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Prevalence and factors associated with fatigue in patients with psoriatic arthritis: a systematic review and meta-analysis

Haoming Tang[1†], Tricia Li Ting Chew[2†] and Warren Fong[3,4,5*]

Abstract

Objectives Fatigue is a prominent symptom in patients with psoriatic arthritis (PsA). There was a wide variety of statistics previously reported on fatigue prevalence in patients. This systematic review examined the current literature to derive the overall prevalence of fatigue and risk factors in PsA patients.

Methods A systematic review of the literature with subsequent meta-analyses was conducted. Publications assessing fatigue severity and prevalence in patients with PsA using validated measurement scores were identified from seven online databases (Cochrane, CINAHL, EMBASE, Google Scholar, MEDLINE, PubMed, and Web of Science), from inception until January 2024. Employing a random effects model, we calculated the pooled fatigue prevalence. Quality assessment of included studies was performed utilising the Joanna Briggs Critical Appraisal Tool.

Results The final analysis included 15 studies with 6482 PsA patients. Pooled fatigue prevalence was 0.51 (95% CI: 0.41, 0.61; I2 = 97.4%). There was substantial heterogenicity across the studies, with biologics use and geographical location in terms of Western versus Eastern countries being possible sources of heterogeneity. Age, disease duration, gender, tender joint count, swollen joint and enthesitis count are among the most commonly reported risk factors for fatigue in multivariate logistic regressions.

Conclusions Approximately half of the patients with PsA experienced fatigue. Biologics use and geographical location of the study were possible sources of heterogeneity in the subgroup analysis.

Clinical trial number Not applicable.

Keywords Fatigue, Psoriatic arthritis, Biologics

[†]Haoming Tang and Tricia Li Ting Chew are both the first authors.

*Correspondence:
Warren Fong
gmsfwsw@nus.edu.sg
[1]Duke-NUS Medical School, Singapore, Singapore
[2]Department of General Medicine, Changi General Hospital, Singapore, Singapore
[3]Department of Rheumatology and Immunology, Singapore General Hospital, Singapore, Singapore
[4]Office of Education, Duke-NUS Medical School, Singapore, Singapore
[5]Department of Medicine, Yong Loo Lin School of Medicine, National University of Singapore, Singapore, Singapore

Introduction

Psoriatic arthritis (PsA) is a systemic inflammatory condition characterised by a high degree of heterogeneity. Beyond articular manifestations, patients also have extensive extra-articular manifestations, such as ocular and dermal involvement [1–3]. Patients diagnosed with PsA also have other comorbidities, such as metabolic syndrome and cardiovascular conditions [4].

Fatigue is a phenomenon studied widely in various fields, affecting patients with a myriad of conditions. It has also been found to affect many patients with PsA [5]. Fatigue can be described as a sensation of exhaustion and a reduction in mental and physical capacity [6]. The experience of fatigue in patients with PsA is associated with multiple mental health comorbidities, reduced physical function, and increased work disability [7]. Its negative associations include reduced cognition, increased occupational accidents, metabolic and reproductive health sequelae, as well as cancer and mortality [8, 9], and greatly affects the quality of life of patients beyond the physical and emotional realm.

In addition, it is interesting to note that a global consensus on a widely accepted set of definitions of fatigue remain inconclusive, and no previous studies have been performed to ascertain the overall prevalence of fatigue in patients with PsA. On this backdrop, this study seeks to conduct a systemic review of the literature to derive the pooled fatigue prevalence in patients with PsA using currently validated measures of fatigue. This study also aims to identify reported potential risk factors of fatigue in fatigue analysis. We hope that this will improve the understanding of fatigue in patients with PsA, and contribute to improving the management fatigue in these patients. If risk factors are identified, more work can be done to develop predictive tools to identify patients at high risk of developing fatigue, so that pre-emptive management strategies can be employed for this group of patients.

Method

We conducted this study in accordance with Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) guidance [10, 11]. To obtain an estimation of fatigue prevalence in PsA patients, we performed a systematic review of the current literature with meta-analyses to identify a pooled fatigue prevalence estimate.

Search strategy

We searched seven online databases from its establishment till January 2024: Cochrane, CINAHL, EMBASE, Google Scholar, MEDLINE, PubMed, and Web of Science. Combinations of keywords regarding psoriatic arthritis and fatigue were employed (Supplementary Data S1). Duplicate studies were removed.

Study selection

Inclusion criteria were listed below: [12] the article was from a peer-reviewed journal; Abstracts lacking complete manuscripts, conference papers, case reports or series, poster presentations, and repeated papers were excluded from the study. (ii) the population identified in the study consisted of only patients with PsA, or patients with PsA were a specific, identifiable subgroup of the whole population whose characteristics could be analysed; (iii) fatigue was determined either as a primary or secondary outcome, with validated measurement tools of fatigue used; and (iv) the language of publication was English.

