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Article

Clinical Characteristics of Patients with Psoriatic Arthritis: Association between Sex and Comorbidity

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Abstract: Many studies have addressed sex differences in patients with psoriatic arthritis, although these are aimed more at describing the phenotype than at investigating the causes underlying the differences. Cross-sectional study of 203 patients. The clinical and demographic variables included age, years of education, time since onset, smoking, type of treatment, clinical presentation, number of entheses affected, dactylitis, fatigue, and cutaneous involvement. Disease activity,functioning and disease was measured. The comorbid conditions evaluated included obesity (and leptin as an associated parameter), anxiety and depression, and sleep quality. Mean age was 54.6, and 46.8% of patients were women. Women less frequently presented axial involvement and more frequently presented enthesitis. They also presented greater disease activity, greater disease impact, and poorer functioning, as well as greater fatigue. As for comorbid conditions, women presented a higher leptin/BMI ratio, higher levels of anxiety and depression, and poorer sleep quality. By sex, pain affecting women was associated with the leptin/BMI ratio and sleep quality. The leptin/BMI ratio was not associated with any component of disease activity in men. Sex was associated with several clinical manifestations, disease activity, functioning, and disease impact. Leptin was associated with intensity of pain in women.

Keywords: arthritis psoriatic; gender perspective; comorbidities

1. Introduction

Psoriatic arthritis (PsA) is an immune-mediated musculoskeletal disease that affects both the joint and the enthesis. It affects men and women equally, although differences have been found in phenotype, impact, and response to treatment [1,2]. In fact, multiple joint involvement is more common among women, in contrast with men, who are more commonly affected by axial presentations, which are associated with positive HLA-B27 values and greater radiological damage [3–5]. As for cutaneous manifestations, most studies report more frequent onychopathy in men [6]. Differences between the sexes have also been found with respect to the frequency of onset of specific comorbid conditions. Anxiety and depression affect up to 30% of patients with PsA, and, in line with the general population, these conditions are more frequent among women [7,8]. Similar data have been reported for fatigue and insomnia [4,9], whose greater frequency in women can act as a confounder owing to their potential effect on specific clinical manifestations of PsA, such as pain. Thus, women perceive pain as being more intense, a finding that has been associated with these comorbid conditions or with concomitant fibromyalgia. Irrespective of the origin, the more intense pain perceived by women leads to greater scores in measures of disease activity (most of which

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include pain as a domain) and to reduced efficacy and persistence of the treatments administered [10–13]. Despite the potential presence of other pathophysiologic mechanisms that account for greater intensity in the perception of pain, most studies continue to accept the presence of these confounders—anxiety, depression, and fibromyalgia—as the only explanation. Therefore, few data have been reported on whether a mechanism underlying sex and independent of confounders. Sex hormones clearly play a role in these mechanisms. Models based on male mice show that spinal microglial cells are associated with persistent hypersensitivity to pain, probably via the Toll-like receptor 4 (TLR4), which depends on testosterone [14]. Estrogens and progestogens, on the other hand, seem to exercise a dual pronociceptive and antinociceptive effect [15]. The hormone leptin is secreted mainly by adipose tissue, stimulated by ovarian sex hormones, and inhibited by testosterone; therefore, its blood levels are higher in women [16]. Together with its metabolic function, leptin intervenes in the proinflammatory response by triggering the production of cytokines such as TNF alpha and IL-6, stimulating differentiation between Th1 and Th17 cells [17–19], and contributing to abnormal pain processing [20].

Therefore, the objective of our study was to evaluate the association between demographic and clinical characteristics and sex-related comorbidities in a cohort of patients with PsA.

2. Materials and Methods

Methods

1. **Type of study**

Cross-sectional study conducted at Salamanca University Hospital (Salamanca, Spain).

