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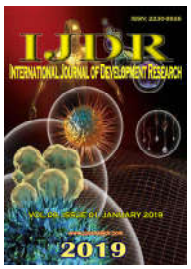

ORIGINAL RESEARCH ARTICLE OPEN ACCESS

OSTEOPOROSIS IN ADULT PATIENTS WITH PSORIASIS AND PSORIATIC ARTHROPATHY

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ABSTRACT

Background and objective: Psoriasis represents a common inflammatory skin disorder, and psoriatic arthritis is a chronic inflammatory disease which characterized by arthritis and enthesitis that can occur in about one-third of patients with psoriasis. Both conditions had been linked to increasing the risk of osteoporosis. **The aims:** this study aims to assess the bone mineral density and the rate of osteoporosis in a group of psoriatic patients with and without arthritis and find the predictors of osteoporosis in such patients. **Patients and methods**: An observational cross-sectional study carried in Rheumatology and Dermatology Unit, Baghdad Medical City and it included 96 patients with psoriasis and psoriatic arthritis. **Results:** The frequency of osteoporosis among our cases was 19.8% in the spine and 4.2% in hips, it was slightly high among patients with psoriatic arthritis (21.1%) compared to 17.9% among patients with psoriasis only. Age, body mass index, the presence of arthritis, duration of arthritis, disease activity score, low hemoglobin, are predictors for osteoporosis in psoriatic patients. **Conclusion**: There is a relationship between osteoporosis and psoriasis especially in presence of arthritis, however in psoriatic population didn't reach the statistically significant level and confounded by same variables that cause normal persons to have reduced bone mass (age, body mass index, nutritional status).

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INTRODUCTION

Psoriasisis a long-lasting autoimmune disease which is characterized by patches of abnormal skin. These skin patches are typically red, itchy, and scaly (Menter, 2008). Psoriatic arthritis (PsA) is a unique, clinically heterogeneous type of inflammatory arthritis associated with skin psoriasis. Early diagnosis and treatment can relieve pain and inflammation, which may achieve disease remission and prevent progressive joint involvement and damage (Gelfand, 2005). Osteoporosis is a progressive metabolic skeletal disorder characterized by compromised bone strength and low bone mineral density predisposing to an increased risk of fractures and diminishing the health related quality of life (Cosman, 2014). National Osteoporosis Foundation has been described osteoporosis as a silent disease as people are not aware of constant loss of their bone mass until they experience a fragility fracture (Rafraf, 2009).

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Osteoporosis in Rheumatic Diseases and Other Conditions: Recently, studies have reported significant bone loss in patients with systemic inflammatory diseases such as rheumatoid arthritis, systemic lupus erythematosus (SLE), and ankylosing spondylitis (Lenore, 2017). Factors that might contribute to osteoporosis in patients with rheumatic diseases include decreased mobility, glucocorticoid therapy, and systemic inflammation (Hansen, 1996). It has been hypothesized that psoriasis is related to an increased risk of osteoporosis due to enhanced activity of IL-6 and TNF-a (Naldi, 2005). Additional explanations linking psoriasis with osteoporosis might include a lack of physical activity, smoking, and alcohol consumption, which are known risk factors for osteoporosis, and are common in patients with psoriasis (Rich, 1992).

PATIENTS AND METHOD

Study design and sample selection: This observational cross sectional study conducted in Rheumatology and Dermatology Unit in Baghdad Teaching hospital, Baghdad, Iraq from

December 2016 to July 2017 carried on 96 patients, age ≥ 20 years with confirmed diagnosis of psoriasis, from them 57 patients had psoriatic arthritis diagnosed according to CASPAR criteria. Thirty seven patients were females. All patients were informed of the objectives of the study and gave verbal consent for their voluntary participation in the study. We excluded pregnant women, patients with renal and hepatic impairment, heart failure and ischemic heart disease, other autoimmune disease, and patients with malignancy

Data collection: Physical examination and patients history were taken including age, gender, BMI, disease duration, family history of psoriasis, and disease activity score (DAS28 and Psoriasis Area and Severity Index (PASI)). Laboratory parameters were also taken including ESR, WBC, hemoglobin, urea, creatinine, ALT, and AST. Bone mineral density was assessed using Z and T score (total hip and lumbar spine) by using dual energy x- ray absorptiometry scan (DXA) scan. Osteopenia is defined as total T score -1 to -2.5, while osteoporosis as total Z score <-2.0 (because all our patients were <50 year age) (Czerwinski 2007).