Following this, 2 authors (H.T. and T.C.L.T) proceeded to execute the full-text screening process independently using the exclusion criteria listed below: [12] the study failed to report data required in the calculation of fatigue prevalence (i.e. the numerator and/or denominator, or fraction)); (ii) the study was conducted exclusively in an inpatient environment (i.e. contributing to overestimation of the primary outcome); (iii) the study was an intervention trial with medications and consequently the study population did not properly represent the general PsA population, and (iv) the study only identified a subgroup of PsA patients (e.g. patients with early PsA or juvenile PsA). A consensus was reached on disagreements that arose during the literature review.

Data extraction

In each article, H.T. extracted data on common study characteristics: geographical area, size of the study population, age, gender, disease duration, disease indices and classification criteria, types of medications used, the study objective's relationship with fatigue, various fatigue severity measurements, and fatigue prevalence. The prevalence of fatigue was the primary outcome of this study.

Methodological quality assessment

The Joanna Briggs Critical Appraisal Tools is a validated study quality assessment tool that can be employed for a variety of different kinds of study designs, including both qualitative and quantitative article designs [13]. It was chosen as it had the broadest relevant range for this systematic review and meta-analysis. This included studies with various designs such as cross-sectional studies, case-control studies, and cohort studies. There were a few options available for each study quality assessment question. One point would be given when the answer was 'yes', and no points were given for all other answers.

Statistical analysis

H.T. conducted the data analysis using RStudio, version 2022.12.0. To estimate fatigue prevalence in PsA patients, the 95% confidence interval was calculated. In view of the expected significant interstudy heterogeneity, the study

employed a random-effects framework to calculate the pooled fatigue prevalence. If the overall PsA estimate was reported by the study, this estimate was used. In scenarios where the studies employed multiple measurements of fatigue to be published in the same study population, measurement tools for patient outcomes were chosen based on the rankings listed below: Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F), Fatigue Severity Scale [14], Short Form 36-item Health Survey (SF-36), Fatigue question in the BASDAI 10 cm visual analog scale (BASDAI-Fatigue), 12-item Psoriatic Arthritis Impact of Disease (PsAID-12) questionnaire, and the rankings were listed as such according to their validity, comprehensiveness and reliability in capturing the patient-reported outcomes [15–19]. Cochran's Q test was employed and I^2 was utilised to assess the variation across studies. We then performed subgroup meta-analyses to establish potential causes of interstudy heterogeneity, demonstrated by an $I^2 > 75\%$, or with a Cochran's Q statistic, with a p-value < 0.1. We analysed and reported the statistical relationship between variables reported in each study and the presence of fatigue. Risk factors were extracted if the analysis of risk factors associated with fatigue was conducted via a univariate or multivariate logistic regression technique, as the presence of fatigue is a binary outcome in the current study. Publication bias was assessed via the Egger test, which was deemed to be present if p-value < 0.05 [20].

Results

Searching framework

The PRISMA flowchart provides a succinct depiction of the search process (Fig. 1). 5628 articles were found based on the initial literature search, and 1 article was identified from the study references. We excluded 1794 articles as they were duplicates, with 3835 articles subsequently

