Original Article

Linking of psoriasis with osteopenia and osteoporosis: A cross-sectional study

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Abstract

Background/Purpose: Psoriasis is a multisystem disease which has been related to vitamin-D deficiency through chronic inflammation. This psoriasis-related inflammatory state and vitamin-D deficiency may induce bone mineral density loss. The purpose of this study is to assess the relationship of psoriasis with bone mineral density, by comparing psoriatic patients with healthy controls and patients with osteopenia/osteoporosis.

Methods: A total of 185 subjects were studied; 58 psoriatic patients who had not been under systemic or biological treatment were included. Age, gender, body mass index, phosphocalcic metabolic parameters and hip and lumbar (L4) bone mineral density data were collected. These variables were compared with those collected in 61 healthy controls and 67 patients with osteopenia/osteoporosis.

Results: Psoriatic patients showed worse hip and lumbar spine bone mineral density levels than healthy controls ($P = 0.001$) and better levels than osteoporotic patients ($P < 0.001$). Multivariate analysis demonstrated a negative association of age and a positive association of body mass index in hip bone mineral density in psoriatic patients.

Limitations: The main limitations are those of cross-sectional studies, such as a lack of follow up period, and a male predominance in the psoriatic group, which is corrected employing a multivariate analysis with an adjusted model for confounding factors.

Conclusions: Bone mineral density levels in psoriatic patients are situated halfway between healthy controls and patients with osteopenia/osteoporosis. In addition, the higher body mass index in patients with psoriasis appears to confer a protective effect against further development of lower bone mineral density.

Key words: Body mass index, bone mineral density, osteopenia, osteoporosis, psoriasis, vitamin-D

Introduction

Psoriasis is a chronic inflammatory disease whose prevalence is estimated to be between 1 and 5% of the world population.[1]

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This condition has been associated with a higher prevalence of metabolic syndrome, obesity, hyperlipidemia, diabetes mellitus, hypertension and arteriosclerosis.[2,3] These comorbidities seem to be responsible for the increased risk of major cardiovascular events in psoriatic patients.[4] Among the comorbidities associated with psoriasis, the association of this disease with vitamin D deficiency is globally recognized. The presence of lower levels of vitamin D in psoriatic patients have been related with higher levels of cholesterol, low-density lipoprotein, triglycerides and glucose.[5,6] The reason for such a large number of pathologies associated with psoriasis appears to lie in the chronic inflammatory state present in psoriatic patients, which has been demonstrated by increased proinflammatory cytokines such as tumor necrosis factor-alpha, interleukin-12, interleukin-23 or interleukin-17 in these patients.[7,8]

Moreover, increased levels of C-reactive protein have been found in psoriatic patients, as well as low levels of vitamin-D metabolizing enzymes, CYP27A1 and CYP27B1, within psoriatic lesions.[9,10] On the other hand, vitamin-D supplementation and treatment with oral calcitriol have been associated with clinical improvement in psoriasis lesions.[11-13]

Osteoporosis is a skeletal disorder characterized by reduced bone mass and micro - architectural changes in bone tissue that result in an increased risk of fractures.[14] The World Health Organization defines osteoporosis as bone mineral density <2.5 standard deviation below the mean for young white adult women (T-score). Osteopenia is defined as the presence of a bone mineral density between 1.5 and 2.5 below the T-score and represents a low bone mass that is not as severe as osteoporosis. This entity is a major public health problem due to the increased risk of development of fractures associated with osteoporosis.[15] However, there is another type of osteoporosis that can occur secondary to various entities such as endocrine pathology, rheumatologic disease, increased chronic inflammation and vitamin-D deficiency.[16] In addition, the presence of a lower bone mineral density has been described in patients with long-term psoriasis in a study without a control group.[17]

Considering this background, a cross-sectional study with a control group was conducted to assess the levels of bone mineral density in patients with psoriasis in comparision to those existing in healthy controls and patients without psoriasis diagnosed with osteopenia or osteoporosis.

Methods

Patients with moderate to severe cutaneous psoriasis were systematically recruited from the outpatient department of the Psoriasis Unit of our hospital. Inclusion criteria were: a clinical diagnosis of psoriasis with a Psoriasis Area Severity Index higher than 4, age 18 years or older, residence in the metropolitan area of Granada (southern Spain) and adequate daily sun exposure, described as staying outdoors for at least 1 hour per day. Exclusion criteria were: personal history of treatment with systemic or biologic agents, or photochemotherapy, personal history of psoriatic arthritis, rheumatoid arthritis, inflammatory bowel disease or other inflammatory diseases and intake of calcium or vitamin-D supplements. Moreover, healthy controls from the same metropolitan area and patients diagnosed with osteopenia or osteoporosis who were followed in the Endocrinology Unit of our hospital were included in the study. All the osteopenia/osteoporosis patients had been recently diagnosed by densitometry and had not received any kind of treatment. Patients who met these selection criteria and signed an informed consent (in accordance with the Helsinki Declaration) were enrolled in the study; no selected patients refused to participate. The study was approved by the Ethics Committee of Hospital Universitario Virgen de las Nieves, Granada, Spain.

