001

Notes: *P-value based on chi-square, Fisher exact test, or independent *t*-test as appropriate. ** N (%) and Mean ± SD are presented as appropriate. ***Comorbidities include: Diabetes mellitus, Hypertension, and Chronic kidney disease.
Abbreviations: RA, rheumatoid arthritis; OP, osteoporosis; BMI, body mass index; DAS28, disease activity score in 28 joints; HAQ –DI, Health Assessment Questionnaire-Disability Index.

Table 3 Disease Activity as Measured by DAS28 Score During the First 3 Clinic Visits in RA-only Patients and RA-OP Patients. Comparison of Patients with Remission & Low Disease Activity to Those with Moderate & High Disease Activity. Data Presented as Number and (%)

Characteristics		All Patients N= 408	RA N= 353	RA and OP N= 55	P value**
DAS 28 score 1st visit	Remission & Low disease activity Moderate to High disease activity	238 (58.3) 170 (41.7)	210 (59.5) 143 (40.5)	28 (50.9) 27 (49.1)	0.23
DAS 28 score 2nd visit	Remission & Low disease activity Moderate to High disease activity	392 (96.1) 16 (3.9)	339 (96.0) 14 (4.0)	53 (96.4) 2 (3.6)	0.90
DAS 28 score 3rd visit	Remission & Low disease activity Moderate to High disease activity	396 (97.3) 11 (2.7)	341 (96.9) 11 (3.1)	55 (100) 0	0.14

Note: ** Chi-square or Fisher exact test as appropriate.
Abbreviations: RA, rheumatoid arthritis; OP, osteoporosis; DAS28, disease activity score in 28 joints.

In contrast to biologic and non-biologic medications, treatment with GCs revealed significant difference (Chi square test, $P = 0.03$) between RA-only patients (41.7%) compared to RA-OP patients (61.7%). Finally, in addition to DMARDs, most patients having RA with OP (61.5%) were receiving a RANK-ligand inhibitor (Denosumab) as

Table 4 Types of Treatment Used by Diseased Groups. N(%)

Type of Treatment		Only RA (N=353)	RA with OP (N=55)	P value*
Biologic RA treatment received	Yes No	196 (55.2) 157(44.8)	24(43.6) 31(56.4)	0.11
Type of biological treatment	Actemra§ Baricitinib Cimzia Enbrel Humira Rituximab Tofacitinib	26(13.3) 3(1.5) 23(11.7) 41(20.9) 43(21.9) 4(2.0) 55(28.1)	1(1.8) 1(1.8) 1(1.8) 3(5.5) 6(10.9) 2(3.6) 10(18.2)	0.07 0.25 0.59 0.48 0.34 0.68 0.78
Non-biologic RA DMARDs received	Yes No	302(85.6) 51(14.4)	47(85.5) 8(14.5)	0.35
Type of non-biological DMARD	Arava Methotrexate Plaquenil Sulfasalazine Methotrexate and plaquenil Methotrexate and Arava Arava and plaquenil Sulfasalazine Cellcept Plaquenil and sulfasalazine Sulfasalazine and Methotrexate	36(11.9) 100(33.1) 86(28.5) 5(1.7) 52(17.2) 12(4.0) 6(2.0) 1(0.3) 0 1(0.3) 2(0.7)	6(12.8) 22(46.8) 11(23.4) 1(2.1) 2(4.3) 0 3(6.4) 0 1(2.1) 1(2.1) 0	0.48 0.09 0.87 0.63 0.47 - - - 0.98 -
Use of Steroids for RA	Yes No	126 (41.7) 176 (58.3)	29 (61.7) 18 (38.3)	0.03
OP treatment	Yes No Fosamax Densukl; mab Protelos	- - - - -	52(94.5) 3(5.5) 19(36.5) 32 (61.5) 1(1.9)	-

Note: *p-value based on chi-square test or Fisher exact test as appropriate.
Abbreviations: RA, rheumatoid arthritis; OP, osteoporosis; DMARDs, disease modifying anti- rheumatic drugs.

anti-osteoporotic medication, but a lower percentage (36.5%) received bisphosphonate (Fosamax) (Table 4).

Discussion

Local and systemic bone loss, in the form of bone erosions and secondary OP respectively, are among the most frequent comorbidities in RA patients. The significant of OP appears to the increased risk of the fragility fracture and thus affecting the individual activity and financially. The main aim of our study was to evaluate the effects of OP on RA disease activity using DAS28-CRP by comparing the outcome between two groups of patients, where RA-OP patients are compared with the reference group of RA-only patients in the same cohort sample. Up to the authors' knowledge, this study is probably one of the first to unveil this area.

Previous studies reported that OP occurs in 30–50% of RA patients[5,6] and had strong relation to multiple risk factors that may affect the progression of RA, so that OP commonly found in older patients[28] and more often female than male,[29] and had lower BMI, a longer disease duration,[30] a corticosteroid treatment,[7] and a higher HAQ-DI score.[7,31] Accordingly, among the cohort sample in the current study, we found 13.5% of treated RA patients developed OP and when compared the demographic data of these patients to RA-only patients, they were significantly older, had longer duration, corticosteroid therapy,

and a higher HAQ-DI score at 2nd and 3rd clinical visit. Hence these results agreed with previous studies[7,28,30,31] except for gender and BMI that showed insignificant difference, while the counterintuitive finding related to the percentage of smoking in RA-OP patients was significantly lower than RA-only patients, a result that opposed to literature reports.[32] We found also, OP commenced in RA patients after a mean duration of 24.6 ± months from the diagnosis of RA that gave a total disease period in RA-OP patients of 106.6 ± 62.6 months at a mean age of 64.8 ± 10.8 years, which means the process of bone loss had occurred at an earlier age. This finding was in consistent with previous results by Kleyer et al,[33] who proved that bone loss in RA patients with ACPA-positive occurs even before the onset of RA clinical features.