2. **Population**

Inclusion criteria: We included consecutive patients aged ≥18 years with a diagnosis of PsA according to the ClASsification criteria for Psoriatic ARthritis (CASPAR) [21] who were seen in outpatient rheumatology clinics between March 2023 and November 2023 and agreed to participate in the study.

Exclusion criteria: We excluded patients who met the American College of Rheumatology diagnostic criteria for fibromyalgia (2016) [22] or had previously been diagnosed and treated for depression, anxiety, diabetes, or dyslipidemia in order to avoid the possible influence of emotional state and obesity on the measurements.

The study was approved by the ethics committee of Salamanca University Hospital (EO 2023 03 1246 - TFG). Patients gave their written informed consent to participate in the study and for the results derived from the research to be published.

3. **Variables assessed**

3.1 **Demographic and clinical characteristics**

Data were collected on the following variables: age; sex; years of education; time since onset; smoking status (smoker/former smoker/never smoker) and the number of cigarettes smoked measured in pack-years [23]; treatment with conventional synthetic disease-modifying antirheumatic drugs (csDMARDs), targeted synthetic DMARDs (tsDMARDs), and biologic DMARDs (bDMARDs) at the time of the study; patients with more than 1 line of treatment with bDMARDs owing to lack of efficacy; form of the disease (peripheral, mixed, or axial), with axial presentations defined as inflammatory lower back pain and radiographic damage (sacroiliitis of at least grade 2 as per New York criteria and/or presence of syndesmophytes) [24,25]; polyarthritis; dactylitis (current or past); and the number of entheses involved as assessed using the modified Maastricht Ankylosing Spondylitis Enthesitis Score (mMASES) [26]. The original MASES [27] focuses on 15 entheses (the bilateral first and seventh costochondral joints, anterior and posterior superior iliac spine, iliac crests, and proximal insertion of the Achilles tendons, as well as the fifth lumbar spinous process); this was modified for PsA to include the plantar fascia, with scores ranging from 0 to 15 [26]. The extent of psoriasis was assessed using the Psoriasis Area Severity Index (PASI) [28]. Fatigue was assessed using the Functional Assessment of Chronic Illness Therapy (FACIT) scale, specifically, the FACIT-fatigue

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scale, which has been validated for PsA [29]) and consists of 13 items assessing self-reported fatigue and its impact on activities of daily living and functioning. Items are rated on a 5-point Likert-type scale from 0 to 4, yielding a total score between 0 and 52, with higher scores indicating less fatigue. Permission was obtained from FACIT.org for the use of the questionnaire in this study.

3.2 Disease activity, functioning, and disease impact.

In patients with peripheral involvement, disease activity was measured using the Disease Activity Index for Psoriatic Arthritis (DAPSA) [30], a composite score designed to assess disease activity in PsA. It is calculated by summing C-reactive protein (CRP, mg/dL), tender joint count (0-68), swollen joint count (0-66), the patient global assessment of disease activity (between 0 and 10 on a numerical rating scale [NRS]), and pain NRS score (0-10). In the case of patients with axial involvement, we used the Ankylosing Spondylitis Disease Activity Score with CRP (ASDAS-CRP) [31]. Functional ability was measured using the Health Assessment Questionnaire-Disability Index (HAQ-DI) for peripheral involvement and the Bath Ankylosing Spondylitis Functional Index (BASFI) for axial involvement. Disease impact was assessed using the 12-item Psoriatic Arthritis Impact of Disease questionnaire (PsAID-12) [32–34].

3.3 Variables related to obesity, emotional state, and sleep quality

Obesity was measured using the body mass index (BMI), which is calculated by dividing weight measured in kg by the height in meters squared [35]. As a parameter associated with obesity, we measured leptin serum levels owing to the association between inflammatory activity and pain in other immune-mediated diseases [19,20]. Leptin was measured using enzyme-linked immunosorbent assay (calibrated according to International Standard WHO/NIBSC 97/594 [recombinant leptin], using a Cobas e411 analyzer with module E170 for modular analytics, and Cobas e601 and e602 analyzers). The leptin/BMI ratio was calculated to determine the association between leptin levels and BMI.