Clinical and laboratory parameters

Data regarding age and sex were collected from all study participants. All patients underwent physical examination, and their weight and height were recorded to calculate their body mass index (kg/m^2), as well as their psoriasis area and severity index. Blood samples were drawn in the early morning for laboratory analysis of biochemical parameters, including serum 25(OH) vitamin-D, calcium, phosphorus, parathyroid hormone and osteocalcin. In addition, bone mineral density was measured by bone densitometry using dual-energy X-ray absorptiometry, employing an Hologic Discovery Wi® (Hologic Inc., USA).T-score values in the Ward triangle of the Hip (tHip), the fourth vertebra in the lumbar spine (tl4) and the whole lumbar spine (tl1-4) were obtained. All laboratory parameters were collected in two consecutive months (March/April 2016).

Statistical analysis

A descriptive analysis by group, psoriasis (P), control (C) and osteopenia/osteoporosis (O), was carried out for all the variables in database. Contingency tables according to group and sex were made using generalization of exact Fisher's test in RXC tables to assess the association between them. One-way analysis of variance was performed for each numerical variable to compare means by group and stratified by sex. Correlation matrix between numerical variables was computed to measure the association between them.

To measure mean differences between P–C and P–O, multiple linear regression was computed. Given that differences between groups were affected by confounding factors (sex, body mass index, vitamin-D, parathyroid hormone and osteocalcin), a crude and an adjusted model are presented, the latter being the main analysis of the study. This type of analysis allows the elimination of existing differences between the various study groups. The outcomes considered were tHip and tl4, and covariates were group, sex, body mass index, vitamin D, parathyroid hormone and osteocalcin.

Fore statistical analysis, STATA 14.1 (Statacorp, College Station, Texas, EEUU) was used.

Results

The final study sample of 185 patients comprised three groups – the psoriasis group (P group) with 58 patients [33 males and 25 females, Table 1], the control group (C group) with 61 patients (19 male and 42 female) and the osteopenia/osteoporosis group (O group) with 67 patients (16 male and 51 female). The three groups [Table 2] differed in the number of males and females included in each group ($P < 0.001$); however, no differences were found in mean age (P group: 48.88 ± 14.04; C group: 51.80 ± 10.33; O group: 51.88 ± 12.27; $P = 0.315$). Body mass index was found to be higher in *P* group than the other groups (P: 30.34 ± 6.50; C: 26.10 ± 3.25; O: 25.22 ± 3.94; $P < 0.001$). Moreover, vitamin-D levels were lower in P group in relation to the other groups ($P < 0.001$). In addition, differences in the parathyroid hormone means were found, showing upper levels in the O group with respect to the other two groups ($P = 0.018$) and higher osteocalcin levels in the P and O groups compared to the C group ($P = 0.002$). Finally, the crude comparison of means concerning the outcomes tHip and tl4 showed significative differences ($P < 0.001$) between different groups. These statistical differences remained stable after stratification by sex [Table 3].

Table 1: General characteristics of the basal features of the psoriatic patients included on the study

Variables	Mean and standard deviation or number and percentage
Age	48±14.05
Gender (%)	
Male	33 (56.9)
Female	25 (43.1)
PASI	7.016±5.08
Time of evolution (years)	12.20±6.14
BMI	30.54±6.50

BMI: Body Mass Index, PASI: Psoriasis Area Severity Index

Table 2: General comparison of the basal characteristics among the three study groups

	Psoriasis	Control	Osteopenia	*p*
Age	48,87±14,05	51,80±10,33	51,88±12,27	0,315
Sex				0,001
M	33	19	16	
F	25	42	51	
BMI	30,34±6,50	26,10±3,25	25,22±3,94	<0,001
VitD ⅂	19,29±7,86	28,08+/7,16	28,93±10,18	<0,001
PTH ⊤	47,00±17,61	45,61±14,97	53,81±18,92	0,018
Osteoc ∪	18,83±7,10	14,58±5,04	18,72±8,76	0,002
tHip Σ	-0,630±0,962	-0,078±0,852	-1,206±0,779	<0,001
tl4 Θ	-1,443±4,701	-0,098±0,732	-2,273±0,724	<0,001