Statistical analysis: All continuous data presented as mean and standard deviation since they follow normal distribution, while categorical variable presented as number and percentage. T test to compare between two independent continuous groups, chi square test to compared between categorical groups. For nonparametric continuous data Mann Whitney U test was used. Binary logistic regression analysis used to calculate the odd ratio (OR) and their 95% confidence intervals, when the outcome can be categorized into 2 binary levels, and if appropriate probability plot used to present the relationship. SPSS 20.0.0, GraphPad Prism 7.0 software package used to make the statistical analysis, p value considered when appropriate to be significant if less than 0.05.

RESULTS

For all psoriatic patients with and without arthritis there was no significant difference among males and females regarding the demographical features except for BMI which was higher in males Table 1. The rate of osteoporosis and osteopenia in psoriatic patients were not significantly differed among males and females as illustrated in Table 2.

Table 1. Demographic and clinical characteristics according to gender

	Female	Male	All	P value
Psoriasis without arthritis				
Number	37	59	96	-
Age	40.38 ± 8.44	41.15 ± 8.88	41.08 ± 8.71	0.337
BMI	26.89 ± 5.38	29.53 ± 4.74	28.51 ± 5.13	0.013
Duration of psoriasis	11.0 (6.5 - 15.0)	10.0 (4.0 - 20.0)	10.5 (5.3 - 19.3)	0.997
Family history of psoriasis				**0.115**
Negative history	33 (89.2%)	45 (76.3%)	78 (81.3%)	
Positive history	4 (10.8%)	14 (23.7%)	18 (18.8%)	
PASI	3.7 (1.7 - 5.6)	4.6 (2.2 - 9.3)	4.1 (2.1 - 8.1)	0.129
Psoriasis with arthritis				
Number	26	31	57	
Age	41.77 ± 7.27	41.52 ± 7.35	41.63 ± 7.65	0.941
BMI	25.09 ± 4.61	28.11 ± 3.54	26.73 ± 4.30	0.007
Duration of psoriasis	12.0 (7.5 - 17.0)	17.0 (7.0 - 25.0)	15.0 (7.5 - 20.0)	0.176
Duration of psoriasis arthritis	5.0 (3.0 - 12.0)	6.0 (3.0 - 9.0)	6.0 (3.0 - 9.0)	0.489
Family history of psoriasis				
Negative history	23 (88.5%)	26 (83.9%)	49 (86.0%)	0.715
Positive history	3 (11.5%)	5 (16.1%)	8 (14.0%)	
Pattern of joint involvement				
DIP involvement	3 (11.5%)	2 (6.5%)	5 (8.8%)	0.603
Mono- oligoarthritis	3 (11.5%)	2 (6.5%)	5 (8.8%)	
Polyarthritis	20 (76.9%)	27 (87.1%)	47 (82.5%)	
PASI	2.9 (1.5 - 4.8)	3.0 (1.6 - 4.6)	2.9 (1.6 - 4.7)	0.526
DAS28	4.5 (2.2 - 5.5)	3.8 (3.1 - 5.7)	4.2 (2.8 - 5.5)	0.847

BMI: body mass index, PASI: Psoriasis Area and Severity Index, DAS28: Disease Activity Score 28