We assessed emotional factors using the Hospital Anxiety and Depression Scale (HADS). The HADS is a 14-item scale designed to identify people with anxiety and depression among individuals with medical conditions. Scores range from 0 to 21 for each subscale (HADS-D for depression and HADS-A for anxiety) and can be classified into 1 of 3 categories: normal (0–7), borderline abnormal indicating a possible clinical disorder (8–10), and abnormal indicating a probable clinical disorder (11-21) [36].

Sleep quality was analyzed using the Insomnia Severity Index (ISI). This self-administered questionnaire comprises 7 items assessing the nature, severity, and impact of insomnia. Responses are rated on a 5-point Likert-type scale ranging from 0 to 4, referring to the previous month. The overall score ranges between 0 and 28 and can be interpreted based on cut-offs, as follows: no clinically significant insomnia (0-7), subthreshold insomnia (8-14), clinical insomnia (moderate severity) (15-21), and clinical insomnia (severe) (22-28) [37].

4. Statistical analysis

Quantitative variables are reported as mean and standard deviation and categorical variables as number and percentage. Comparisons between groups were carried out using the *t* test for normally distributed quantitative variables and the Mann-Whitney test for ordinal variables or non-normally distributed quantitative variables. Comparisons between more than 2 groups were performed using 1-factor analysis of variance for normally distributed quantitative variables and the Kruskal-Wallis test for ordinal variables or non-normally distributed quantitative variables. Correlations between quantitative variables were assessed using Pearson's correlation coefficient. p Values <0.05 were considered statistically significant.

Bivariate correlations were calculated between the leptin/BMI ratio, ISI, HADS-A, HADS-D, and the components of DAPSA for women and men. Given the effect of leptin on pain [20],linear regression analysis was performed for both sexes, with the dependent variable being pain according to the visual analog scale (VAS) and the independent variables being the leptin/BMI ratio and the findings for ISI, HADS-A, and HADS-D. Both models were adjusted for treatment with tsDMARDs and bDMARDs. The independent variables were selected based on data published elsewhere [9,38].

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This analysis was performed with IBM SPSS Statistics for Windows, Version 23.0.

3. Results

3.1. Demographic and Clinical Characteristics

Mean age was 54.6±11.3 years, and 46.8% of patients were women. Time since onset of the disease was 10.0±7.0 years, and 27.1% of patients were receiving tsDMARDS or bDMARDs. The mean DAPSA score was 14.9±7.4. The remaining data are summarized in Table 1.

Table 1. Demographic, clinical, and disease-related characteristics of patients with psoriatic arthritis.

Total	**n=203** mean ± standard deviation or number (%)
Years of education	11.0 ± 7.0
Smoking status	
Smoker	53 (26)
Former smoker	93(46)
Non-smoker	57 (28)
Pack-years	20.0 ± 19.8
Conventional synthetic DMARDs	153 (75)
Methotrexate	105 (52)
Sulfasalazine	38 (19)
Leflunomide	10 (5)
tsDMARDs	4 (2)
bDMARDs	55 (27)
TNF inhibitor	34 (17)
Other	17 (8)
Failure of tsDMARDs or bDMARDs, N (%)	28(50)
Clinical form	
Peripheral	
Mixed	166(82)
Axial	31(15)
Polyarthritis	6(3)
Dactylitis	20(9.9)
	41(20.2)
mMASES	1.4 ± 2.0
PASI	1.2 ± 7.7
FACIT-Fatigue	35.8+11.3
DAPSA*	14.9 ± 7.4
Pain VAS*	4.5 ± 2.7
Activity VAS*	4.0 ± 2.6
TJC*	3.7 ± 2.4
SJC*	1.7 ± 1.8