□ Vitamin-D; □ Parathyroid hormone; □ Osteocalcin; □ Hip T-Score; □ L4 T-Score. Hip T-Score and L4 T-Score values reflect number of standard deviations of the bone mineral density with respect to the average value of the population of 20 to 39 years of the same sex

The multiple linear regression for hip T-score adjusted for confounding factors, including sex, age, body mass index, vitamin-D, parathyroid hormone and osteocalcin [Table 4], showed that the mean hip T-score in group C was higher than group P ($P = 0.001$), whereas the average T-score in the O group was lower than P group, not reaching statistical significance ($P = 0.129$). Furthermore, age showed an independent effect on the levels of hip T-score, decreasing its value with the increased age of patients ($P = 0.001$). Furthermore, the body mass index variable also showed a significant effect on hip T-score, increasing its value with the body mass index rising [$r = 0.272$; $P = 0.035$, Figure 1]. On the contrary, an inverse association between hip T-score and Psoriasis Area Severity Indexwas found, although this association was nearly significant [$r = -0.230$; $P = 0.091$, Figure 2]. The variables such as gender, vitamin-D, parathyroid hormone and osteocalcin did not show any significant effect on hip T-score.

The multiple linear regression for L4 T-score adjusted for confounding factors [Table 5] revealed that the average T-score in C was higher than P ($P = 0.002$), while the mean T-score in O was significantly lower than P ($P < 0.001$). None of the other variables showed a significant effect on L4 T-score.

Discussion

General data

In this study, bone mineral density values in patients with psoriasis were significantly lower than in healthy controls from the general population. In addition, a trend was observed in psoriasis patients, who presented with better levels of bone mineral density than patients of osteopenia/osteoporosis. Significant differences between group P and group O were only observed in the T-score of L4 after adjustment for confounding factors.

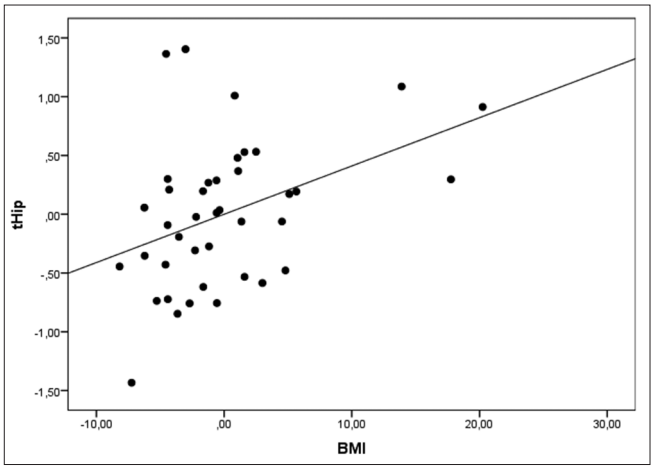

Figure 1: Correlation between body mass index and hip T-score ($r = 0.272$)

Table 3: General comparison of the basal characteristics among the three study groups stratified by sex

Variables	Male				Female			
	Psoriasis	Control	Osteoporosis	*P*	Psoriasis	Control	Osteoporosis	*P*
Age	47.91±11.02	50.85±9.85	50.68±10.92	0.291	50.18±15.23	52.44±10.98	52.65±11.08	0.428
BMI	31.28±8.28	26.40±4.21	26.04±3.83	<0.001	29.42±7.31	25.92±3.45	24.98±4.32	<0.001
Vitamin D	20.03±7.45	28.35±7.33	29.14±8.04	<0.001	18.98±8.30	27.46±7.82	28.04±7.21	<0.001
PTH	47.80±18.45	46.52±15.28	52.25±17.21	0.041	46.10±17.22	45.14±14.49	54.12±19.06	0.024
Osteocalcin	18.68±7.22	14.16±5.42	18.54±6.82	0.032	18.97±8.34	14.82±6.09	18.86±7.04	0.016
tHip	−0.545±0.842	0.032±0.721	−1.145±0.842	<0.001	−0.702±0.823	−0.144±0.842	−1.296±0.722	<0.001
tl4	−1.338±4.682	0.009±0.635	−2.105±0.773	<0.001	−1.526±4.971	−0.178±0.801	−2.342±0.823	<0.001
tl1-4	−1.294±3.647	0.066±0.834	−2.099±0.745	<0.001	−1.472±4.122	−0.109±0.769	−2.301±0.797	<0.001

