Depression and Anxiety in Psoriatic Disease: Prevalence and Associated Factors

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ABSTRACT. ***Objective.*** (1) To determine the prevalence of depression and anxiety in patients with psoriatic arthritis (PsA) and to identify associated demographic and disease-related factors. (2) To determine whether there is a difference in the prevalence of depression and anxiety between patients with PsA and those with psoriasis without PsA (PsC).

Methods. Consecutive patients attending PsA and dermatology clinics were assessed for depression and anxiety using the Hospital Anxiety and Depression Scale. Patients underwent a clinical assessment according to a standard protocol and completed questionnaires assessing their health and quality of life. T tests, ANOVA, and univariate and multivariate models were used to compare depression and anxiety prevalence between patient cohorts and to determine factors associated with depression and anxiety.

Results. We assessed 306 patients with PsA and 135 with PsC. There were significantly more men in the PsA group (61.4% vs 48% with PsC) and they were more likely to be unemployed. The prevalence of both anxiety and depression was higher in patients with PsA (36.6% and 22.2%, respectively) compared to those with PsC (24.4% and 9.6%; p = 0.012, 0.002). Depression and/or anxiety were associated with unemployment, female sex, and higher actively inflamed joint count as well as disability, pain, and fatigue. In the multivariate reduced model, employment was protective for depression (OR 0.36) and a 1-unit increase on the fatigue severity scale was associated with an increased risk of depression (OR 1.5).

Conclusion. The rate of depression and anxiety is significantly higher in patients with PsA than in those with PsC. Depression and anxiety are associated with disease-related factors. (First Release April 1 2014; J Rheumatol 2014;41: 887–96; doi:10.3899/jrheum.130797)

Key Indexing Terms:
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Psoriasis is a chronic inflammatory disease, characterized by erythematous scaly plaques that may be pruritic[1], and is estimated to affect between 1% to 3% of the population[2,3]. Psoriatic arthritis (PsA), occurring in 30% of patients with psoriasis[4], is characterized by pain, tenderness, and swelling of the joints.

The prevalence of depression in patients with psoriasis ranges from 19.2% to 62%[5,6,7,8] and anxiety is reported to be as high as 43%[9]. The prevalence rate of suicidal ideation among patients with psoriasis (5.5%) is higher than that reported in numerous studies of general medical patients (2.4% to 3.3%)[10,11,12,13]. Further, patients with PsA have been found to have a worse quality of life (QOL) than patients with psoriasis alone[14], and the presence of joint pain is associated with higher rates of depression[15]. Anxiety and depression are also common among patients with rheumatoid arthritis (RA), the prototype of inflammatory arthritis, with 13.4% having a diagnosis of anxiety and 41.5% of depression[16]. Therefore, for patients with PsA, the combination of joint and skin disease may increase the risk for depression and anxiety, and may be associated with unique factors.

While a number of studies have measured the prevalence

of depression and anxiety in patients with PsA (ranging from 7.9% to 29.7%)[17,18,19,20], few have examined depression and anxiety separately or as the main focus of the study. The only 2 studies (by Freire, *et al*[17] and Kotsis, *et al*[20]) that examined anxiety and depression in patients with PsA were both conducted in Europe. There is yet to be a study focusing on the prevalence of depression and anxiety in North American patients with PsA. Further, the study by Kotsis, *et al*[20] compared PsA and patients with RA, but no study has compared patients with psoriasis alone (PsC) to those with PsA. The aims of our study were therefore (1) to measure and compare the prevalence of depression and anxiety in patients with PsC and patients with PsA, and (2) to identify demographic and disease-related factors associated with poorer mental health that are unique to PsA and PsC, and those factors that are common to psoriatic disease.

MATERIALS AND METHODS

Setting and study population. Consecutive patients attending the PsA and dermatology clinics at Toronto Western Hospital were assessed for depression and anxiety using the Hospital Anxiety and Depression Scale (HADS)[21]. Patients were referred to the clinics from the greater Toronto area as well as from other parts of the province of Ontario. Patients with PsA satisfied the Classification Criteria for Psoriatic Arthritis (CASPAR)[22]. Patients with PsC had their psoriasis confirmed by a dermatologist and were assessed by a rheumatologist to exclude the diagnosis of PsA, and were reevaluated annually for the possible development of PsA[23].

Outcome measure. HADS[21] is a 14-item scale designed to identify people with anxiety and depression among individuals with medical conditions. Good reliability and validity coefficients were reported specifically for dermatology patients[24]. Scores for each subscale (HADS-D for depression and HADS-A for anxiety) range from 0–21 and can be classified into 3 categories: normal (0–7), borderline abnormal indicating a possible clinical disorder (8–10), and abnormal indicating a probable clinical disorder (11–21). HADS has good sensitivity and specificity in identifying cases of psychiatric distress as detected by the Structured Clinical Interview for *Diagnostic and Statistical Manual of Mental Disorders-IV*[25]. Cases of depression or anxiety can be defined using a cutoff score of 8 with both sensitivity and specificity of 0.8[21].

Clinical assessment. Patients with PsA were routinely reviewed at 6-month to 12-month intervals with a detailed assessment according to a standard protocol[23,26]. Demographic data and a complete medical history were taken at baseline and updated at each visit. Smoking status and alcohol consumption habits were obtained at each visit. A detailed medication history was obtained. Radiographs were done at 2-year intervals. Physical examination at each visit included number of actively inflamed joints (stress pain, joint line tenderness, and/or swelling, 0–68 scale) and the number of deformed joints (ankylosis, subluxation, or decreased range of motion of more than 20%, attributable to joint damage rather than inflammation, 0–68 scale). Fibromyalgia was also assessed[27]. The severity of psoriasis was assessed by the Psoriasis Area and Severity Index (PASI) score[28,29]. Overall disease activity was scored using the Physician Global Assessment. Global health, joint disease, psoriasis, and global skin and joint disease were rated on a 5-point scale ranging from "very good" to "very poor". Patients with psoriasis without arthritis were followed at 12-month intervals according to the same protocol. All patients were recruited for this study between June 2011 and March 2013. The study was approved by the University Health Network research ethics board and all patients provided informed consent.