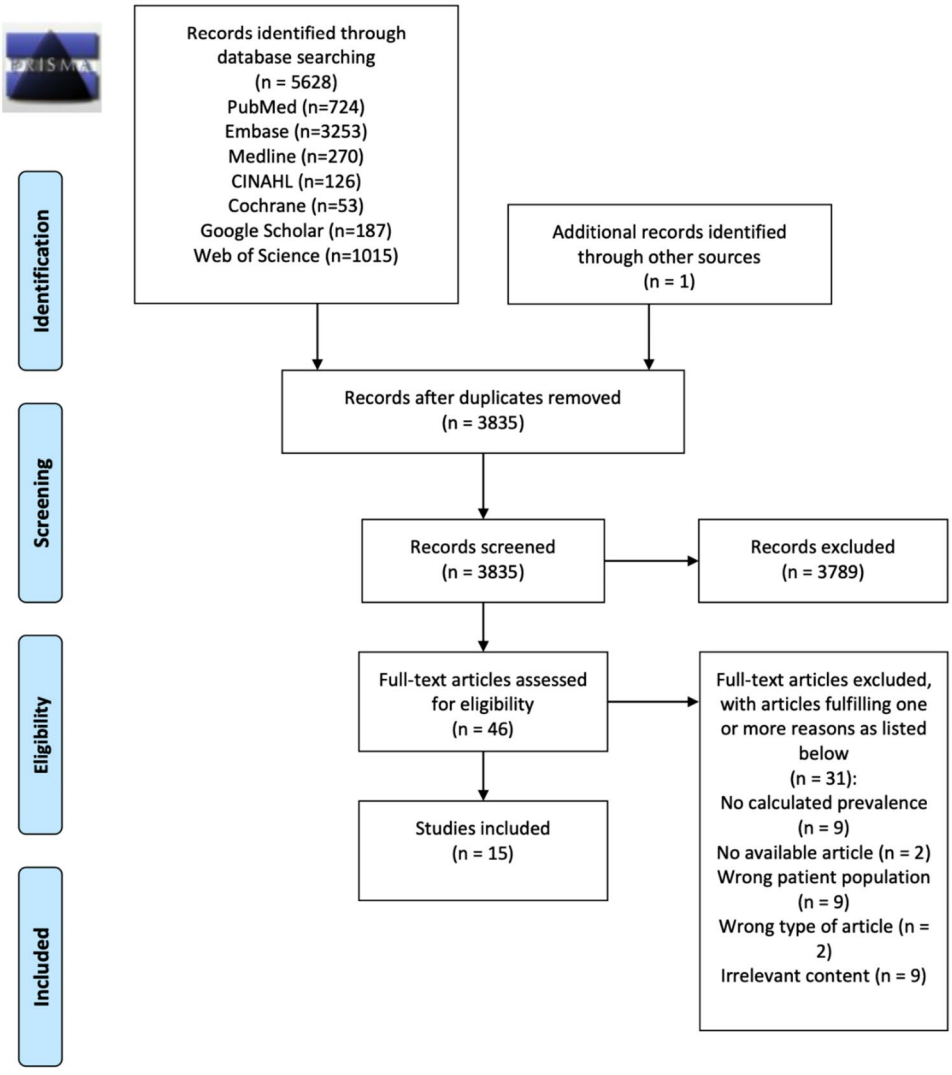

Fig. 1 PRISMA study flowchart

proceeding to the next stage of abstract reviewing. In this stage, 3789 articles were excluded. The full-text review was conducted based on the final 46 articles included, and 15 studies were included in the systemic review in the end, totalling 6482 patients (Fig. 2).

Characteristics of the incorporated studies

All studies included were cross-sectional studies, with the majority conducted in the Western (i.e. Europe, America, Australia, and New Zealand) Hemisphere ($n = 10$). The fatigue prevalence in PsA was reported or calculated in accordance with available data (Supplementary Tables S1 and S2).

Study quality assessment

According to the Joanna Briggs Institute Critical Appraisal tools, most studies had satisfactory study quality for analysis. The score mean was 91% (95% CI: 85 – 97%), with 14 studies obtaining a score of > 70%, indicating an overall satisfactory study quality (Supplementary Table S3). All studies were eventually included for analysis.

Assessment of fatigue

Frequently employed measurement tools included FACIT-F, FSS, SF-36, 0–100 mm visual analog scale, BASDAI-Fatigue, 10 cm/100 mm visual analog scale, Chalder Fatigue Scale, 12-item Psoriatic Arthritis Impact of Disease (PsAID-12) questionnaire, Vitality scale of the RAND version of the SF 36-item Health Survey, and fatigue Numeric Rating Scale. The fatigue definition was different across the studies included, but could be broadly dichotomised to the presence of 'any fatigue' or 'significant fatigue', according to the definitions provided in the studies in the measurement of fatigue.

The pooled fatigue prevalence in PsA patients was 0.51 (95% CI: 0.41, 0.61; $I^2 = 97.4\%$). There was substantial heterogeneity across the studies. To explore sources of heterogeneity across studies, stratified subgroup analyses were conducted. The variables used included male percentage, study population size, disease duration, fatigue either as the primary or secondary purpose of the included study, fatigue definition criteria in the study, geographic location of the study, and the use of biologics. The Egger test $p = 0.8595$ revealed no publication bias (Supplementary Figure S1).

Subgroup analysis

As can be seen in Table 1, the use of biologics and region where the study was conducted (Western/Eastern) were found to be statistically significant in predicting fatigue. The current review dichotomised the studies according to the geographical region where they were conducted. If done in the Eastern hemisphere, they were classified as "Eastern" and vice versa. The prevalence of fatigue was 0.58 (CI = 0.44–0.70) in Western countries compared to the Eastern countries, namely Asia and the Middle East (0.33, CI = 0.11–0.65, where $p = 0.007$).

