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Prevalence and variables associated with fatigue in psoriatic arthritis: a cross-sectional study

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Abstract

Objective To describe the prevalence of and evaluate the factors associated with fatigue patients with psoriatic arthritis (PsA) in an Asian population.

Methods We used baseline data from a registry of patients with PsA attending an outpatient clinic of a tertiary hospital in Singapore. Demographic data and disease characteristics were evaluated. Fatigue was assessed by question one of the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI-F) and the vitality domain of the Medical Outcome Survey, Short-Form 36 (SF-36 VT). We evaluated clusters of variables, and individual variables in association with fatigue.

Results We included 131 patients (50.4% men, 63.4% Chinese, median PsA duration 21.0 months) with completed data for fatigue. Forty-five patients (34%) experienced severe fatigue (defined by BASDAI-F > 5/10). We used principal component analysis and identified five clusters of variables that explained 62.9% of the variance of all factors. Of these, disease activity and impact, and disease chronicity were significantly associated with BASDAI-F and SF-36 VT. In multivariable analyses, back pain, peripheral joint pain and patient global assessment were associated with BASDAI-F, whereas peripheral joint pain and mental health were associated with SF-36 VT.

Conclusion PsA-associated fatigue is prevalent in this Asian PsA cohort and is associated with disease activity, impact and chronicity.

Keywords Arthritis · Psoriatic · Fatigue · Rheumatic diseases

Introduction

Psoriatic arthritis (PsA) is a chronic autoimmune disease with musculoskeletal manifestations of arthritis, dactylitis, enthesitis and spondylitis associated with skin psoriasis. Fatigue is ranked among the three most important domains according to patients with PsA [1, 2]. Its significance is formally recognised in the inner core of the OMERACT core set of domains and it is required to be reported in all clinical trials and longitudinal observational studies [3].

Fatigue has a detrimental impact on quality of life and physical fitness of patients with PsA [4]. It impairs activity participation, daily activities and contributes to work absenteeism [5], and should be treated as an independent outcome [6]. Fatigue is also a useful prodromal symptom of flares which patients can recognise to avoid flares of pain [7]. Despite its importance, fatigue as a subjective feeling of patients may not be readily recognized by healthcare providers [8, 9]. The pathogenesis of PsA-associated fatigue is not clearly understood, but generally thought to be multifactorial with immunologic, psychologic and physiologic components [10, 11]. Increased fatigue levels in PsA cohorts have been found to be associated with higher disease activity [12] and severe skin psoriasis [12, 13].

Most studies reporting on PsA-associated fatigue have been conducted in western populations and there are currently no data from Asian countries. It is well-known that

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ethnic, cultural and environmental factors influence the clinical manifestations of rheumatic illnesses including PsA [14, 15]. In a multinational study in rheumatoid arthritis, country of residence was shown to have a significant impact on fatigue [16]. These variations may arise from the interaction of one's genetic background, socio-economic environment, symptom perception, as well as cultural influences on self-reporting of symptoms [14].

In this study, we aim to evaluate the prevalence of fatigue and the variables associated with fatigue in patients with PsA within a multi-ethnic Asian population.

Methods

Study design

We used baseline data from the PRESPOND (PREcision medicine in SPondyloarthritis for better Outcomes aNd Disease remission) registry with patients recruited from March 2013 to February 2018. We recruited consecutive patients attending a designated PsA clinic in Singapore General Hospital who were above the age of 18 years and fulfilled the Classification Criteria for Psoriatic Arthritis (CASPAR) [17]. The SingHealth Centralized Institutional Review Board approved the study protocol (CIRB Ref: 2012/498/E) and all patients provided written consent prior to the study.

Data collection

We collected demographic characteristics, clinical data and patient-reported outcomes (PROs) from each patient according to a standardized protocol. Patients were invited to complete self-administered questionnaires collecting data on their age, gender, ethnicity, highest education level and PROs. Body weight and height were measured in the clinic and the duration of PsA was derived from the date of diagnosis in clinical records.