Patient reported outcomes. Patients completed questionnaires annually in paper or online format[30]. These included the Health Assessment Questionnaire (HAQ)[31,32], the Medical Outcomes Study Short Form-36 (SF-36)[33], the Dermatology Quality of Life Index (DLQI)[34], the Fatigue Severity Scale (FSS), and the Patient Global Assessment (PGA). Data from these questionnaires were included in the analysis if they were obtained within 3 months prior to completion of the HADS.

The HAQ has been validated in studies of PsA as a measure of disability in activities of daily living (hygiene, walking, eating, arising, dressing, and grooming). The SF-36 questionnaire assesses functional status, well-being, and general health perceptions and consists of 8 subscales, including bodily pain and mental subscales. The DLQI, consisting of 10 questions, assesses the effect of skin disease on a patient's QOL. It addresses symptoms (including pruritus), feelings, daily activities, work and school, personal relationships, and the effects of treatment on daily life[35]. The FSS assesses the effect of fatigue on activities of daily living. A score is computed as the average of 9 responses to questions relating to fatigue. Lastly, the PGA is a 7-item questionnaire asking the patient to rate their overall health and the effect of psoriasis and PsA on their life. A number of the patient-derived questionnaires (HAQ and SF-36) have been validated at the University of Toronto Psoriatic Arthritis Clinic[36,37].

All the information collected was entered into an Oracle database, along with current treatments, laboratory assessments, radiological evaluation, and patient-reported outcomes. Data obtained within 3 months of the completion of the HADS questionnaire was used in the analyses.

Statistical analysis. T tests for continuous variables and chi-squared tests for categorical variables were used to compare the prevalence of depression or anxiety between PsA and PsC cohorts. Further, patients were grouped by likelihood of depression or anxiety, and ANOVA tests were used to determine which factors were associated with an increase in depression or anxiety. A p value < 0.05 was considered statistically significant. Statistical analyses were conducted using SAS 9.3 software.

RESULTS

A total of 306 patients with PsA and 135 patients with PsC were included in the study (Table 1). We compared the 306 patients with PsA who completed the HADS to 91 who attended the clinic in the same period (June 2012–March 2013) who did not complete the questionnaires, and the 135 patients with PsC who completed the HADS to 43 patients who did not. The comparison included demographics, disease characteristics, medication use, and patient-reported outcomes. The only variable that was statistically significant was PsA duration, which was longer among those who completed the questionnaires. No differences were detected among the patients with PsC.

The age of patients with PsA and those with PsC was similar (53.8 and 52.4 yrs, respectively). The mean age at diagnosis for psoriasis was significantly younger in the PsA group (27.5 yrs vs 30.9 yrs for patients with PsC), and the duration of psoriasis was longer (mean duration 26.4 yrs vs 21.6 yrs). Patients with PsA were significantly more likely to be men (61% vs 49% for PsC) and were more likely to be unemployed (40% vs 29% for PsC). Smoking status and alcohol consumption were similar in both groups. Severity of psoriasis was worse in the PsC group (as measured by the PASI) while the Physician Global Assessment score was worse in the PsA group. In patients with PsA, the mean

Table 1. Sociodemographic and clinical characteristics of patients with PsA or PsC.

Characteristic	Frequency (%) or Mean (SD)		p
	PsA, n = 306	PsC, n = 135	
Age, yrs	53.8 (12.9)	52.4 (13.2)	0.29
Age at diagnosis of psoriasis	27.5 (13.8)	30.9 (16.6)	0.04
Age at diagnosis of PsA	36.5 (13.0)	—	—
Sex, female	118 (39%)	69 (51.5%)	0.01
Unemployed	122 (40%)	39 (29.1%)	0.03
Education status, college/university	248 (81.3%)	117 (87.3%)	0.12
Married/common-law	219 (71.8%)	77 (57.5%)	0.003
Smoking status			0.09
No	182 (59.7%)	65 (48.5%)	
Current	31 (10.2%)	19 (14.2%)	
Past	92 (30.2%)	50 (37.0%)	
Alcohol consumption			0.20
None	142 (46.6%)	50 (37.0%)	
Social	139 (45.6%)	69 (51.9%)	
Daily	24 (7.9%)	14 (10.5%)	
PASI	3.3 (4.1)	4.4 (4.6)	0.03
Active joint count	6.13 (7.01)	—	—
Damaged joint count	12.2 (12.9)	—	—
Physician global assessment (fair–very poor)	55 (18.8%)	2 (1.6%)	< 0.0001
HAQ	0.61 (0.65)	0.08 (0.23)	< 0.0001
HAQ pain (0–100)	29.7 (25.4)	9.1 (6.2)	< 0.0001
SF-36 MCS	48.7 (11.1)	50.3 (11.0)	0.18
SF-36 PCS	40.9 (12.2)	51.7 (7.7)	< 0.0001
Patient's global assessment (fair–very poor)	128 (42.1%)	21 (16.4%)	< 0.0001
DLQI	3.47 (4.85)	4.36 (5.16)	0.09
FSS	4.49 (3.18)	2.89 (2.50)	< 0.0001
Ultraviolet therapy	4 (1.3%)	30 (22.4%)	< 0.0001
Topicals for psoriasis	163 (53.8%)	113 (84.3%)	< 0.0001
NSAID	184 (60.7%)	9 (6.9%)	< 0.0001
DMARD	178 (58.8%)	19 (14.5%)	< 0.0001
Biologic agents	145 (47.9%)	12 (9.2%)	< 0.0001
Antidepressants	41 (13.5%)	14 (10.5%)	0.37

PsA: psoriatic arthritis; PsC: psoriasis without arthritis; PASI: Psoriasis Area and Severity Index; HAQ: Health Assessment Questionnaire; SF-36 MCS and PCS: Medical Outcomes Study Short-form 36 Mental Component Subscale and Physical Component Subscale; DLQI: Dermatology Quality of Life Index; FSS: Fatigue Severity Scale; NSAID: nonsteroidal antiinflammatory drugs; DMARD: disease-modifying antirheumatic drugs.

number of actively inflamed joints and clinically damaged joints were 6.13 and 12.2, respectively. They were more likely to have taken nonsteroidal antiinflammatory drugs (NSAID), disease-modifying antirheumatic drugs (DMARD), and biologic agents than patients with PsC, but were less likely to have received ultraviolet phototherapy and topical medications for psoriasis. Patients with PsA fared worse on measures of disability and QOL such as the HAQ, SF-36 PCS, PGA, and FSS. Scores on the DLQI and SF-36 MCS, however, were similar between PsA and PsC groups. A similar proportion of patients in each group were currently taking antidepressant medication (13.5% and 10.5%, respectively).