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C-reactive protein (mg/dL)	0.8 ± 1.0
HAQ*	0.6 ± 0.6
ASDAS-CRP**	1.7 ± 0.8
BASFI**	3.5 ± 2.8
PsAID-12	3.4 ± 2.1
BMI (kg/m²)	27.0 ± 4.4
Leptin (ng/dL)	16.8 ± 18.9
Leptin/BMI	0.5 ± 0.6
HADS anxiety	5.7 ± 3.7
HADS depression	4.1 ± 3.6
ISI	8.1 ± 4.7

Abbreviations: ***ASDAS-CRP***: Ankylosing Spondylitis Disease Activity Score with C-reactive protein; ***BASFI:*** Bath Ankylosing Spondylitis Functional Index; ***BMI:*** body mass index; ***DAPSA:*** Disease Activity Index for PSoriatic Arthritis; ***DMARD:*** disease-modifying antirheumatic drug; ***bDMARD:*** biologic DMARD; ***tsDMARD:*** targeted synthetic DMARD; ***FACIT:*** Functional Assessment of Chronic Illness Therapy; ***HADS:*** Hospital Anxiety and Depression Scale; ***HAQ-DI:*** Health Assessment Questionnaire-Disability Index; ***ISI:*** Insomnia Severity Index; ***mMASES:*** modified Maastricht Ankylosing Spondylitis Enthesitis Score; ***PASI:*** Psoriasis Area Severity Index; ***PsAID-12:*** 12-item Psoriatic Arthritis Impact of Disease questionnaire; ***SJC:*** swollen joint count; ***TJC:*** tender joint count; ***TNF:*** tumor necrosis factor; ***VAS:*** visual analog scale. *In peripheral forms (n= 197).**In axial forms (n= 37).

3.1.1. Demographic and Clinical Variables, Disease Activity, Functioning, Disease Impact, and Comorbid Conditions: Comparison between the Sexes

Axial involvement was less common and enthesitis more common in women. Women also had more marked disease activity and impact and poorer functioning in peripheral presentations. No differences in BMI were found between the sexes. Women had a greater leptin/BMI ratio and more severe fatigue. As for the remaining comorbid conditions, women had higher degrees of anxiety, depression, and fatigue and poorer sleep quality.

The results of the comparisons are summarized in Table 2.

Table 2. Demographic, clinical, and disease-related characteristics of patients with psoriatic arthritis by sex.

Variable	Women (n=95)	Men (n=108)	P
Age*	54.2 ± 10.2	55.0 ± 12.3	0.4
Years of education*	11.5 ± 4.9	10.7 ± 5.10	0.5
Years since onset*	9.5 ± 6.2	10.4 ± 7.7	0.2
Smoking status (%)			0.001
Smoker	33 (35)	20 (18)	
Former smoker	31 (33)	62 (57)	
Non-smoker	31 (32)	26 (24)	
Smoking, pack-years	15.7 ± 14.2	23.3 ± 21.8	0.1
ts DMARDs or bDMARDs, N (%)	26 (25.2)	33 (28.7)	0.5
Failure of tsDMARDs or bDMARDs, N (%)	16 (64)	12 (38.7)	0.06