The prevalence of fatigue was also lower in patients who required biologic administration, and this was statistically significant. No significant difference in the prevalence of PsA was found when assessed if fatigue was classified as a primary or secondary objective of the study, disease duration, or fatigue definition (severe fatigue versus any fatigue). There was no significant difference in fatigue prevalence between those studies that reported a specific cutoff score for the definition of fatigue and those that did not.

There was also no significant difference in the fatigue prevalence between genders. In cohorts with less than or equal to 50% males, the prevalence was 0.44 (CI: 0.35–0.54), compared to that of 0.53 (0.21–0.83) in a population comprising more than 50% males ($p = 0.84$).

When evaluating the reported risk factors of fatigue presence, a variety of risk factors were extracted based on analyses from univariate or multivariate logistic

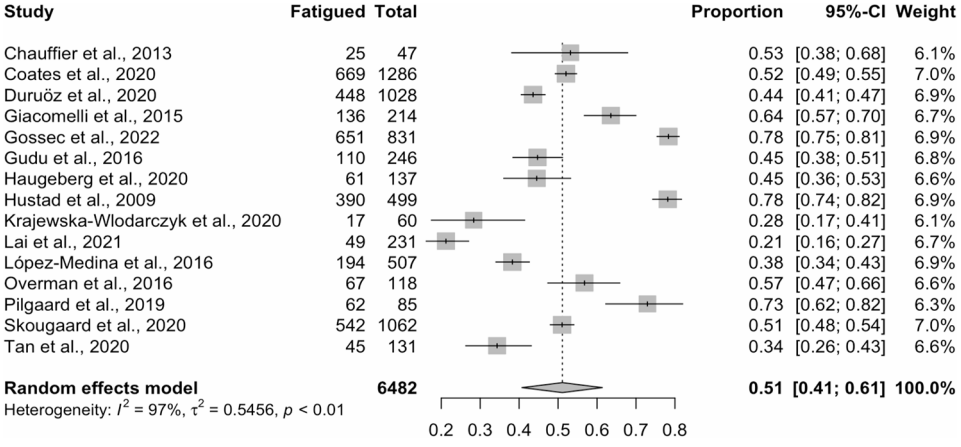

Fig. 2 Pooled fatigue prevalence in psoriatic arthritis patients

Table 1 Subgroup analysis

Variables	Number of studies	Pooled estimates (95% CI)	I^2 (%)	*P*-value
Sample Size				
≤ 200	6	0.48 (0.31–0.66)	88.2%	0.6507
> 200	9	0.53 (0.37–0.68)	98.3%	
Male (%)				
≤ 50	5	0.44 (0.35–0.54)	84.9%	0.4950
> 50	5	0.53 (0.21–0.83)	98.9%	
Disease duration (y)				
≤ 8	3	0.48 (0.37–0.59)	68.7%	0.8430
> 8	3	0.51 (0.06–0.95)	99.1%	
Fatigue as the study's primary objective				
Yes	6	0.46 (0.25–0.68)	98.3%	0.2682
No	2	0.57 (0.06–0.96)	89.7%	
Definition of fatigue				
Any fatigue	6	0.58 (0.37–0.76)	97.3%	0.2907
Significant fatigue	9	0.47 (0.34–0.60)	97.0%	
Divergent reporting of fatigue				
Reporting of cutoff scores	13	0.50 (0.38–0.62)	97.7%	0.3558
No reporting of cutoff scores	2	0.57 (0.06–0.96)	89.7%	
Classification criteria use				
Yes	5	0.41 (0.23–0.62)	95.0%	0.1032
No	3	0.61 (0.22–0.90)	98.8%	
Region of the Study				
Western	10	0.58 (0.44–0.70)	97.4%	0.0078
Eastern	3	0.33 (0.11–0.65)	94.9%	
Biologic use				
≤ 40%	4	0.62 (0.39–0.80)	98.3%	0.0054
> 40%	4	0.36 (0.20–0.56)	91.0%	

y: year

regression were reported for these variables (Table 2). Commonly reported possible risk factors included, age, disease duration, and enthesitis. Potential risk factors that were consistently noticed to correlate with the presence of fatigue include lesser educational status, with data from two studies available. Of the three articles for which the data were available, all of them utilised multivariate logistic regressions for the presence of fatigue. However, Lai et al. only reported the p-values in the analysis without the corresponding odds ratios and confidence intervals [21]. A meta-analysis of the individual risk factors to derive pooled odds ratios was not conducted due to the lack of sufficient studies for each risk factor and the varied forms of reporting utilised.

Discussion

There was a high fatigue prevalence in patients with psoriatic arthritis, similar to patients with rheumatoid arthritis as well as ankylosing spondylitis [22, 23].