BMI: Body mass index, tHip: Triangle of the Hip, tl4: Fourth vertebra in the lumbar spine, tl1-4: The hole lumbar spine, PTH: Parathyroid hormone

Table 4: Crude and adjusted for confounding factors regression model in the comparisons of triangle of the hip levels between psoriasis and control group and psoriasis and osteopenia/osteoporosis group

Variables	Crude model			Adjusted model		
	Coefficient	95% CI	*P*	Coefficient	95% CI	*P*
P-C	0.551	0.283 to 0.865	0.001	0.679	0.272 to 1.086	0.001
P-O	−0.576	−0.883 to−0.269	<0.001	−0.307	−0.704 to 0.091	0.129
M-F	−0.276	−0.883 to−0.269	0.065	−0.049	−0.359 to 0.260	0.753
Age	−0.012	−0.024 to−0.001	0.036	−0.049	−0.359 to−0.009	0.001
BMI	0.033	0.004 to 0.061	0.025	0.034	0.002 to 0.065	0.035
Vitamin-D	−0.004	−0.019 to 0.011	0.629	0.000	−0.015 to 0.016	0.954
PTH	−0.009	−0.017 to−0.001	0.027	0.000	−0.009 to 0.008	0.947
Osteocalcin	−0.026	−0.045 to−0.007	0.007	−0.006	−0.025 to 0.013	0.546

Coefficient reflects the differences in the mean values of the bone mineral density in the P-C, P-O and M-F comparisons (adjusted for the other variables in the adjusted model) and the increase or decrease of the bone mineral density regarding the other variables in the other lines (adjusted for confounding factors in the adjusted model). BMI: Body mass index, PTH: Parathyroid hormone, P-C: Psoriasis/control relationship, P-O: Psoriasis-osteopenia/osteoporosis relationship, M-F: Male/female relationship, CI: Confidence interval

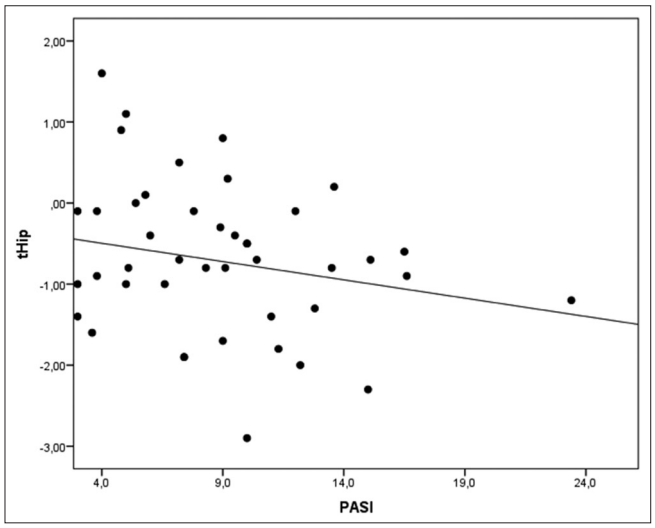

Figure 2: Correlation between psoriasis area severity index and hip T-score ($r = -0.230$)

Although not related to the primary objective of the study, some of the current results deserve comment. First, in the psoriatic group the percentage of men was slightly higher than women (56.9% vs 43.1%), while in the control group and osteoporosis group the percentage of women was higher (68.9 and 76.1%, respectively). These results are consistent with the findings of a recent American review[18] and another study carried out in Spanish population.[19] On the contrary, the high percentage of women in the O group is similar to that found in other epidemiological studies in industrialized countries.[20,21] Likewise, a higher body mass index in psoriatic patients has also been described.[22] In addition, previous studies have demonstrated that increased body mass index was positively correlated with increased risk of developing psoriasis.[23,24]

Relationship between psoriasis and lower levels of bone mineral density

In our study, we have observed lower levels of bone mineral density in patients with psoriasis as compared to healthy controls. There are several studies that reinforce the idea of the association of psoriasis with lower levels of bone mineral density. A recent cross-sectional study without control group performed in patients with psoriasis and psoriatic arthritis showed that 63% of patients had deficient levels of vitamin-D, which is inversely correlated with body mass index of patients.[25] In addition, in this study no significant association between vitamin-D levels and bone mineral density was found, which is consistent with our findings. In 2011, Attia*et al*. demonstrated that patients with psoriasis and/or psoriatic arthritis showed worse bone mineral density levels relative to healthy

Table 5: Crude and adjusted for the confounding factors regression model in the comparison of fourth vertebra in the lumbar spine levels between psoriasis and control group and psoriasis and osteopenia/osteoporosis group