Prevalence of depression and anxiety in psoriatic disease. The prevalence of anxiety and depression was determined by a HADS subscale score of ≥ 8. The prevalence of depression was 22.2% in patients with PsA and 9.6% in patients with PsC (p = 0.002; Table 2). The mean HADS depression score was also significantly higher in the PsA group [4.5 (3.8) vs 2.8 (2.9), p < 0.0001]. The prevalence of anxiety was 36.6% in patients with PsA and 24.4% in patients with PsC (p = 0.012). The prevalence of patients with comorbid depression and anxiety was 17.7% in the PsA group compared to 6.7% in the PsC group (p = 0.002).

Factors associated with depression in PsA. Patients with PsA were grouped into 3 categories based on likelihood of depression. Patients with a HADS-D score of ≤ 7 were unlikely to be depressed, 8–10 had possible clinical depression, and ≥ 11 had probable clinical depression. Variation in demographics, disease severity, and patient outcomes between these 3 groups were measured using ANOVA (Table 3). The only demographic variable associated with an increased likelihood of depression was unemployment. Other factors such as age, disease duration, sex, marital status, education, and smoking or alcohol consumption were not significantly associated with likelihood of depression. Of the measures of disease severity, a

Table 2. Prevalence of anxiety and depression among patients with PsA and PsC.

Variables	Frequency (%) or Mean (SD)		p
	PsC, n = 135	PsA, n = 306	
Anxiety			
HADS-A score	5.59 (3.62)	6.13 (3.86)	0.17
Possible clinical disorder	21 (15.6%)	66 (21.6%)	0.14
Probable clinical disorder	12 (8.9%)	46 (15.0%)	0.08
Total	33 (24.4%)	112 (36.6%)	0.01
Depression			
HADS-D score	2.76 (2.94)	4.51 (3.76)	< 0.0001
Possible clinical disorder	10 (7.4%)	40 (13.1%)	0.08
Probable clinical disorder	2 (2.2%)	28 (9.2%)	0.01
Total	13 (9.6%)	68 (22.3%)	0.002
Anxiety and depression			
Both probable clinical disorders	3 (2.2%)	12 (3.9%)	0.36
Both possible or probable (total)	9 (6.7%)	54 (17.7%)	0.002

Possible clinical disorder: HADS 8–10. Probable clinical disorder: HADS ≥ 11. Total: HADS ≥ 8. HADS: Hospital Anxiety and Depression Scale; HADS-A: HADS anxiety subscale; HADS-D: HADS depression subscale; PsA: psoriatic arthritis; PsC: psoriasis without PsA.

higher actively inflamed joint count and a higher score on the Physician Global Assessment were associated with increased likelihood of depression. PASI score and the number of damaged joints were not found to be significant factors in measuring psoriasis severity. All patient-reported outcomes were poorer in patients with depression, including the HAQ, SF-36 PCS, MCS-PGA, DLQI, and FSS. Treatments for PsA were not associated with an increased risk of depression.

Factors associated with anxiety in PsA. Patients with PsA were grouped into 3 categories based on likelihood of anxiety. Patients with a HADS-A score of ≤ 7 were unlikely to be anxious, 8–10 had possible clinical anxiety, and ≥ 11 had probable clinical anxiety. Variations in demographics, disease severity, and patient outcomes between these 3 groups were measured using ANOVA (Table 4). Anxiety was associated with a higher unemployment rate. Women were more likely than men to be anxious, while other factors such as age, disease duration, marital status, and education were not significant. Patients with PsA who had anxiety were more likely to be current smokers, while alcohol consumption was similar in all groups. A higher actively inflamed joint count and poorer score on the Physician Global Assessment were associated with higher rates of anxiety, while the PASI was not. All patient-reported outcomes, including the HAQ, SF-36, PGA, DLQI, and FSS, were poorer with increased likelihood of anxiety. Treatments for PsA were not associated with an increased risk of anxiety.

Factors associated with depression in PsC. Patients with PsC were stratified based on likelihood of depression (HADS-D score), and variations in demographics, disease severity, and patient-reported outcomes between these 3 groups were measured using ANOVA (Table 5). Like those with PsA, patients with PsC who were unemployed were more likely to be depressed. A lower level of education was also associated with increased likelihood of depression in PsC, while age, sex, and marital status were not significant. Depressed patients with PsC were more likely to be current smokers and less likely to consume alcohol. As with patients with PsA, the PASI score was not associated with an increased risk of depression while all patient-reported outcomes (HAQ, SF-36, PGA, DLQI, and FSS) were poorer, with an increased likelihood of depression. Treatments for PsC were not associated with depression with the exception of topical agents for psoriasis, which were less commonly used in the depressed group.

Factors associated with anxiety in PsC. Patients with PsC were stratified based on the likelihood of anxiety (HADS-A score) and variation in demographics, disease severity, and patient-reported outcomes between the 3 categories of likelihood of depression were measured using ANOVA (Table 6). Like patients with PsA, those with PsC who were female were more likely to be anxious. Other demographic factors such as unemployment, age, marital status, and education were not significantly associated with the likelihood of anxiety in patients with PsC. Patients with PsC and anxiety had similar smoking and alcohol consumption to their non-anxious counterparts. Poorer outcomes in the objective measures of disease severity (PASI and Physician Global Assessment) were not associated with increased risk of anxiety, while poorer scores on the patient-reported outcomes (HAQ, SF-36 MCS, PGA, DLQI, and FSS) were highly associated. Patients with PsC treated with NSAID were more anxious, but other treatment regimens had no significant association.

Table 3. Comparison of demographics, disease characteristics, and treatments of patients with PsA by likelihood of depression.