Fatigue has often been investigated in patients with PsA. There currently exists no standardized assessment tool, and studies worldwide adopt various fatigue assessment tools that have been validated in various populations, with their own cutoff values. The lack of standardized assessment tools can pose a challenge when attempting to draw comparative conclusions across the different studies. The current review attempted to mitigate this by broadly dichotomising to the presence of 'any fatigue' or 'significant fatigue', according to the definitions provided in the studies in the measurement of fatigue, to allow us to draw meaningful comparisons from the data.

Although there was a significant ($p < 0.05$) correlation between fatigue prevalence in Western compared to Eastern countries, this should take into consideration that majority of the included studies took place in the Western hemisphere, with few focusing on fatigue prevalence in Asia. Thus, this association could be confounded by variable reporting of PsA across the globe. For example, reports on the prevalence of psoriatic arthritis in China are limited, with a growing awareness of its prevalence only in recent years. A recent study in 2023 reported a doubling in the prevalence of PsA in the Chinese population [24]. Thus, variable reporting globally can further limit the true understanding of the prevalence of fatigue in various geographical populations, and this information should be interpreted in context. Future studies on the underreported areas, such as Asia, should be conducted to investigate fatigue prevalence in PsA patients. In addition, the differences in fatigue prevalence could also be contributed by cultural differences in fatigue reporting. There are limited studies done to assess cultural differences in fatigue reporting in Psoriatic arthritis patients. However, extrapolating from non-PsA populations, a paper by Alison et al. highlighted differences in cultural perception of fatigue. In this study, participants from Caucasian ethnicities were more likely to view fatigue as a symptom of an underlying medical problem and regard it more seriously than study participants of Asian ethnicity, who were likely to view fatigue as consequences of systemic deficiencies (as a result of various psychosocial factors) than a disease process, hence viewing it less seriously [25]. This could suggest that differences in cultural perceptions of fatigue affect fatigue reporting. In addition, there could be a lack of awareness of patients of their PsA diagnosis as seen by a paper by Anshul et al. [26]. As a result of varying levels of awareness in patient populations, underreporting of fatigue as a symptom may result. A study done by Hifinger et al. also showed variations in level of fatigue reporting dependent on country of residence- suggesting an interplay between cultural and socioeconomic factors on fatigue reporting and prevalence [27].

Table 2 Potential risk factors of fatigue

Risk factors	Risk factor definition	Measurement of effect in odds ratio[a]	Other measurement of effect
Gender	With reference to female [23, 24]	OR 0.62, CI 0.32–1.20, p-value 0.16 [23] OR 1.81, CI 0.97–3.44, p-value 0.06 [24]	With significant fatigue (59.2% male) Without significant fatigue (67% male) p-value > 0.05 [22]
Age		OR 1.00, CI 0.97–1.03, p-value 0.99 [23] OR 0.99, CI 0.97–1.02, p-value 0.89 [24]	With significant fatigue (mean: 50.4, SD: 12.7) Without significant fatigue (mean: 51.6, SD: 12) p-value > 0.05 [22]
Disease duration		OR 1.00, CI 0.96–1.05, p-value 0.94 [23] OR 1.00, CI 0.97–1.03, p-value 0.90 [24]	With significant fatigue (median: 4, IQR: 2–10) Without significant fatigue (median: 5, IQR: 2–10) p-value > 0.05 [22]
Education	With reference to primary school [23] For each year less of education [24]	Middle school: OR 0.24, CI 0.10–0.59, p-value < 0.01 [23] High school and above: OR 0.23 CI 0.01–0.51, p-value < 0.01 [23] OR 1.09, CI 1.02–1.23, p-value 0.02 [24]	
Tender joints	For each 5 extra joints [24]	OR 1.30, CI 1.01–1.68, p-value 0.05 [24]	
Swollen joints		OR 1.04, CI 0.94–1.14, p-value 0.43 [24] OR 1.03, CI 0.82–1.30, p-value 0.77 [23]	
Skin PsO	Skin PsO > 5% of body surface [24]	OR 4.67, CI 1.05–20.72, p-value 0.04 [24]	
Axial involvement	Current inflammatory back pain considered related to the inflammatory rheumatism [24]	OR 0.98, CI 0.51–1.87, p-value 0.94 [24]	
Enthesitis	Enthesitis count [23] Current inflammatory entheseal disease considered related to the inflammatory rheumatism [24] Leeds Enthesitis Index [22]	OR 1.04, CI 0.90–1.19, p-value 0.62 [23] OR 1.53, CI 0.76–3.05, p-value 0.23 [24]	With significant fatigue (median: 0, IQR: 0–1) Without significant fatigue (median: 0) p-value > 0.05 [22]
Dactylitis	Current diffuse swelling of a digit considered related to the inflammatory rheumatism [22]	OR 0.56, CI 0.23–1.37, p-value 0.20 [24]	With significant fatigue (median: 0, IQR: 0–3) Without significant fatigue (median: 0, IQR: 0–1) p-value > 0.05 [22]
DAPSA		OR 0.89, CI 0.76–1.14, p-value 0.94 [23]	With significant fatigue (median: 18.3, IQR: 11.4–29.9) Without significant fatigue (median: 11.3, IQR: 5.3–18) p-value < 0.01 [22]
PASI			With significant fatigue (median: 4.2, IQR: 1.2–10.7) Without significant fatigue (median: 2.1, IQR: 0.3–5.6) p-value 0.04 [22]
MDA	Satisfying five out of of seven of the following: tender joint count ≤ 1, swollen joint count ≤ 1, enthesitis count ≤ 1, PASI ≤ 1 or body surface area ≤ 3, PtGA ≤ 20 mm, patient pain VAS ≤ 15 mm, and health assessment questionnaire ≤ 0.5 [23]	OR 1.00, CI 0.42–2.40, p-value 0.99 [23]	