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Clinical presentation, N (%)			
Peripheral	88 (92)	78 (72)	0.001
Mixed	7 (8)	24 (22)	
Axial	0 (0)	6 (6)	
Polyarthritis (yes/no) (%)	8/87 (8)	12/90 (11)	0.4
Dactylitis (yes/no) (%)	12/83 (12.6)	24/84 (22.2)	0.07
Enthesitis	2.2 ± 2.4	0.7 ± 1.2	0.001
PASI*	1.1 ± 1.7	1.3 ± 1.7	0.2
FACIT-F	32.7 ± 11.2	38.5 ± 10.8	0.001
CRP (mg/dL)*	0.8 ± 1.1	0.8 ± 0.9	0.4
Pain VAS *	5.2 ± 2.5	3.9 ± 2.8	0.001
Activity VAS *	4.4 ± 2.4	3.6 ± 2.8	0.03
SJC *	1.6 ± 1.7	1.7 ± 1.8	0.7
TJC *	4.2 ± 2.5	3.2 ± 2.3	0.02
DAPSA	16.4 ± 7.1	13.4 ± 7.5	0.001
ASDAS-CRP*	2.4 ± 0.8	1.5 ± 0.7	0.02
HAQ-DI*	0.8 ± 0. 5	0.5 ± 0.5	0.001
BASFI*	4.9 ± 2.5	3.0 ± 2.8	0.95
PsAID-12	4.0 ± 2.1	3.0 ± 2.1	0.001
BMI (kg/m²)	26.7 ± 5.2	27.3 ± 3.5	0.06
Leptin (ng/mL)	26.4 ± 22.6	8.4 ± 8.6	0.001
Leptin/BMI	2.4 ± 0.8	1.5 ± 0.7	0.001
HAS-A	6.9 ± 3.8	4.7 ± 3.2	0.001
HAS-D	4.9 ± 3.4	3.4 ± 3.5	0.004
ISI	9.3 ± 4.9	7.0 ± 4.3	0.001

Abbreviations: ***ASDAS-CRP:*** Ankylosing Spondylitis Disease Activity Score with C-reactive protein; ***BASFI:*** Bath Ankylosing Spondylitis Functional Index; ***DAPSA:*** Disease Activity Index for PSoriatic Arthritis; ***tsDMARD:*** targeted synthetic disease-modifying antirheumatic drug; ***bDMARD:*** biologic disease-modifying antirheumatic drug; ***FACIT:*** Functional Assessment of Chronic Illness Therapy; ***HADS:*** Hospital Anxiety and Depression Scale; ***HAQ-DI:*** Health Assessment Questionnaire - Disability Index; ***ISI:*** Insomnia Severity Index; ***SJC:*** swollen joint count; ***TNF:*** tumor necrosis factor; ***TJC:*** tender joint count; ***VAS:*** visual analog scale; ***BMI:*** body mass index, ***mMASES:*** modified Maastricht Ankylosing Spondylitis Enthesitis Score; ***PASI:*** Psoriasis Area Severity Index; ***PsAID-12:*** 12-item Psoriatic Arthritis Impact of Disease questionnaire. *In peripheral presentations (n= 197).**In axial presentations (n= 37).

3.1.1.1. Association between comorbid conditions and disease activity (peripheral and axial) by sex

- Women

1. Peripheral

Table 3 summarizes the correlation between the DAPSA components and the leptin/BMI ratio, anxiety, depression, and sleep quality.

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Table 3. Correlation between DAPSA components and leptin levels, HADS, and ISI in women.

	CRP	VAS pain	VAS activity	TJC	SJC
Leptin/BMI	r: 0.0 p=0.8	r: 0.2 **p<0.02**	r: 0.1 p=0.1	r: 0.0 p=0.5	r: 0.1 p=0.1
HADS-A	r: 0.0 p=0.8	r: 0.1 p=0.09	**r:0.2 p<0.03**	r: 0.0 p=0.9	r: 0.0 p=0.9
HADS-D	r: 0.1 p=0.1	r: 0.2 **p<0.005**	**r: 0.2 p<0.02**	r: 0.1 p=0.08	r: 0.2 p<0.04
ISI	r: 0.0 p=0.9	r: 0.35 **p<0 .001**	r: 0.1 p=0.1	r: 0.2 p<0.01	r: 0.2 p<0.04

Abbreviations: ***BMI:*** body mass index; ***HADS:*** Hospital Anxiety and Depression Scale; ***ISI:*** Insomnia Severity Index; ***SJC:*** swollen joint count; ***TJC:*** tender joint count, ***VAS:*** visual analog scale.