Variables	Frequency (%) or Mean (SD)			p
	Unlikely Depression (HADS ≤ 7), n = 238	Possible Clinical Depression (HADS 8–10), n = 40	Probable Clinical Depression (HADS ≥ 11), n = 28	
Age, yrs	53.7 (12.8)	53.7 (13.9)	55.0 (12.7)	0.88
Age at diagnosis of PsC, yrs	27.1 (13.6)	30.6 (14.2)	26.5 (14.4)	0.32
Age at diagnosis of PsA, yrs	36.2 (12.9)	38.7 (14.3)	35.5 (11.7)	0.49
Sex (female)	84 (35.3%)	22 (55%)	12 (42.9%)	0.05
Unemployed	80 (33.6%)	22 (55%)	20 (71.4%)	< 0.0001
Education status (college/university)	197 (82.8%)	30 (76.9%)	21 (75%)	0.46
Married/common-law	172 (72.3%)	28 (71.8%)	19 (67.9%)	0.89
Smoking status				0.24
Nonsmoker	147 (61.8%)	21 (53.9%)	14 (50%)	
Current	20 (8.4%)	5 (12.8%)	6 (21.4%)	
Past	71 (29.8%)	12 (33.3%)	8 (28.6%)	
Alcohol consumption				0.06
None	102 (42.9%)	21 (53.9%)	19 (67.9%)	
Social	117 (49.2%)	16 (41.0%)	6 (21.4%)	
Daily	19 (8.0%)	2 (5.1%)	3 (10.7%)	
PASI	3.4 (3.9)	2.3 (3.1)	3.96 (6.2)	0.35
Active joint count	4.3 (5.2)	10 (10.0)	11.4 (7.5)	< 0.0001
Damaged joint count	12.2 (12.6)	10.4 (14.0)	14.2 (14.9)	0.66
Physician global assessment (fair-very poor)	33 (14.5%)	9 (24.3%)	13 (48.2%)	< 0.0001
HAQ	0.48 (0.60)	0.95 (0.64)	1.26 (0.50)	< 0.0001
HAQ pain (0–100)	24.7 (24)	43.8 (26.8)	56.8 (26.5)	< 0.0001
SF-36 MCS	51.6 (9.3)	40.6 (10.0)	35.3 (11.4)	< 0.0001
SF-36 PCS	43.6 (11.5)	34.1 (9.7)	27.4 (7.1)	< 0.0001
Patient's global assessment (fair-very poor)	73 (30.9%)	32 (80%)	23 (82.1%)	< 0.0001
DLQI	2.92 (3.96)	5.3 (6.1)	5.5 (7.8)	0.001
FSS	3.56 (2.79)	7.2 (2.2)	8.5 (1.8)	< 0.0001
Ultraviolet therapy	4 (1.7%)	0 (0%)	0 (0%)	0.56
Topicals for psoriasis	134 (56.8%)	19 (48.7%)	10 (35.7%)	0.09
NSAID	135 (57.2%)	28 (71.8%)	21 (75%)	0.06
DMARD	138 (58.5%)	24 (61.5%)	16 (57.1%)	0.92
Biologic agents	113 (47.9%)	16 (41%)	16 (57.1%)	0.43
Anti-depressants	24 (10.2%)	9 (23.1%)	8 (28.6%)	0.005

PsA: psoriatic arthritis; HADS: Hospital Anxiety and Depression Scale; PsC: psoriasis without PsA; PASI: Psoriasis Area and Severity Index; HAQ: Health Assessment Questionnaire; SF-36: Medical Outcomes Study Short Form-36; MCS: SF-36 mental subscale; PCS: SF-36 bodily pain subscale; DLQI: Dermatology Quality of Life Index; FSS: Fatigue Severity Scale; NSAID: nonsteroidal antiinflammatory drugs; DMARD: disease-modifying antirheumatic drugs.

DISCUSSION

Our study is unique because it compares patients with PsA and patients with PsC using a standard questionnaire (HADS) and a standard clinical protocol. The results of our study indicate a higher rate of both anxiety and depression in patients with PsA compared to those with PsC. Anxiety was highest in the PsA group at 36.6%, while depression in this group was 22.2%. The prevalence of both anxiety and depression in patients with PsA was 17.7%. The prevalence for the PsC group was 24.4% for anxiety, 9.6% for depression, and 6.7% for both anxiety and depression. While anxiety was highest in both groups, the rate of depression in the PsA group was more than double that in the PsC group. This is particularly interesting because it is well documented that patients with PsC have a high rate of depression due to skin disease alone, and the PASI scores among patients with PsA were lower than those with PsC[5,6,7,8].

The prevalence of depression in patients with PsC in our study, 9.6%, was lower than that reported in the literature (19.2% to 62%)[5,6,7,8], but is consistent with the 9% estimated for the general population[38]. The lower prevalence of depression among our patients with PsC may be because ours were outpatients with mild and often

Table 4. Comparison of demographics, disease characteristics and treatments of PsA patients by likelihood of anxiety.