Table 2 (continued)

Risk factors	Risk factor definition	Measurement of effect in odds ratio[a]	Other measurement of effect
VLDA	Satisfying seven out of of seven of the following: tender joint count ≤ 1, swollen joint count ≤ 1, enthesitis count ≤ 1, PASI ≤ 1 or body surface area ≤ 3, PtGA ≤ 20 mm, patient pain VAS ≤ 15 mm, and health assessment questionnaire ≤ 0.5 [23]	OR 0.16, CI 0.03, 0.92, p-value 0.04 [23]	
Medication use	Including cDMARDs, MTX, SSZ, LEF, CsA, ACT, biologics [22]		p-value > 0.05 [22]
PsO Duration			With significant fatigue (median: 12, IQR: 10–23) Without significant fatigue (median: 14, IQR: 7–22) p-value > 0.05 [22]
HAQ	HAQ [23] HAQ-DI [22]	OR 2.06, CI 0.55–7.76, p-value 0.29 [23]	With significant fatigue (median: 0.75, IQR: 0.03–1.13) Without significant fatigue (median: 0, IQR: 0 -0.38) p-value > 0.05 [22]
Diabetes mellitus			With significant fatigue (diabetes mellitus: 14.3%) Without significant fatigue (diabetes mellitus: 19.2%) p-value > 0.05 [22]
Ischemic heart disease			With significant fatigue (ischemic heart disease: 4.1%) Without significant fatigue (ischemic heart disease: 4.4%) p-value > 0.05 [22]
Renal function	Creatinine clearance [22]		With significant fatigue (median: 89, IQR: 76–120) Without significant fatigue (median: 94, IQR: 78–110) p-value > 0.05 [22]
BMI		OR 0.95, CI 0.90–1.01, p-value 0.09 [23]	With significant fatigue (mean: 24.8, SD: 5.5) Without significant fatigue (mean: 24.9, SD: 3.9) p-value > 0.05 [22]
Inflammatory markers	CRP [23] ESR and CRP [22]	OR 1.01, CI 0.98–1.04, p-value 0.67 [23]	ESR: With significant fatigue (median: 18, IQR: 11–47) Without significant fatigue (median: 20, IQR: 10–35) p-value > 0.05 [22] CRP: With significant fatigue (median: 4.6, IQR: 3.1–11.1) Without significant fatigue (median: 11.3, IQR: 3.1–9.5) p-value > 0.05 [22]
VAS Pain	VAS, 0–100 mm [22, 23]	OR 1.02, CI 0.98–1.05, p-value 0.33 [23]	With significant fatigue (median: 50, IQR: 15–70) Without significant fatigue (median: 10, IQR: 0–43) p-value > 0.05 [22]
Quality of life	PsAQoL [23] General health VAS [22]	OR 1.05, CI 0.95–1.16, p-value 0.03 [23]	With significant fatigue (median: 60, IQR: 40–80) Without significant fatigue (median: 40, IQR: 20–60) p-value > 0.05 [22]
Fibromyalgia	FiRST [23]	OR 1.41, CI 1.09–1.82, p-value 0.01 [23]	
BASDAI		OR 1.53, CI 1.15–2.04, p-value < 0.01 [23]	
Anxiety	HAD-A [23]	OR 1.14, CI 1.02–1.26, p-value 0.02 [23]	