On the other hand, our study did not prove any significant difference in DAS28-CRP scores between RA-only and RA-OP patients during the three clinical visits either by simple statistical comparison or via multivariable regression analysis. Therefore, indicating that OP did not affect the disease activity and the outcome of RA patients, and would not interfere with the management of RA patients. Having examined the association between various risk factors in our data, we did not find any significant association related specifically to the development of OP among RA patients than those who did not have OP except for the age factor that showed the RA-OP group significantly decreased with age compared to patients with RA-only (OR 0.952, 95% CI 0.909–0.997; P=0.036) (Table 1). The reason for this is most probably in our study of RA-OP group, we deal mainly with glucocorticoid induced OP (GIOP), which is a secondary OP, since our statistical analysis revealed the use of glucocorticoid by RA-OP patients was significantly higher than RA-only patients (61.7% vs. 41.7%, P = 0.03) (Table 4). This finding is consistent with a comprehensive review done by Sadat-Ali et al,[34] who reported that secondary OP occurred at a young age group (mean age and SD, 37.4 years) and its prevalence was higher than primary OP both in men and women (46.4 to 31.9, P<0.001, 95% CI<-13.4486). Moreover, the increased relative use ofGCs in RA-OP patients may reflect the increased short term RA activity in this group of patients, and the associated increased risk for occurrence of OP.

Concerning overall principle that we followed in this cohort of patients was treat to target principles regardless the type of DMARDs used to achieve the target. There were no significant differences of various DMARDs received (biologic and non-biologic) between RA-only and RA-OP patients. This entailing that both groups had received and tolerated same medications and there was no difference in their management plan, although most of them having various comorbidities other than OP, the management plan was the same for all RA patients. Following treatment, both groups of RA patients experienced continuing improvement in disease activity, as measured by DAS28-CRP score, and overall, up to 96–97% patients reach remission and low disease activity after the 2nd clinical visit and continue so to the 3rd clinical visit. Unlike our finding, previous studies on RA patients by Darawankul et al[35] and Barnabe et al[36] showed lower remission rates at 14.6 and 37% respectively. In addition, when evaluating the patients' disabilities by HAQ-DI score, we found much improvement in all RA patients' disabilities by the end of the three clinical visits, although there were more significant disabilities with bone loss in RA-OP patients compared to the other group (P = 0.001 at 2nd and 3rd visits) (Table 2). These finding were similar to the Hafiz et al report, where HAQ-DI scores tended to increase with increasing radiographic progression of bone loss.[37]

In our cohort study, denosumab was used mostly in conjunction with methotrexate for the treatment of RA-OP patients. This combination has been reported to be beneficial for RA patients with risk factors for joint destruction.[38] Denosumab was found also useful in combination with DMARDs in suppressing joint destruction and increasing BMD, although it did not affect joint space narrowing or disease activity scores.[39]

There were several limitations to this study. This was a single center study and may not reflect findings of patients treated elsewhere in Saudi Arabia. It was lacking in some data, including the detailed history of smoking, dosing of various DMARDs therapy, duration and dose of GCs, and information about the progression and severity of OP. Moreover, patients in Saudi Arabia have early access to biologic modifiers and DMARDs, which may not be the case in other countries.

In conclusion, the current study revealed that OP has insignificant effects on RA disease activity and thus the development of OP among RA patients will not change the management plan for them. However, we found that the RA-OP group significantly decreased with age compared to patients with RA-only, indicating that this secondary OP might be mostly GIOP, which supported by finding a significant higher consumption of glucocorticoid by RA-

OP patients. In addition, RA-OP patients had greater disabilities than RA-only patients since the first clinical visit and even though decreased by 2nd and 3rd visit, disabilities remained significantly higher in RA-OP patients. Hence our recommendation is to focus on aggressive, appropriate and treat to target approach for RA patients regardless of whether they have OP or not to control the RA disease activity. As well as perform early screening for OP and prompt treatment for the newly confirmed RA-OP cases.

Abbreviations

ACR, American College of Rheumatology; BMI, Body mass index; BMD, Bone mineral density; CKD, Chronic kidney disease; ACPA, Citrullinated proteins antibodies; CRP, C-reactive protein; DM, Diabetes mellitus; Dkk-1, Dickkopf-related protein-1; DMARDs, Disease modifying antirheumatic drugs; DSFH, Doctor Soliman Fakeeh Hospital; DEXA, Dual-energy X-ray absorptiometry; GIOP, Glucocorticoid-induced osteoporosis; GCs, Glucocorticoids; HAQ-DI, Health Assessment Questionnaire-Disability Index; HTN, Hypertension; IFN-γ, Interferon gamma ; IL-1b, Interleukin −1b; IL-4, Interleukin-4; IL-6, Interleukin-6; IL-11, Interleukin-11; IL-17, Interleukin-17; RANKL, Nuclear factor, kappa-B ligand; OP, Osteoporosis; OPG, Osteoprotegerin; RA, Rheumatoid arthritis; RF, Rheumatoid factor; RASD, Saudi registry of the Rheumatoid Arthritis Saudi Database; SD, Standard deviation; SPSS, Statistical Package for Social science; Th1, T helper cell 1; Th17, T helper cell 17; DAS28-CRP, The Disease Activity Score 28 for Rheumatoid, Arthritis with CRP; TGF-β, Transforming growth factor-β; TNF, Tumor necrosis factor; WHO, World health organization.

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Disclosure

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