The linear regression analysis showed pain to be associated with the leptin/BMI ratio (β: 0.29; p<0.004; 95%CI: 0.3-1.6) and sleep quality (β: 0.31; p<0.004; 95%CI: 0.04-0.25; R^2: 0.26). The values for HADS-A and HADS-D were p=0.4 and p=0.09, respectively.

2. Axial

No statistically significant differences were found between ASDAS-CRP and the leptin/BMI ratio (r: 0.3; p=0.3), anxiety (HADS-A r: 0.5; p=0.2), depression (HADS-D r:0.0; p=0.9), and sleep quality (ISI r: 0.3; p=0.4).

- Men

1. Peripheral

Table 4 summarizes the correlation between the components of DAPSA and the leptin/BMI ratio, anxiety, depression, and sleep quality.

Table 4. Correlation between the components of DAPSA and leptin levels, HADS, and ISI in men.

	CRP	VAS pain	VAS activity	TJC	SJC
Leptin/BMI	r: 0.02 p=0.7	r: 0.07 p=0.46	r: 0.0 p=0.47	r: 0.02 p=0.7	r: 0.06 p=0.5
HADS-A	r: -0.0 p=0.3	**r: 0.37 p<0.001**	r: 0.1 p=0.2	r: 0.0 p=0.3	r: 0.0 p=0.7
HADS-D	r: -0.1 p=0.2	**r: 0.4 p<0.005**	r: 0.1 p=0.06	r: 0.0 p=0.3	r: -0.1p=0.8
ISI	r: -0.7 p=0.4	**r: 0.51 p<0.001**	**r: 0.36 p<0.001**	**r: 0.30 p<0.01**	r:-0.0 p=0.5

Abbreviations: ***BMI:*** body mass index; ***HADS:*** Hospital Anxiety and Depression Scale; ***ISI:*** Insomnia Severity Index; ***SJC:*** swollen joint count; ***TJC:*** tender joint count, ***VAS:*** visual analog scale.

The linear regression analysis showed pain to be associated with sleep quality (ISI β: 0.4; p<0.001; 95%CI: 0.15-0.41; R^2: 0.27). Values for the remaining variables were as follows: leptin/BMI (p=0.7), HADS-A (p=0.9), and HADS-D (p=0.4).

2. Axial

A statistically significant association was identified between ASDAS-CRP and sleep quality using ISI (r: 0.6, p=0.001). This was not the case for the leptin/BMI ratio (r: 0.0, p= 0.7), anxiety (HADS-A r: 0.3, p=0.08), and depression (HADS-D r: 0.2, p=0.1).

Missing data accounted for less than 3%.

4. Discussion

Many studies have addressed sex differences in patients with PsA, although these are aimed more at describing the phenotype than at investigating the causes underlying the differences. We found sex to be associated with the presence of specific clinical manifestations; in most of the subjective variables, the association was with disease activity and functioning. Higher leptin concentrations, while not directly associated with obesity, may have intervened in the perception of pain among women.

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In most previous studies, the clinical presentation differed between the sexes, mainly in the greater frequency of axial disease affecting men [3,5]. Consistent with previous reports, we found a greater presence of axial disease, defined according to the degree of radiological damage. Furthermore, Eder et al. [3]found that male sex was associated not only with more frequent axial presentation, but also with greater radiological damage. However, these results were not confirmed in recent studies in Turkish and Chinese populations [39,40]. In contrast with data reported by Queiró et al. [5], our results are similar to those from various cohort studies [3,39,40], which did not reveal more frequent polyarticular presentation in women. As for other clinical manifestations, enthesitis was more common among women than among men. These results are consistent with those from the cohorts CORRONA [41]and ASAS [42]. However, most studies report no association between sex and the predominance of enthesitis. These differences can be explained by the various methods of measurement applied [39,40]. As in other studies, we found no association between sex differences and dactylitis or severity of psoriasis [3–5,39,40].