The designated physician (YYL) assessed patients' tender, swollen and damaged joint counts on a 66/68/68 diarthrodial joints diagram as previously described [14], dactylitis count (0–20), enthesitis count according to the 6-point Leeds Enthesitis Index (LEI), and Psoriasis Area and Severity Index (PASI). Data on physician's global assessment (PhGA) were collected on a 0–10 numeric rating scale (NRS) (0 no disease activity to 10 worse disease activity). Erythrocyte sedimentation rate (ESR) was measured in each patient as part of routine care. Current conventional (c) disease-modifying anti-rheumatic drugs (DMARDs) or biological (b) DMARDs were recorded (yes/no). The presence or absence of prevalent hypertension, hyperlipidemia, diabetes mellitus, coronary heart disease and stroke was collected from case records.

For PROs, we collected patient global assessment (PGA) of disease activity in the past week on a 0–100 mm visual analogue scale (VAS) (0 very good to 100 very bad), Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) [18], Health Assessment Questionnaire Disability Index (HAQ-DI) (0 no disability to 3 severe disability), and 36-item Short-Form Health Survey version 2 (SF-36v2). Perceptions of axial and peripheral joint pain were assessed with the second and third questions of BASDAI, collected on a 0–10 NRS (0 none to 10 very severe). The criteria for minimal disease activity (MDA) were evaluated for each patient [19].

Measurements of fatigue

We used two fatigue measures—the first question of BASDAI (BASDAI-F) that asked the severity of fatigue in the past week, rated on a 0–10 NRS (0 none to 10 very severe) and the vitality domain of SF-36 (SF-36 VT). We defined severe fatigue as having a BASDAI-F score of > 5/10 [12, 20] and deemed a BASDAI-F score from 0 to 5 as nil-to-moderate fatigue. The SF-36 VT, one of the 8 SF-36 domains, is computed as a standardized score (0–100) based on responses to 4 questions on "feeling full of life", "having a lot of energy", "feeling worn out" and "feeling tired". The SF-36 VT is a reverse concept of fatigue; higher SF-36 VT scores suggest lower levels of fatigue.

Statistical analysis

Results were shown as median (interquartile range, IQR), or mean (standard deviation, SD) when specified, for continuous variables; and number and percentages (%) of patients for categorical variables. We described and compared baseline characteristics of patients with severe and nil-to-moderate fatigue with chi-squared tests for categorical variables and Student's *t* tests or Mann–Whitney *U* tests as appropriate for continuous variables.

We performed a principal component analysis (PCA), without rotation, to identify clusters of variables that were clinically relevant and distinct. These variables were selected based on theoretical link and results of previous studies [12, 13, 16, 21–30]. We only allowed variables with a predefined maximum collinearity of 0.6 into the model. Variables measuring similar concepts or had high collinearity were selected through a discussion among domain experts (YYL, WF, YHK).

Swollen joint count was chosen instead of tender joint count as it may better represent disease activity [31]; BASDAI-axial pain and BASDAI-peripheral joint pain were included separately as they measure different concepts; PhGA was excluded due to high collinearity with tender and swollen joint counts; SF-36 summary scores were not

chosen as the eight domains of the SF-36 represent better-defined concepts. From the eight domains of SF-36, we included the mental health (MH) domain as it may represent the psychological status of patients that has been previously associated with fatigue [20, 32, 33]. Variables included in the final PCA were age, gender, ethnicity (Chinese *vs*. non-Chinese), education level (primary or below, secondary, tertiary), body mass index (BMI), duration of PsA, swollen joint count, clinically damaged joints, dactylitis, LEI, PASI, ESR, PGA, BASDAI-axial pain, BASDAI-peripheral joint pain, HAQ-DI and SF-36 MH. We evaluated the associations of the identified clusters of variables (components) with both fatigue measurement using linear regression models.

We conducted a univariable analysis for the association of variables with BASDAI-F and SF-36 VT using Spearman's rho correlations. A Spearman's rho > 0.7 was considered strong, > 0.5–0.7 was considered moderate, > 0.3–0.5 was considered weak, and < 0.3 was considered negligible [34].