[a]adjusted estimate

OR: odds ratio; CI: confidence interval; SD: standard deviation; IQR: interquartile range; PsO: psoriasis; DAPSA: disease activity in psoriatic arthritis; PASI: psoriasis area and severity index; MDA: minimal disease activity; PtGA: patient global assessment; cDMARDs: conventional disease-modifying anti-rheumatic drugs; MTX: methotrexate; SSZ: sulphasalazine; LEF: lefluonamide; CsA: cyclosporine; ACT: acitretin; HAQ: health assessment questionnaire; HAQ-DI: health assessment questionnaire-disability index; BMI: body mass index; ESR: erythrocyte sedimentation rate; CRP: c-reactive protein; VAS: visual analogue scale; PsAQoL: psoriatic arthritis quality of life; FiRST: fibromyalgia rapid screening tool; VLDA: very low disease activity; BASDAI: bath ankylosing spondylitis disease activity index; HAD-A: hospital anxiety and depression scale-anxiety

Not surprisingly, higher prevalence of fatigue was seen in patients with greater disease severity, as measured by the PASI, VLDA, DAPSA, which are measurements that involve standardised assessments by a clinician. Conversely, a higher prevalence of fatigue was not found to be statistically significant with a worse performance on the HAQ, a patient-reported outcome measure. This further supports that while fatigue may be a subjective sensation patients experience, there is an objective basis for the pathogenesis of fatigue which may be correlated to disease severity and the pathogenesis of PsA.

There was a lower prevalence of fatigue in patients who received biologic therapy. Only one paper by Lai et al. mentioned the type of biologic use (anti-tumour necrosis factor) [21]. Further work can be done to assess whether there are any significant differences in the prevalence of fatigue based on the type of biologic used pre- and post-biologic administration, to potential causative factors for fatigue. Differences in fatigue severity based on type of biologic use can potentially help in eliciting commonalities in their mechanisms in relation to fatigue. In addition, more can be done to assess the duration of biologics used for patients currently on biologics, or the indication of biologics in the first place (e.g. inadequate response to conventional DMARDs, side effects from conventional DMARDs, contraindications against conventional DMARDs) as these reasons may confound the difference in prevalence between the two subgroups.

In addition, the presence of anxiety was also found to be a significant risk factor for fatigue. IL-17 and TNF, which are pro-inflammatory cytokines in the pathogenesis of PsA, have also been found to be associated with anxiety and depression [12]. This could highlight the potential for parallel treatments to target similar pathogenetic pathways to address anxiety to reduce fatigue in PsA patients.

Fatigue was also found to be statistically associated with the diagnosis of fibromyalgia in patients. It is known that the presence of fibromyalgia and fatigue more commonly observed in patient with PsA compared to controls [28]. However, it is currently unclear from our data if patients with both fibromyalgia and PsA experience a greater severity of fatigue.

Patients with higher educational level attainment were also less likely to develop fatigue. Several previous studies have documented between higher educational attainment's negative association with fatigue, potentially indicating improved health literacy and access to health information is significant for patient's disease control [29]. Patients who attended middle school or high school in comparison to those who had only primary school education, had a statistically significant difference in fatigue prevalence. This is useful information where it could help clinicians assess which patients may be at higher risk of developing fatigue when managing PsA, and to aid in instituting pre-emptive measures to this patient population.

There does not seem to be any significant difference in the prevalence of fatigue between genders. Previous studies on the association of gender and disease burden showed that while its prevalence may be equal in males and females, current literature suggested that the burden of disease may be higher in females compared to males, with some studies reporting it in terms of disease activity, pain, and fatigue [30]. However, it is important to consider that many studies in the current literature comparing the impact of gender on patient-reported outcomes, including fatigue, have not taken potential confounders into account [31]. Data from this current study did not highlight any predilection in fatigue based on gender in comparison to the previous studies.

Commonly reported risk factors of fatigue included concomitant enthesitis, dactylitis, lower educational level attained, disease severity, higher pain score, and inflammatory markers. Notably, depression was absent from the list of possible contributors from the current study due to the lack of data. However, it is underdiagnosed in PsA, and along with anxiety, it is known to present in approximately 20–30% of the patients with PsA with a bidirectional relationship with pain. A full assessment of such disease-related clinical factors would be crucial in targeting patients with fatigue to improve their quality of life [32–35]. Although the present study was unable to pool the estimates for the potential risk factors reported, understanding and assessing risk factors of fatigue in patients with PsA is critical for providing clinicians and health professionals with quintessential knowledge of psychological aspects of the disease that need to be addressed when treating patients with significant fatigue in a multidisciplinary team and patient-centered approach [35].