Variables	Frequency (%) or Mean (SD)			p
	Unlikely Anxiety (HADS ≤ 7), n = 194	Possible Clinical Anxiety (HADS 8–10), n = 66	Probable Clinical Anxiety (HADS ≥ 11), n = 46	
Age, yrs	54.3 (12.9)	54.1 (12.9)	51.5 (13.1)	0.41
Age at diagnosis of PsC, yrs	28.0 (14.0)	27.9 (13.0)	24.6 (13.9)	0.33
Age at diagnosis of PsA, yrs	36.9 (13.0)	35.1 (12.5)	36.3 (14.1)	0.63
Sex (female)	65 (33.5%)	29 (43.9%)	24 (52.2%)	0.039
Unemployed	68 (35.1%)	28 (42.4%)	26 (57.8%)	0.02
Education status (college/university)	160 (82.5%)	52 (78.8%)	36 (80%)	0.78
Married/common-law	139 (71.7%)	49 (74.2%)	31 (68.9%)	0.82
Smoking status				0.04
Nonsmoker	121 (62.4%)	38 (57.6%)	23 (51%)	
Current	12 (6.2%)	10 (15.2%)	9 (20%)	
Past	61 (31.4%)	18 (27.3%)	13 (28.9%)	
Alcohol consumption				0.07
None	82 (42.3%)	35 (53%)	23 (51%)	
Social	96 (49.5%)	10 (15.2%)	9 (20%)	
Daily	16 (8.3%)	18 (27.3%)	13 (28.9%)	
PASI	3.3 (4.0)	3.1 (3.5)	3.8 (5.3)	0.76
Active joint count	4.7 (5.7)	6.1 (6.5)	10.7 (9.1)	0.0005
Damaged joint count	12.2 (12.4)	14.3 (15.7)	6.9 (6.1)	0.17
Physician global assessment (fair-very poor)	25 (13.3%)	14 (23%)	16 (37.2%)	0.0009
HAQ	0.44 (0.56)	0.81 (0.69)	1.04 (0.68)	< 0.0001
HAQ pain (0–100)	25.5 (24.3)	28.0 (24.3)	51.1 (28.9)	< 0.0001
SF-36 MCS	53.4 (7.8)	43.0 (10.8)	38.0 (11.2)	< 0.0001
SF-36 PCS	43.3 (11.8)	38.6 (12.6)	34.7 (10.6)	< 0.0001
Patient's global assessment (fair-very poor)	56 (29.2%)	36 (54.6%)	36 (78.3%)	< 0.0001
DLQI	2.6 (3.8)	4.2 (5.2)	5.07 (6.8)	< 0.0001
FSS	3.5 (2.9)	5.7 (3.0)	7.19 (2.46)	< 0.0001
Ultraviolet therapy	4 (2.1%)	0 (0%)	0 (0%)	0.32
Topicals for psoriasis	108 (55.7%)	35 (55.6%)	20 (43.5%)	0.31
NSAID	110 (56.7%)	43 (68.3%)	31 (67.4%)	0.16
DMARD	113 (58.3%)	41 (65.1%)	24 (52.2%)	0.39
Biologic agents	86 (44.3%)	31 (49.2%)	28 (60.9%)	0.13
Anti-depressants	19 (9.8%)	13 (20.6%)	9 (19.6%)	0.04

PsA: psoriatic arthritis; HADS: Hospital Anxiety and Depression Scale; PsC: psoriasis without PsA; PASI: Psoriasis Area and Severity Index; HAQ: Health Assessment Questionnaire; SF-36: Medical Outcomes Study Short Form-36; MCS: SF-36 mental subscale; PCS: SF-36 bodily pain subscale; DLQI: Dermatology Quality of Life Index; FSS: Fatigue Severity Scale; NSAID: nonsteroidal antiinflammatory drugs; DMARD: disease-modifying antirheumatic drugs.

well-managed psoriasis, indicated by a lower mean body surface area (BSA) affected of 5.9%, while previous studies reported on patients with BSA as high as 53%[13].

The results in our patients with PsA are consistent with several recent studies of depression and/or anxiety in PsA. Freire, *et al* reported a prevalence of anxiety of 29.7% and depression of 17.6%[17], while Khraishi, *et al*, reported the overall prevalence of depression and anxiety at 7.9% based on patient self-report[18]. A previous study of 611 patients with PsA and 449 patients with PsC carried out at the University of Toronto PsA and dermatology clinics reported a prevalence of depression/anxiety of 20.7% in PsA and 9.3% in PsC, based on patient self-report[19]. Kotsis, *et al* measured depression in patients with PsA compared to patients with RA using the Patient Health Questionnaire-9 and reported a prevalence of depression in PsA of 21.7%, very similar to our study's prevalence of 22.2%[20]. From these reports, it is clear that the rate of depression in patients with PsA is about 1 in 5 and the rate of anxiety may be even higher. A study that assessed anxiety and depression among US adults with arthritis also reported a higher prevalence of anxiety (31%) than depression (18%), measured by the Arthritis Impact Measurement Scale[39]. A recent study using the HADS in early as well as late PsA also found a high prevalence of anxiety and depression similar to the levels reported in our study[40].

Table 5. Comparison of demographics, disease characteristics and treatments of patients with PsC by likelihood of depression.

Variables	Frequency (%) or Mean (SD)			p
	Unlikely Depression (HADS ≤ 7), n = 122	Possible Clinical Depression (HADS 8–10), n = 10	Probable Clinical Depression (HADS ≥ 11), n = 3	
Age, yrs	52.5 (13.5)	54.1 (10.3)	43.7 (2.9)	0.48
Age at diagnosis of PsC, yrs	31.1 (16.9)	29.6 (15.5)	29.7 (11.0)	0.96
Sex (female)	61 (50.4%)	7 (70%)	1 (33.3%)	0.69
Unemployed	31 (25.6%)	6 (60%)	2 (66.7%)	0.02
Education status (college/university)	106 (87.6%)	10 (100%)	1 (33.3%)	0.03
Married/common-law	71 (58.7%)	5 (50%)	1 (33.3%)	0.60
Smoking status				0.04
Nonsmoker	61 (50.4%)	3 (30%)	1 (33.3%)	
Current	14 (11.6%)	3 (30%)	2 (66.7%)	
Past	46 (38.0%)	4 (40%)	0 (0%)	
Alcohol consumption				0.02
None	41 (34.2%)	8 (80%)	1 (33.3%)	
Social	67 (55.8%)	0 (0%)	2 (66.7%)	
Daily	12 (10%)	2 (20%)	0 (0%)	
PASI	4.5 (4.8)	3.1 (2.3)	4.7 (1.5)	0.71
Physician global assessment (fair-very poor)	2 (1.7%)	0 (0%)	0 (0%)	NS
HAQ	0.05 (0.16)	0.41 (0.54)	0.29 (0.31)	< 0.0001
HAQ pain (0–100)	7.3 (12.9)	25.8 (27.5)	30.5 (43.1)	0.0004
SF-36 MCS	51.7 (9.8)	41.4 (8.2)	20.6 (2.2)	< 0.0001
SF-36 PCS	52.2 (7.2)	48.3 (7.6)	42.8 (20.2)	0.048
Patient's global assessment (fair-very poor)	16 (13.9%)	2 (20%)	2 (66.7%)	0.026
DLQI	3.8 (4.3)	8.7 (7.4)	13.5 (19.1)	0.0005
FSS	2.6 (2.2)	5.3 (3.0)	6.3 (3.7)	0.0002
Ultraviolet therapy	27 (22.3%)	2 (20%)	1 (33.3%)	0.86
Topicals for psoriasis	102 (84.3%)	10 (100%)	1 (33.3%)	0.03
NSAID	7 (6.0%)	1 (10%)	1 (33.3%)	0.12
DMARD	17 (14.4%)	2 (20%)	0 (0%)	0.78
Biologic agents	11 (9.3%)	1 (10%)	0 (0%)	NS
Anti-depressants	10 (8.3%)	3 (30%)	1 (33.3%)	0.053