We included in the multivariable analysis variables that had an association with fatigue with a significance level of $p < 0.2$ in the univariable analysis and other important variables as suggested by literature. Selected variables were analysed using stepwise linear regression models with both fatigue measurements.

We considered two-sided p values less than 0.05 as statistically significant. We performed all statistical analyses with IBM SPSS Statistic Package, version 24 (IBM, Armonk, NY).

Results

Patient characteristics

We recruited 142 patients with PsA to the registry, of which 131 had completed data for both BASDAI-F and SF-36 VT at baseline and were included in the analysis. Characteristics of the total patient cohort with stratification to nil-to-moderate fatigue and severe fatigue are presented in Table 1. The mean (standard deviation, SD) age and median (interquartile range, IQR) duration of PsA were 50.1 (13.5) years and 21.0 (95.0) months, respectively. There were 66 (50.4%) men and 83 (63.4%) Chinese patients. Severe fatigue (BASDAI-F > 5/10) was experienced by 45 patients (34.4%).

Patients who reported severe fatigue had higher tender and swollen joint counts, enthesitis count and PhGA than those with nil-to-moderate fatigue. Patients with severe fatigue also reported significantly higher PGA, axial and peripheral joint pain, more disability by HAQ-DI and poorer health-related quality of life across all SF-36 domains. A significantly lower proportion of patients met the MDA criteria in the severe fatigue group as compared to the nil-to-moderate fatigue group (15.6% *vs.* 50.6%; $p < 0.001$). Among the 50 patients who were in MDA, 7 (14%) reported severe fatigue by BASDAI-F.

Principal component analysis

In the PCA of 17 selected variables, variables clustered to five components explaining a total of 62.9% of the variance (Fig. 1 and Supplementary Table S1 [Online Resource]). The largest component, explaining 24.1% of the variance, reflected disease activity and impact. This component comprised HAQ-DI, BASDAI-peripheral joint pain, BASDAI-axial pain, PGA, SF-36 MH, swollen joint count, LEI, ESR, dactylitis and PASI. The second component, explaining 13.5% of the variance, reflected disease chronicity. This second component comprised age, education level, clinically damaged joints and ESR. In linear regression analyses of the five components, the first two components were statistically significantly associated with fatigue measured by both BASDAI-F and SF-36 VT. These 2 components representing (a) disease activity and impact and (b) disease chronicity explained 44.2% and 51.3% of the total variance of BASDAI-F and SF-36 VT, respectively.

Univariable and multivariable analyses

In the univariable analysis (Table 2), PGA, BASDAI-axial and BASDAI-peripheral joint pain moderately and significantly correlated with BASDAI-F (rho ranges 0.52–0.59). Tender joint count, LEI, PhGA, HAQ-DI and SF-36 MH correlated weakly and significantly with BASDAI-F (rho ranges 0.31–0.40). The correlations between BASDAI-F and both ethnicity and swollen joint count were negligible but statistically significant.

In the univariable analysis for SF-36 VT, SF-36 MH was strongly and significantly correlated with SF-36 VT (rho = 0.70). Tender joint count, LEI, PhGA, PGA, BASDAI-axial pain, BASDAI-peripheral joint pain, and HAQ-DI weakly and significantly correlated with SF-36 VT (rho ranges 0.31–0.50). Age, BMI, dactylitis and ESR correlated significantly with SF-36 VT at negligible ranges.

In the multivariable analysis, age, ethnicity, BMI, duration of PsA, swollen joint count, LEI, PASI, ESR, PGA, BASDAI-axial pain, BASDAI-peripheral joint pain, HAQ-DI and SF-36 MH were included based on association with BASDAI-F with a p value < 0.2 in the univariable analysis. In addition, we included gender [12, 24] and education level [12] as they were associated with fatigue in previous studies. We also included the duration of PsA and clinically damaged joints to investigate chronicity and physical joint damage as potential variables which have been found to be associated with fatigue in a previous study [26].