Variables	Crude model			Adjusted model		
	Coefficient	CI (95%)	*P*	Coefficient	CI (95%)	*P*
P-C	1.346	0.373 to 2.319	0.007	0.860	0.320 to 1.400	0.002
P-O	−0.829	−1.781 to 0.123	0.087	−1.185	−1.709 to −0.661	<0.001
M-F	−0.570	−1.417 to 0.278	0.186	−0.096	−0.508 to 0.317	0.648
Age	−0.024	−0.057 to 0.010	0.163	0.002	−0.015 to 0.018	0.826
BMI	0.052	−0.033 to 0.060	0.233	0.020	−0.022 to 0.061	0.353
Vitamin-D	0.014	−0.032 to 0.060	0.553	0.004	−0.017 to 0.025	0.733
PTH	−0.014	−0.037 to 0.010	0.259	−0.005	−0.017 to 0.007	0.408
Osteocalcin	−0.061	−0.088 to −0.034	0.007	−0.026	−0.052 to 0.000	0.052

BMI: Body mass index, PTH: Parathyroid hormone, P-C: Psoriasis/control relationship, P-O: Psoriasis-osteopenia/osteoporosis relationship, M-F: Male/female relationship, CI: Confidence interval

controls.[26] Similar results have been recently published in a study performed in Turkish population.[27] In this paper, the presence of lower levels of bone mineral density in women with psoriasis relative to healthy controls is described, while no differences were found in the comparison between men. However, both these studies did not perform an adjustment for possible confounders such as body mass index or age.

An inverse association between body mass index and serum levels of vitamin D have been demonstrated by several studies, both in patients with psoriasis[7,25] and in healthy and obese patients.[28-30]

Correlation between body mass index and bone mineral density

This possible association between the two parameters could suggest that patients with psoriasis and high body mass index have lower levels of bone mineral density at the expense of reduced serum levels of vitamin-D. However, in our study we have found a positive association between body mass index and hip T-score in patients with psoriasis. These results are consistent with other publications, in which it is described that a low body mass index correlates with lower bone mineral density in postmenopausal women.[31] In 2011, Pedreira*et al*. conducted a cross-sectional study with a control group, comparing the association of bone mineral density levels with various anthropometric parameters in patients with psoriasis.[32] In this paper, a positive correlation between bone mineral density and body mass index was observed. Recently, Honma*et al*. have reported a similar positive correlation in psoriatic patients.[33] In addition, Skrzek *et al*. have determined that the risk of developing osteopenia/osteoporosis in postmenopausal women is lower in those with a body mass index of 26–27.9.[34] Thus, after adjustment for confounding factors, the high body mass index present in patients with psoriasis appears to protect these patients against osteopenia/osteoporosis, mitigating the negative effect on bone mineral density produced by chronic inflammation and low levels of vitamin D present therein. This protective effect is particularly evident by observing the lower difference in bone mineral density between the psoriatic group and the osteopenia/osteoporosis group after the adjustment.

The association between psoriasis and chronic inflammation has been extensively described in literature, being one of the most common immune-mediated inflammatory skin disorders.[35] This increase in systemic chronic inflammation has also been related with lower vitamin-D and bone mineral density levels.[7,17]

Limitations and need for future studies

The limitations of this study are those of cross-sectional studies with control group, such as the lack of follow up and the inability of making causality inferences. Although there is a male predominance in the *P* group, the use of a multivariate analysis with adjusted model eliminates the differences between the study groups mediated by this variable, making the groups fully comparable. On the contrary, despite the multiple studies describingthe association between psoriasis and low bone mineral density levels, a recent Norwegian population-based study has not found a reduced bone mineral density level or an increased risk of osteoporosis in psoriatic patients.[36] Moreover, despite the deficit of vitamin D found in patients with psoriasis, treatment with oral calcium and/or vitamin D to prevent osteoporotic fractures remains controversial.[37,38]

Conclusions

In conclusion, a cross-sectional study comparing bone mineral density in psoriatic patients vshealthy controls and patients with osteopenia/osteoporosis is presented. We were unable to find any report of the last comparison in literature. According to our results, levels of bone mineral density in patients with moderate to severe psoriasis are situated halfway between those present in healthy controls and patients with osteopenia/osteoporosis. The higher body mass index found in the psoriatic group could be a protective factor against the development of osteopenia/osteoporosis in these patients. However, more studies would be needed to demonstrate a causal association

between psoriasis and the risk of developing osteopenia/osteoporosis.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patients have given their consent for their images and other clinical information to be reported in the journal. The patients understand that name and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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