Table 2. Bone status in spine and total hip

	Female	Male	All	P value
Psoriasis without arthritis				
Number	37	59	96	-
Spine	-1.40 ± 1.10	-1.48 ± 1.06	-1.45 ± 1.07	0.720
Normal	15 (40.5%)	20 (33.9%)	35 (36.5%)	0.716
Osteopenia	16 (43.2%)	26 (44.1%)	42 (43.8%)	
Osteoporosis	6 (16.2%)	13 (22.0%)	19 (19.8%)	
Total Hip	-0.71 ± 0.95	-0.91 ± 0.81	-0.83 ± 0.87	0.284
Normal	23 (62.2%)	33 (55.9%)	56 (58.3%)	0.675
Osteopenia	12 (32.4%)	24 (40.7%)	36 (37.5%)	
Osteoporosis	2 (5.4%)	2 (3.4%)	4 (4.2%)	
Psoriasis with arthritis				
Number	26	31	57	-
Spine	-1.63 ± 1.21	-1.45 ± 1.05	-1.53 ± 1.12	0.553
Normal	7 (26.9%)	13 (41.9%)	20 (35.1%)	0.494
Osteopenia	13 (50.0%)	12 (38.7%)	25 (43.9%)	
Osteoporosis	6 (23.1%)	6 (19.4%)	12 (21.1%)	
Hip	-0.93 ± 0.97	-0.98 ± 0.85	-0.96 ± 0.90	0.860
Normal	13 (50.0%)	17 (54.8%)	30 (52.6%)	0.933
Osteopenia	11 (42.3%)	12 (38.7%)	23 (40.4%)	
Osteoporosis	2 (7.7%)	2 (6.5%)	4 (7.0%)	

Table 3. Predictors of Osteoporosis in Psoriasis patients

	Univariate analysis		Multivariate analysis [a]	
Variables	OR (95%CI)	P value	OR (95%CI)	P value
Age	*1.066 (1.024 - 1.109)*	*0.002*	1.403 (1.131 - 1.741)	0.002
Gender	1.460 (0.501 - 4.253)	0.488		
BMI	1.020 (0.925 - 1.126)	0.689	0.648 (0.459 - 0.915)	0.014
Presence of PSA	1.219 (0.432 - 3.437)	0.708	20.572 (0.705 - 600.121)	0.079
Duration of psoriasis	1.013 (0.952 - 1.077)	0.685		
PASI	*1.149 (1.042 - 1.266)*	*0.005*	2.091 (1.246 - 3.510)	0.005
ESR	*1.024 (0.999 - 1.049)*	*0.059*		
WBC	1.125 (0.933 - 1.358)	0.218		
Hb	0.793 (0.586 - 1.075)	0.135	0.343 (0.152 - 0.773)	0.010
Urea	1.000 (0.964 - 1.038)	0.985	0.827 (0.730 - 0.938)	0.003
Creatinine	0.993 (0.239 - 4.133)	0.993		
ALT	*1.018 (1.002 - 1.035)*	*0.030*		
AST	*1.037 (1.009 - 1.066)*	*0.010*	1.143 (1.031 - 1.268)	0.011

[a] R^2= 0.461 (Cox and Snell), Backward elimination methods used to estimate the optimal model for the predictors of osteoporosis in psoriasis

BMI: body mass index, PASI: Psoriasis Area and Severity Index, AST: Aspartate transaminase, ALT: Alanine transaminase, WBC: White blood cells, Hb: Hemoglobin, ESR: Erythrocyte sedimentation rate

Table 4. Predictors of Osteoporosis in Psoriasis arthritis patients

	Univariate analysis		Multivariate analysis	
Variables	OR (95%CI)	P value	OR (95%CI)	P value
Age	*1.069 (1.011 - 1.130)*	*0.018*	1.185 (1.049 - 1.338)	0.006
Gender	0.800 (0.223 - 2.864)	0.732		
BMI	1.030 (0.884 - 1.201)	0.701		
Duration of psoriasis	0.933 (0.857 - 1.017)	0.114		
Duration of psoriasis arthritis	*0.852 (0.713 - 1.017)*	*0.076*	0.769 (0.603 - 0.980)	0.034
PASI	*1.139 (0.980 - 1.325)*	*0.090*	0.441 (0.191 - 1.018)	0.055
DAS28	*1.798 (1.098 - 2.943)*	*0.020*	1.586 (0.728 - 3.456)	0.246
ESR	1.011 (0.983 - 1.039)	0.444		
WBC	0.980 (0.781 - 1.229)	0.861		
Hemoglobin	0.924 (0.612 - 1.394)	0.707		
Urea	0.984 (0.933 - 1.038)	0.557		
Creatinine	0.776 (0.142 - 4.246)	0.770		
ALT	1.014 (0.992 - 1.036)	0.212		
AST	*1.044 (1.000 - 1.090)*	*0.049*	1.208 (1.036 - 1.410)	0.016

[a] R^2= 0.412 (Cox and Snell)