Table 3 summarizes the results of the multivariable analysis for BASDAI-F and SF-36 VT, respectively. Variables that

Table 1 Baseline characteristics of patients with psoriatic arthritis ($n=131$)

	Total ($n=131$)	Nil to moderate fatigue BASDAI-F ≤ 5/10 ($n=86$)	Severe fatigue BASDAI-F > 5/10 ($n=45$)	p value
Demographics				
Age, years[a]	50.1 (13.5)	50.9 (12.8)	48.6 (14.6)	0.349
Gender, male (%)	50.4	45.3	60.0	0.111
Ethnicity				
Chinese (%)	63.4	67.4	55.6	
Malay (%)	8.4	7.0	11.1	
Indian (%)	26.0	23.3	31.1	
Others (%)	2.3	2.3	2.2	0.580
Education, secondary or below (%)	56.9	56.5	57.8	0.886
BMI, kg/m^2[b]	25.6 (22.8–29.4)	25.5 (22.8–28.7)	26.0 (22.7–30.3)	0.241
Duration of PsA, months[b]	21.0 (4.0–99.0)	21.0 (4.5–96.3)	23.0 (4.0–109.0)	0.907
Current drug use (%)				
bDMARDs	11.8	8.5	17.8	0.123
cDMARDs	74.8	74.4	75.6	0.885
Comorbidities (%)				
Hypertension	31.0	29.6	33.3	0.667
Hyperlipidemia	46.0	43.2	51.1	0.394
Diabetes mellitus	17.5	18.5	15.6	0.675
Coronary heart disease	6.3	3.7	11.1	0.133[c]
Stroke	0.0	0.0	0.0	NA
Clinical assessments				
Tender joint count (0–66)[b]	2 (0–5)	1 (0–3)	4 (1–9)	< 0.001***
Swollen joint count (0–68)[b]	1 (0–3)	1 (0–2)	3 (1–5)	0.004**
Clinically damaged joints (0–68)[b]	1 (0–4)	1 (0–4)	0 (0–3)	0.630
Dactylitis count (0–20)[b]	0 (0–1)	0 (0–1)	0 (0–1)	0.566
LEI (0–6)[b]	0 (0–1)	0 (0–0)	0 (0–2)	0.002**
PASI (0–72)[b]	1.50 (0.20–3.40)	1.30 (0.20–3.23)	1.80 (0.35–6.10)	0.090
ESR, mm/h[b]	21.0 (8.0–39.0)	17.0 (7.0–33.0)	23.0 (9.5–52.0)	0.062
PhGA (0–10)[b]	3 (1–4)	3 (1–4)	4 (3–6)	0.001**
Achieved MDA (%)	38.5	50.6	15.6	< 0.001***
Patient-reported outcomes				
PGA (0–100)[b]	32.0 (13.0–50.0)	25.0 (11.0–45.5)	51.0 (32.5–70.5)	< 0.001***
BASDAI-axial pain (0–10)[b]	3 (1–5)	2 (0–3)	5 (2–7)	< 0.001***
BASDAI-peripheral joint pain (0–10) [b]	4 (2–6)	3 (1–5)	6 (4–8)	< 0.001***
HAQ-DI (0–3)[b]	0.25 (0.00–0.66)	0.13 (0.00–0.44)	0.50 (0.00–1.06)	0.001**
SF-36 domains[b]				
PF (0–100)	75 (50–90)	75 (55–95)	60 (35–80)	< 0.001***
RP (0–100)	75 (50–100)	81 (56–100)	56 (44–81)	0.002**
BP (0–100)	62 (41–74)	72 (51–74)	41 (32–62)	< 0.001***
GH (0–100)	52 (40–67)	57 (47–72)	40 (30–57)	< 0.001***
VT (0–100)	50 (44–62)	63 (50–75)	44 (31–50)	< 0.001***
SF (0–100)	75 (63–100)	88 (63–100)	63 (50–75)	< 0.001***
RE (0–100)	83 (50–100)	100 (75–100)	75 (42–100)	0.001**
MH (0–100)	70 (55–80)	75 (55–86)	60 (48–75)	0.001**
PCS (norm-based)	42.6 (30.1–51.4)	46.1 (35.3–52.5)	35.8 (25–46.4)	< 0.001***
MCS (norm-based)	42.3 (35.3–50.1)	46.1 (37.6–54.7)	37.3 (28.7–44.3)	< 0.001***