This is the first study looking into fatigue prevalence in patients with PsA using a pooled analysis from studies of good quality and measured using validated instruments. From our results, given that tender and swollen joints and enthesitis were identified risk factors for PsA, this highlights that control of underlying disease activity will be important to reduce fatigue. Given that cultural factors have been found to influence fatigue reporting, this study also highlights the need for proactive assessment of fatique using locally validated instruments during clinical consultations. There is also a need to screen for concomittant anxiety and depression, as these are associated risk factors of fatigue. This is in keeping with current recommendations and guidelines on fatigue evaluation and management - which should span across multiple domains - biological, psychosocial, to inform clinical care.

However, our study does have some limitations. Firstly, the number of studies included in the subgroup analysis was low and might result in an inadequate analysis of parameters contributing to heterogeneity in the prevalence of fatigue in PsA patients. This was due to variables that were not measured consistently across studies. Studies that were not published in and those which were drug trials were excluded, potentially limiting the generalizability of the study. Secondly, the scales used to measure fatigue and definitions of fatigue varied across studies. Although the current review attempted to mitigate this through broadly dichotomising to the presence of 'any fatigue' or 'significant fatigue' according to the definitions provided in the individual studies, the definitions which formed the basis of this were not identical. This could limit the generalizability of our findings. An international standardized measurement of fatigue would be ideal, but in the absence of that, perhaps more research can be done to allow for inter-measurement comparisons and interpretations. Next, because the scales used to measure fatigue and definitions of fatigue varied across studies, this contributed to heterogeneity in the derived pooled prevalence of fatigue and resulted in potentially suboptimal pooling of the fatigue estimates. In addition, although this study found that patients receiving biologic therapy reported less fatigue, the papers did not elaborate on the biologic type and duration of biologic use. This highlights that more research can be done into this area to evaluate how biologic class and treatment duration affects fatigue in patients with PsA. Last but not least, we were unable to conduct a meta-analysis of the risk factors associated with the presence of fatigue. Commonly examined risk factors of fatigue for autoimmune diseases, such as sleep deprivation, anxiety, depression and quality of life, were unable to be adequately examined due to the lack of sufficient studies [36]. In addition, there was a lack of studies reporting the potential risk factors using the same measurement scale and cut-off scores using a univariate or multivariate logistic regression technique specifically for patients with PsA from the existing literature. Therefore, our findings may not be generalizable to all patients with PsA. There is a need for future studies to use a common definition of fatigue and utilise validated fatigue scales to understand the impact of fatigue in PsA better.

Conclusions

About half of the patients with PsA experienced fatigue. The current review attempted to mitigate the heterogeneity in the assessment tools by broadly classifying patients into "any fatigue" and "significant fatigue". Patients who did not receive biologic therapy, had concomitant anxiety or fibromyalgia, or had a lower educational attainment were found to have a higher prevalence of fatigue. With such information, we can identify patient populations at greater risk of developing fatigue and take pre-emptive measures in their therapy. In addition, our results highlight that control of underlying disease activity will be important to reduce fatigue. There is also a need to screen for concomittant anxiety and depression, as these are associated risk factors of fatigue. More can be done to push for an international collaboration on the establishment of a global consensus on the fatigue definition and objective standardised assessment, taking into account cross-cultural and socioeconomic differences in the fatigue perception, as well as the multifaceted, intricate comorbidities that accompany fatigue. This would better help clinicians translate research literature to practical assessment and management framework of patients' fatigue.

Abbreviations

BASDAI-Fatigue	Fatigue question in the BASDAI 10 cm visual analog scale
CI	Confidence interval
DAPSA	Disease Activity in Psoriatic Arthritis
DMARD	Disease-modifying anti-rheumatic drug
FACIT-F	Functional Assessment of Chronic Illness Therapy-Fatigue
HAQ	Health Assessment Questionnaire
IL-17	Interleukin-17
PASI	Psoriasis Area and Severity Index
PsA	Psoriatic arthritis
PsAID-12	12-item Psoriatic Arthritis Impact of Disease questionnaire
PRISMA	Preferred Reporting Items for Systematic Review and Meta-Analysis
TNF	Tumor Necrosis Factor
VLDA	Very Low Disease Activity

Supplementary Information

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Supplementary Material 1

Supplementary Material 2

Supplementary Material 3

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Author contributions
W.F. designed the systematic review, undertook the conception of the study, and critically evaluated the manuscript for revision. H.T. and T.C.L.T. collected, analysed, and interpreted the data and drafted the manuscript.

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Data availability
The datasets generated during the current study are available from the corresponding author upon request.

Declarations

Human ethics and consent to participate declarations
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Competing interests
The authors declare no competing interests.

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