AST: Aspartate transaminase, ALT: Alanine transaminase, WBC: White blood cells, Hb: Hemoglobin, ESR: Erythrocyte sedimentation rate

Table 5. Demographic and clinical characteristics according to the presence of arthritis

	Psoriasis	Psoriatic arthritis	All	P value
Number	39	57	96	-
Age	40.74 ± 10.28	40.63 ± 10.65	40.08 ± 10.71	0.699
Gender				**0.085**
Female	11 (28.2%)	26 (45.6%)	37 (38.5%)	
Male	28 (71.8%)	31 (54.4%)	59 (61.5%)	
Smoking status				**0.002**
Smoker	17 (43.6%)	43 (75.4%)	60 (62.5%)	
None smoker	22 (56.4%)	14 (24.6%)	36 (37.5%)	
BMI	31.12 ± 5.18	26.73 ± 4.30	28.51 ± 5.13	<0.001
Duration of psoriasis	10 (4 – 12)	15 (7.5 – 20)	10.5 (5.3 - 19.3)	0.004
Family history of psoriasis				**0.152**
Negative history	29 (74.4%)	49 (86.0%)	78 (81.3%)	
Positive history	10 (25.6%)	8 (14.0%)	18 (18.8%)	
PASI	5.7 (4.1 – 12)	2.9 (1.6 – 4.7)	4.1 (2.1 - 8.1)	<0.001

BMI; body mass index, PASI; psoriasis area and severity index.

Table 6. Bone status for Psoriatic adult patients with and without arthritis

	Psoriasis	Psoriatic arthritis	All	P value
Number	39	57	96	-
Spine	-1.33 ± 1.00	-1.53 ± 1.12	-1.45 ± 1.07	0.381
Normal	15 (38.5%)	20 (35.1%)	35 (36.5%)	0.911
Osteopenia	17 (43.6%)	25 (43.9%)	42 (43.8%)	
Osteoporosis	7 (17.9%)	12 (21.1%)	19 (19.8%)	
Hip	-0.65 ± 0.79	-0.96 ± 0.90	-0.83 ± 0.87	0.084
Normal	26 (66.7%)	30 (52.6%)	56 (58.3%)	0.148
Osteopenia	13 (33.3%)	23 (40.4%)	36 (37.5%)	
Osteoporosis	0 (0.0%)	4 (7.0%)	4 (4.2%)	

In multivariate analysis; age, presence of arthritis, high PASI score, elevated AST, low hemoglobin and low blood urea were found to increase the risk of osteoporosis in psoriatic patients (all these variables are independent predictors of osteoporosis) as illustrated in Table 3. Also the rate of Osteoporosis and Osteopenia in patients with psoriatic arthritis were not statistically differed among males and females as illustrated in Table 2. Only age, duration of arthritis and AST independently correlated with Osteoporosis, while DAS28 showed correlation only in univariate analysis (i.e. dependent predictor) as illustrated in Table 4. PASI score, duration of psoriasis, and BMI were significantly differed among psoriatic patients who had arthritis and those who had not, as illustrated in Table 5. The rate of osteoporosis and osteopenia among

Psoriatic patients who had arthritis and those who had not were not significantly differed as illustrated in Table 6.

DISCUSSION

In this study we analyzed the frequency of osteoporosis in a sample of 96 patients with psoriasis and psoriatic arthritis. The prevalence of osteoporosis in psoriatic patients was 19.8% (4.2% of the cases had osteoporosis in both hips and spine), which was in agreement with Drieher *et al.* study (Dreiher 2009) which involved 7936 psoriatic patients when 12.4% had osteoporosis. Also in this study the frequency of osteoporosis in psoriatic arthritis was higher than in psoriasis patients without (spine: 21.1% vs. 17.9%; hip: 7.0% vs. 0% respectively) however this differences did not reach statistical significance (p value > 0.05). The frequency of osteopenia in psoriatic arthritis was similar to that in psoriatic patients without arthritis (spine 43.9% and hips 40.4% vs spine 43.6% and hip 33.3% respectively). (Busquets 2014) found a lower rate of osteoporosis in lumbar spine (7%) and slightly higher in the hip (11%). In a small study that involved 47 patients which included 18 patients with psoriatic arthritis; they reported (one patient) 5% of the psoriatic arthritis having osteoporosis and 50% (9 patients) having osteopenia, while in the patients without arthritis no one had osteoporosis and only 8 (27.5%) had osteopenia; so they reported lower rates of osteoporosis compare to our study but similar rates of osteopenia (Borman 2008). In a recent (2016) literature review that involved 21 studies (16 case-control, 4 cross sectional and 1 prospective cohort) the prevalence of osteoporosis range from 1.4% in hipto 68.8% in wrist, while the prevalence of osteopenia was 6.3% to 61%. This put the findings of our study in line with this large literature review (Chandran 2016). In our study T score was higher in hip compared to spine (-0.83 ± 0.87 vs. -1.45 ± 1.07) for all patients with no significant difference between males and females (p value > 0.05).