PsA: psoriatic arthritis; HADS: Hospital Anxiety and Depression Scale; PsC: psoriasis without PsA; PASI: Psoriasis Area and Severity Index; HAQ: Health Assessment Questionnaire; SF-36: Medical Outcomes Study Short Form-36; MCS: SF-36 mental subscale; PCS: SF-36 bodily pain subscale; DLQI: Dermatology Quality of Life Index; FSS: Fatigue Severity Scale; NSAID: nonsteroidal antiinflammatory drugs; DMARD: disease-modifying antirheumatic drugs; NS: not significant.

We found that being unemployed was associated with a higher likelihood of depression and anxiety, while being female was associated with an increase in anxiety only. This is consistent with the findings of Freire, *et al*, where a logistic regression analysis revealed women and the unemployed as more anxious and depressed[17]. These factors were associated with depression and anxiety in both patients with PsA and those with PsC in our study.

Of the objective measures of disease severity, a higher actively inflamed joint count was associated with a higher likelihood of both depression and anxiety. This is consistent with a study of anxiety and depression among patients with RA where anxiety was associated with the Ritchie index[41]. The PASI, a measure of skin involvement, was not significantly associated with psychological symptoms in either cohort. This is consistent with studies suggesting that the objective severity of skin disease is less important than patients' perceptions and stigmatization experienced as a result of psoriasis[9,42]. A similar observation was noted by Bandinelli, *et al*[40], who found that anxiety and depression were independent of the PASI, which may explain why patients with PsA have more anxiety and depression than those with PsC.

Richards, *et al* reported a greater PASI score in men[9]. However, women scored higher in the HADS and reported a higher stigmatization experience[9,43]. That same study found that perceptions of stigmatization and depression both contributed significantly to variance in disability, and

Table 6. Comparison of demographics, disease characteristics and treatments of PsC patients by likelihood of anxiety.

Variables	Frequency (%) or Mean (SD)			p
	Unlikely Anxiety (HADS ≤ 7), n = 102	Possible Clinical Anxiety (HADS 8–10), n = 21	Probable Clinical Anxiety (HADS ≥ 11), n = 12	
Age, yrs	54.3 (12.9)	54.1 (12.9)	51.5 (13.1)	0.85
Age at diagnosis of PsC, yrs	28.0 (14.0)	27.9 (13.0)	24.6 (13.9)	0.16
Sex (female)	43 (42.6%)	15 (76.2%)	10 (83.3%)	0.0013
Unemployed	28 (27.7%)	5 (23.8%)	6 (50%)	0.23
Education status (college/university)	90 (88.2%)	19 (90.5%)	8 (66.7%)	0.10
Married/common-law	55 (54.5%)	14 (66.7%)	8 (66.7%)	0.47
Smoking status				0.29
Nonsmoker	52 (51.5%)	9 (42.9%)	4 (33.3%)	
Current	15 (14.9%)	1 (4.8%)	3 (25%)	
Past	34 (33.7%)	11 (52.4%)	5 (41.7%)	
Alcohol consumption				0.051
None	35 (34.3%)	6 (28.6%)	9 (75%)	
Social	55 (53.9%)	1 (4.8%)	3 (25%)	
Daily	10 (9.8%)	4 (19.1%)	0 (0%)	
PASI	3.3 (4.0)	3.1 (3.5)	3.8 (5.3)	0.58
Physician global assessment (fair-very poor)	2 (2%)	0 (0%)	0 (0%)	NS
HAQ	0.44 (0.56)	0.81 (0.69)	1.04 (0.68)	0.0002
HAQ pain (0–100)	25.5 (24.3)	28.0 (24.3)	51.1 (28.9)	< 0.0001
SF-36 MCS	53.4 (7.8)	43.0 (10.8)	38.0 (11.2)	< 0.0001
SF-36 PCS	43.3 (11.8)	38.7 (12.6)	34.7 (10.6)	0.12
Patient's global assessment (fair-very poor)	11 (10.8%)	4 (19.1%)	6 (54.5%)	0.003
DLQI	2.6 (3.8)	4.2 (5.3)	6.1 (6.8)	< 0.0001
FSS	3.5 (2.9)	5.66 (12.7)	22.2 (12.9)	< 0.0001
Ultraviolet therapy	24 (23.8%)	3 (14.3%)	3 (25%)	0.68
Topicals for psoriasis	85 (84.2%)	18 (85.7%)	10 (83.3%)	NS
NSAID	3 (2.9%)	2 (10%)	4 (33.3%)	0.002
DMARD	13 (12.7%)	2 (9.5%)	4 (33.3%)	0.18
Biologic agents	8 (7.8%)	3 (14.3%)	1 (8.3%)	0.67
Anti-depressants	9 (8.9%)	3 (14.3%)	2 (16.7%)	0.43

HADS: Hospital Anxiety and Depression Scale; PsC: psoriasis without psoriatic arthritis; PASI: Psoriasis Area and Severity Index; HAQ: Health Assessment Questionnaire; SF-36: Medical Outcomes Study Short Form-36; MCS: SF-36 mental subscale; PCS: SF-36 bodily pain subscale; DLQI: Dermatology Quality of Life Index; FSS: Fatigue Severity Scale; NSAID: nonsteroidal antiinflammatory drugs; DMARD: disease-modifying antirheumatic drugs; NS: not significant.

suggested that psychological factors play a stronger role in disability than clinical severity or disease duration.