We recorded greater disease activity and poorer functioning in patients with peripheral manifestations. These findings are consistent with those of Orbai et al. [43], whose multinational study covered 14 countries. With respect to disease activity, the findings are also consistent with the data obtained from the Turkish cohort using DAS28, although not with those reported for functioning [39]. As for axial presentations, we found differences in disease activity but not in functioning. These results are consistent with those reported by Nas et al.[44] for a study population comprising patients with axial PsA. In the ASAS cohort, significant differences were found in activity and functioning, although the study population was not separated according to whether the patients had axial or peripheral manifestations [42].

Disease impact was also greater in women, consistent with data reported by Gossec et al. [4].

As for comorbidity, we did not find statistically significant differences in BMI between the sexes. Some previous studies report greater BMI in women [39,42], possibly because of the inclusion criteria more than the presence of any real sex differences. Serum leptin levels, such as those adjusted for BMI, were higher in women. In physiological terms, this hormone is predominant in women; however, to our knowledge, differences have not been studied in patients with PsA [16]. In our study population, we found that leptin levels adjusted for BMI were associated with perception of pain. Eder et al. [3] found no differences between leptin levels and the number of active joints (r: 10; p=0.05). In a further study, these authors did not examine the association between intensity of pain and leptin levels [45]. A recent study of patients with rheumatoid arthritis found an association between leptin levels and pain, although the authors did not analyze the results by sex[46]. This association has also been found in other diseases, such as arthrosis [47]. Animal models have revealed a cellular link between the effects of leptin on the spinal column and the extrasynaptic NMDAR-nNOS–mediated cellular mechanism underlying neuropathic pain [48].

As for axial manifestations, Hernández-Breijo et al. [49] studied a cohort of patients with axial spondyloarthritis and reported an association between response to treatment with TNF inhibitors and baseline leptin levels. We found no correlation between axial disease activity and the leptin/BMI ratio. This observation could be explained by the small number of patients included.

Although we excluded patients with fibromyalgia, anxiety, and depression, the scores on the questionnaires associated with these conditions, either directly or indirectly, were higher in women. Moreover, they affected various items on the DAPSA for both sexes. Anxiety and depression have been associated with increased disease activity, especially in terms of the subjective components of the instrument [38]. However, the fact that they more frequently affect women, irrespective of whether they have PsA, means that they must be considered confounders and not a sex-associated characteristic of the disease. Furthermore, these comorbid conditions affected the subjective variables of disease activity for both sexes, although they were more frequent in women. As for sleep quality, while this can be considered to be closely linked to anxiety and depression, a recent study by our group found an association between sleep quality and disease activity, irrespective of these conditions [9]. To our knowledge, no other studies have previously associated sleep quality with sex in PsA.

Our study is limited by its cross-sectional design, and although it is not possible to establish causal relationships, in the case of the association between leptin/BMI ratio and intensity of pain, the association favors the effect of leptin on intensity and not the reverse. Studies with other characteristics could better consolidate the effect of higher leptin concentrations in women in more pronounced disease activity, without considering their role in obesity. Our study was also limited by the fact that we did not investigate women's hormonal status, even though secretion of leptin is known to be associated with estrogen production. Lastly, while there is a direct correlation between BMI and leptin secretion, BMI may not be the best marker to accurately reflect adiposity leading to greater leptin secretion.

Despite its limitations, our study is the first, to our knowledge, to address the role of leptin, a hormone whose secretion is closely linked to sex, as a possible cause of the difference in disease activity observed in women with PsA.

5. Conclusions

Sex played a role in the subjective parameters associated with disease activity and impact and functioning. An association was observed between the highest leptin concentrations—a characteristic of female sex and not obesity in our study—and perception of pain.

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Institutional Review Board Statement: The study was conducted in accordance with the Declaration of Helsinki, and approved by the ethics committee of Salamanca University Hospital (EO 2023 03 1246 - TFG).

Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

Data Availability Statement: The data presented in this study are available on request from the corresponding author.

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Conflicts of Interest: The authors declare no conflicts of interest.

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