In psoriatic arthritic patients T score also was higher in hip as compared to spine (-0.96 ± 0.90 vs. -1.53 ± 1.12) with no significant difference among males and females (p value >0.05). In both spine and hip psoriatic arthritis patients had lower T score than patients without arthritis but it did not reach statistical significance level. Our findings agree partially with Busquets *et al.* (2014) since we have similar T score in the hip (-0.92 ± 1.16) in all psoriatic patients but disagree with them on T score of spine (-0.63 ± 1.24) as it was higher than ours and higher than these of hip. The disagreement caused by different subjects involved in their study compared to ours, as they included large number of postmenopausal women. Our study is in a line with Borman *et al.* (2008) findings in which no statistical difference observed in lumbar spine and hip Z and T scores of the psoriatic patients with and without arthritis, however like our findings psoriatic arthritis patients had lower scores. Also in this study age appears to be independently correlated with osteoporosis in both psoriatic patients (OR=1.403, p <0.01) and in psoriatic arthritis patients (OR=1.185, p < 0.01).This findings is in agreement with Dreiher et al(Dreiher 2009)We found smoking to be significantly associated with lower bone mineral density in psoriatic arthritis (p value <0.01), which is similar to previous finding of the association between smoking and low bone mineral density and osteoporosis is PsA (Chandran 2016). The following predictors in this study appear to predict osteoporosis in all patients: advance age, presence of arthritis, high PASI score, elevated AST, low hemoglobin, low urea, and low BMI (these variables explain 46.1% of osteoporosis in psoriatic patients). Our findings were not agreed with Pedriera *et al.* (2011) in which PASI score, duration of psoriasis did not correlate with osteoporosis. Also our findings were not agreed with Borman *et al.* (2008) study in which ESR, CRP did not correlate with osteoporosis while there was strong inverse correlation between duration of arthritis and BMD in lumbar and hip (this in line with our findings). Frediani *et al.* (2001) also found no correlation between ESR, CRP nor duration of psoriasis with BMD. The lack of relationship between the inflammatory biomarker (i.e. ESR) with bone mass reduction (i.e. osteoporosis) in their study may be caused by the low productivity of ESR in such cases or that its low sensitivity that its elevation is not high enough to correlate with BMD loss and better inflammatory marker are required such as interleukins and tumor necrosis factors. The results of this study show that AST was independently predicted osteoporosis in both uni- and multivariate analysis (p value <0.01), however no previous study shed a light on this relationship, and to our knowledge this the first reported relationship with AST, a possible explanation is that AST elevation can be attributed to various organ abnormalities like in liver, muscles and bones etc; but we can link AST elevation to bone resorption rather than its effect by the liver; which could explain why ALT (which is more specific for hepatic involvement) in our study was dependently correlated (i.e. in univariate analysis) with osteoporosis and lose the relationship in multivariate analysis. In this study hemoglobin was inversely correlated with osteoporosis (OR=0.343, P = 0.010), this is the first reported study concerning this relationship, a possible explanation that hemoglobin linked to nutritional status so low hemoglobin indicate malnutrition and chronic active disease which possibly lead to low BMD. In conclusion there is relationship between osteoporosis and psoriasis especially in presence of psoriatic arthritis, however its magnitude on psoriatic population is mild and confounded by same variables that cause normal persons to have reduce bone mass (age, BMI, nutritional status). In psoriatic arthritis there was strong correlation between osteoporosis and disease activity score (DAS28).

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