Patient-reported factors such as disability, pain, and fatigue appear to be highly correlated with an increased likelihood of both depression and anxiety in both patient cohorts. The HAQ, a measure of disability in the activities of daily living, was an important factor in our study as well as in the study by Freire, *et al*[17]. The HAQ pain section was also closely associated with higher depression and anxiety in our study as well as in 2 previous studies[17,31]. Greater fatigue, as measured by the FSS, was associated with a higher likelihood of depression and anxiety. However, fatigue is a common symptom of depression, so whether it is a predictor or the result of depression remains unclear.

Treatment with DMARD and/or biologic agents did not have any significant association with either depression or anxiety in our study, although in the study by Freire, *et al* treatment with biologic agents as monotherapy or in combination with a DMARD was associated with a lower prevalence of anxiety[17]. Although our analysis did not indicate an effect of biologic treatment, this issue would be interesting to explore further. Increased concentrations of proinflammatory cytokines, such as tumor necrosis factor-α, are associated with major depression, and it has been suggested that blocking these cytokines with biologic therapy may improve depressive symptoms[44,45,46] as well as symptoms of fatigue[5]. A study by Tyring, *et al* found that a greater proportion of patients with psoriasis receiving the biologic

etanercept had at least a 50% improvement in depression scores (as measured by Ham-D or Beck Depression Index) and had significant improvements in fatigue (FACIT-F score) at Week 12 compared with the placebo group[46].

Of those we found to be depressed, only 25% of patients with PsA and 31% of patients with PsC were currently taking antidepressant medication. This finding is not surprising because there is evidence that doctors may have difficulty identifying psoriasis patients who are in distress. In one study, only half of probable cases of anxiety and a third of depressed patients were identified by physicians in consultation compared to the HADS. This is unfortunate given that psychosocial interventions in the treatment of psoriasis have shown benefit in enhancing QOL and reducing disease burden. In one study, pharmacotherapy plus a 6-week structured program in cognitive behavioral therapy resulted in greater decreases in psoriasis severity and self-reported disability than pharmacotherapy alone[47]. This highlights the value of identifying patients with depression and applying a multidisciplinary approach to their treatment. Our study, however, could not identify those patients who may have chosen to forgo treatment, decided not to share their psychological symptoms with their physicians, or chose nonpharmacological treatment for their depression.

The strength of our study is the accurate phenotype of the patients with psoriasis and PsA, the use of a validated instrument to measure anxiety and depression in this patient population, and the availability of data on demographic and clinical features to relate to the presence of anxiety and depression in patients with psoriasis and those with PsA followed in an outpatient setting. The limitation of our study is the cross-sectional design, which prevents us from determining or commenting on causality.

Additionally, a single HADS score, which assesses depressive/anxious symptoms in the last 2 weeks, may or may not be representative of patients' general mental health. Longitudinal studies will be useful in elucidating the interaction between mental health, disease activity, and patient-reported health and disability.

These results indicate a high rate of depression and anxiety in patients with PsA that may be underrecognized and undertreated. The factors most closely associated with higher rates of depression are those in which patients express the negative effects this disease has on their QOL. A greater understanding of the factors related to depression and anxiety in psoriatic disease will be helpful in planning and evaluating future treatments. Depression and anxiety are known to influence treatment adherence, health behaviors, and perceived health[47], and therefore cannot be forgotten when treating any chronic disease. A multi-disciplinary approach is needed to best treat both the psychological and physical consequences of psoriatic disease.

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REFERENCES

1. Griffiths CE, Barker JM. Pathogenesis and clinical features of psoriasis. Lancet 2007;370:263-71.
2. Myers WA, Gottlieb AB, Mease P. Psoriasis and psoriatic arthritis: clinical features and disease mechanisms. Clin Dermatol 2006;24:438-47.
3. Langley RG, Krueger GG, Griffiths CE. Psoriasis: epidemiology, clinical features, and quality of life. Ann Rheum Dis 2005;64 Suppl 2:18-25.
4. Gladman DD. Psoriatic arthritis. Dermatol Ther 2009;22:40-55.
5. Biljan D, Laufer D, Filakovic P, Situm M, Brataljenovic T. Psoriasis, mental disorders and stress. Coll Antropol 2009; 33:889-92.
6. Akay A, Pekcanlar A, Bozdag KE, Altintas L, Karaman A. Assessment of depression in subjects with psoriasis vulgaris and lichen planus. J Eur Acad Dermatol Venereol 2002;16:347-52.
7. Schmitt JM, Ford DE. Role of depression in quality of life for patients with psoriasis. Dermatology 2007;215:17-27.
8. Esposito M, Saraceno R, Giunta A, Maccarone M, Chimenti S. An Italian study on psoriasis and depression. Dermatology 2006;212:123-7.
9. Richards HL, Fortune DG, Griffiths CE, Main CJ. The contribution of perceptions of stigmatisation to disability in patients with psoriasis. J Psychosom Res 2001;50:11-5.
10. Zimmerman M, Lish JD, Lush DT, Farber NJ, Plescia G, Kuzma MA. Suicidal ideation among urban medical outpatients. J Gen Intern Med 1995;10:573-6.
11. Cooper-Patrick L, Crum RM, Ford DE. Identifying suicidal ideation in general medical patients. JAMA 1994;272:1757-62.
12. Olfson M, Weissman MM, Leon AC, Sheehan DV, Farber L. Suicidal ideation in primary care. J Gen Intern Med 1996; 11:447-53.
13. Gupta MA, Gupta AK. Depression and suicidal ideation in dermatology patients with acne, alopecia areata, atopic dermatitis and psoriasis. Br J Dermatol 1998;139:846-50.
14. Rosen CF, Mussani F, Chandran V, Eder L, Thavaneswaran A, Gladman DD. Patients with psoriatic arthritis have worse quality of life than those with psoriasis alone. Rheumatology 2012;51:571-6.
15. Harvima RJ, Viinamaki H, Harvima IT, Naukkarinen A, Savolainen L, Aalto ML, et al. Association of psychic stress with clinical severity and symptoms of psoriatic patients. Acta Derm Venereol 1996;76:467-71.
16. Isik A, Koca SS, Ozturk A, Mermi O. Anxiety and depression in patients with rheumatoid arthritis. Clin Rheumatol 2007;26:872-8.
17. Freire M, Rodriguez J, Moller I, Valcarcel A, Tornero C, Diaz G, et al. Prevalence of symptoms of anxiety and depression in patients with psoriatic arthritis attending rheumatology clinics [Spanish]. Reumatol Clin 2011;7:20-6.
18. Khraishi M, MacDonald D, Rampakakis E, Vaillancourt J, Sampalis JS. Prevalence of patient-reported comorbidities in early and established psoriatic arthritis cohorts. Clin Rheumatol 2011; 30:877-85.
19. Husted JA, Thavaneswaran A, Chandran V, Eder L, Rosen CF, Cook RJ, et al. Cardiovascular and other comorbidities in patients with psoriatic arthritis: a comparison with patients with psoriasis. Arthritis Care Res 2011;63:1729-35.
20. Kotsis K, Voulgari PV, Tsifetaki N, Machado MO, Carvalho AF, Creed F, et al. Anxiety and depressive symptoms and illness perceptions in psoriatic arthritis and associations with physical health-related quality of life. Arthritis Care Res 2012;64:1593-601.

21. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. Acta Psychiatrica Scandinavica 1983;67:361-70.
22. Taylor W, Gladman DD, Helliwell PS, Marchesoni A, Mease P, Mielants H. Classification criteria for psoriatic arthritis: development of new criteria from a large international study. Arthritis Rheum 2006;54:2665-73.
23. Gladman DD, Chandran V. Observational cohort studies: lessons learnt from the University of Toronto Psoriatic Arthritis Program. Rheumatology 2011;50:25-31.
24. Lewis G, Wessely S. Comparison of the General Health Questionnaire and the Hospital Anxiety and Depression Scale. Br J Psychiatry 1990;157:860-4.
25. Strik JJ, Honig A, Lousberg R, Denollet J. Sensitivity and specificity of observer and self-report questionnaires in major and minor depression following myocardial infarction. Psychosomatics 2001;42:423-8.
26. Gladman DD, Shuckett R, Russell ML, Thorne JC, Schachter RK. Psoriatic arthritis (PSA)-an analysis of 220 patients. Q J Med 1987;62:127-41.
27. Wolfe F, Smythe HA, Yunus MB, Bennett RM, Bombardier C, Goldenberg DL, et al. The American College of Rheumatology 1990 Criteria for the Classification of Fibromyalgia. Report of the Multicenter Criteria Committee. Arthritis Rheum 1990;33:160-72.
28. Marks R, Barton SP, Shuttleworth D, Finlay AY. Assessment of disease progress in psoriasis. Arch Dermatol 1989;125:235-40.
29. Fredriksson T, Pettersson U. Severe psoriasis—oral therapy with a new retinoid. Dermatologica 1978;157:238-44.
30. Mackenzie H, Thavaneswaran A, Chandran V, Gladman DD. Patient-reported outcome in psoriatic arthritis: a comparison of Web-based versus paper-completed questionnaires. J Rheumatol 2011;38:2619-24.
31. Husted JA, Gladman DD, Farewell VT, Cook R. Health-related quality of life of patients with psoriatic arthritis: a comparison with patients with rheumatoid arthritis. Arthritis Care Res 2001; 45:151-8.
32. Sokoll KB, Helliwell PS. Comparison of disability and quality of life in rheumatoid and psoriatic arthritis. J Rheumatol 2001;28:1842-6.
33. Ware JE Jr., Sherbourne CD. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. Med Care 1992;30:473-83.
34. Fries JF, Spitz P, Kraines RG, Holman HR. Measurement of patient outcome in arthritis. Arthritis Rheum 1980;23:137-45.
35. Finlay AY, Khan GK. Dermatology Life Quality Index (DLQI)—a simple practical measure for routine clinical use. Clin Exp Dermatol 1994;19:210-6.
36. Blackmore M, Gladman DD, Husted J, Long J, Farewell VT. Measuring health status in psoriatic arthritis: the Health Assessment Questionnaire and its modification. J Rheumatol 1995;22:886-93.
37. Husted J, Gladman DD, Long JA, Farewell VT, Cook R. Validating the SF-36 health questionnaire in patients with psoriatic arthritis. J Rheumatol 1997;24:511-7.
38. Current depression among adults – United States, 2006 and 2008. MMWR Morb Mortal Wkly Rep 2010;59:1229-35.
39. Murphy LB, Sacks JJ, Brady TJ, Hootman JM, Chapman DP. Anxiety and depression among US adults with arthritis: prevalence and correlates. Arthritis Care Res 2012;64:968-76.
40. Bandinelli F, Prignano F, Bonciani D, Pallanti S, Lotti T, Salaffi F, et al. Clinical and demographic factors influence on anxiety and depression in early psoriatic arthritis (ePsA). Clin Exp Rheumatol 2013;31:318-9.
41. El-Miedany YM, El Rasheed AH. Is anxiety a more common disorder than depression in rheumatoid arthritis? Joint Bone Spine 2002;69:300-6.
42. Schmitt J, Ford DE. Understanding the relationship between objective disease severity, psoriatic symptoms, illness-related stress, health-related quality of life and depressive symptoms in patients with psoriasis - a structural equations modeling approach. Gen Hosp Psychiatry 2007;29:134-40.
43. Ginsburg IH, Link BG. Feelings of stigmatization in patients with psoriasis. J Am Acad Dermatol 1989;20:53-63.
44. O'Brien SM, Scott LV, Dinan TG. Cytokines: abnormalities in major depression and implications for pharmacological treatment. Hum Psychopharmacol 2004;19:397-403.
45. Patarca R, Klimas NG, Lugtendorf S, Antoni M, Fletcher MA. Dysregulated expression of tumor necrosis factor in chronic fatigue syndrome: interrelations with cellular sources and patterns of soluble immune mediator expression. Clin Infect Dis 1994;18 Suppl 1:S147-53.
46. Tyring S, Gottlieb A, Papp K, Gordon K, Leonardi C, Wang A, et al. Etanercept and clinical outcomes, fatigue, and depression in psoriasis: double-blind placebo-controlled randomised phase III trial. Lancet 2006;367:29-35.
47. Carroll CL, Feldman SR, Camacho FT, Balkrishnan R. Better medication adherence results in greater improvement in severity of psoriasis. Br J Dermatol 2004;151:895-7.