BMI body mass index; *cDMARDs* conventional disease-modifying anti-rheumatic drugs; *bDMARD* biological DMARDs; *LEI* Leeds Enthesitis Index; *PASI* Psoriasis Area and Severity Index; *ESR* erythrocyte sedimentation rate; *PGA* patient global assessment; *PhGA* physician global assessment; *MDA* minimal disease activity; *BASDAI* Bath Ankylosing Spondylitis Disease Activity Index; *HAQ-DI* Health Assessment Questionnaire disability index; *SF-36* Medical Outcome Short Form-36; *PF* physical function; *RP* role-physical; *BP* bodily pain; *GH* general health; *VT* vitality; *SF* social functioning; *RE* role-emotional; *MH* mental health; *PCS* physical health component summary; *MCS* mental health component summary

*p<0.05; **p<0.01; ***p<0.001

Table 1 (continued)

[a]Mean (standard deviation)

[b]Median (interquartile range)

[c]Fisher's exact test

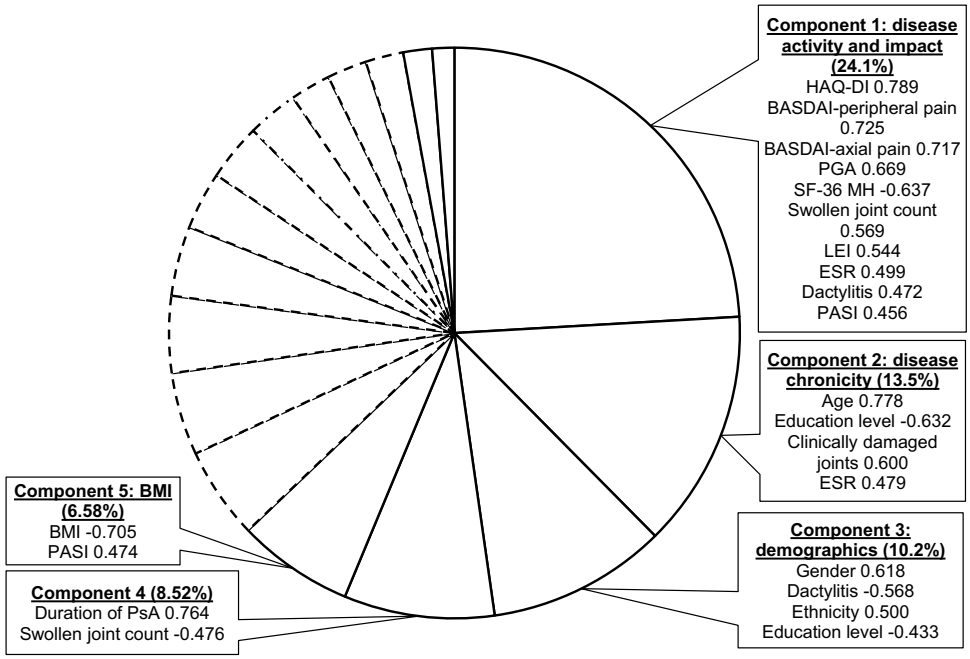

Fig. 1 Principal component analysis with 5 components and residuals (in dotted lines). Only factor loadings of magnitude greater than 0.40 are shown. *PsA* psoriatic arthritis; *BMI* body mass index; *LEI* Leeds Enthesitis Index; *PASI* Psoriasis Area and Severity Index; *ESR* erythrocyte sedimentation rate; *PGA* patient global assessment; *BASDAI* Bath Ankylosing Spondylitis Disease Activity Index; *HAQ-DI* Health Assessment Questionnaire disability index; *SF-36* Medical Outcome Short Form-36; *MH*, mental health

remained statistically significantly associated with BASDAI-F were BASDAI-axial pain, BASDAI-peripheral joint pain and PGA. Variables associated with SF-36 VT were BASDAI-peripheral joint pain and SF-36 MH.

Discussion

Fatigue is prevalent in our study cohort of Asian patients with PsA. More than a third (34.4%) of patients experienced severe fatigue with greater disease activity, disability and reduced health-related quality of life. In the PCA, fatigue was associated with clusters of variables representing concepts of disease activity and impact, and second, disease chronicity. In the multivariable analysis, variables of disease activity were the main drivers of fatigue after controlling for other variables. PGA, BASDAI-axial pain and peripheral joint pain were associated with BASDAI-F, while BASDAI-peripheral joint pain and SF-36 MH were associated with SF-36 VT.

The prevalence of severe fatigue in the current study was similar to that reported in the western literature [26, 30, 33, 35]. In a multinational study across 13 European countries in 246 PsA patients, 44.7% experienced high fatigue with the same definition of severe fatigue as this study (NRS fatigue score > 5/10) [12]. In a Canadian study of 499 PsA patients, 49.5% and 28.7% of patients with PsA experienced at least moderate and severe fatigue as defined by the modified fatigue severity scale ≥ 5 and ≥ 7, respectively [24]. In addition, we found that 14% of patients were in MDA and still reported having severe fatigue. Within our multi-ethnic cohort of PsA patients, non-Chinese patients were more likely to experience greater fatigue, but ethnicity was not statistically significantly associated with both measurements of fatigue in the multivariable analysis.

In the PCA, the clusters of variables explaining fatigue were disease activity and disease impact; disease chronicity came second. Disease chronicity may be contributed by structural damage from long-standing active PsA. These two components, namely disease activity and disease chronicity, were also found to have significant associations with fatigue in a PCA conducted within a Danish registry for PsA [26]. From both the PCA and regression models in the current study, the key driver of fatigue was disease activity. In the BASDAI-F model, both peripheral joint and axial pain were significantly associated with fatigue, while in the SF-36 VT model, only peripheral joint pain was associated with fatigue. Disease activity being the key driver of fatigue corroborates with findings from other PsA cohort studies conducted mainly among Caucasians [12, 20, 24, 27, 36].

Table 2 Spearman's rho correlation between fatigue measures and patient characteristics

	BASDAI-F Correlation coefficient	SF-36 VT Correlation coefficient
Age	−0.12	0.22*
Gender	−0.10	0.11
Ethnicity	0.20*	−0.13
Education level	−0.02	−0.07
BMI	0.17	−0.23**
Duration of PsA	−0.01	0.09
Tender joint count	0.37***	−0.32***
Swollen joint count	0.29**	−0.17
Clinically damaged joints	−0.11	0.09
Dactylitis count	0.04	−0.20*
LEI	0.31***	−0.31***
PASI	0.13	−0.05
ESR	0.14	−0.26**
PhGA	0.34***	−0.32***
PGA	0.52***	−0.44***
BASDAI-axial pain	0.57***	−0.48***
BASDAI-peripheral joint pain	0.59***	−0.45***
HAQ-DI	0.40***	−0.50***
SF-36 MH	−0.37***	0.70***

BMI body mass index; *LEI*, Leeds Enthesitis Index; *PASI*, Psoriasis Area and Severity Index; *ESR* erythrocyte sedimentation rate; *PGA* patient global assessment; *PhGA* physician global assessment; *BASDAI* Bath Ankylosing Spondylitis Disease Activity Index; *HAQ-DI* Health Assessment Questionnaire disability index; *SF-36* Medical Outcome Short Form-36; *VT* vitality; *MH* mental health

*$p < 0.05$; **$p < 0.01$, ***$p < 0.001$

Table 3 Multivariable analysis for variables associated with BASDAI-F and SF-36 VT

	BASDAI-F			SF-36 VT		
	b	95% CI	*p*	*b*	95% CI	*p*
BASDAI-axial pain (0–10)	0.292	(0.138–0.447)	< 0.001			
BASDAI-peripheral joint pain (0–10)	0.244	(0.095–0.394)	0.002	−2.499	(−3.336 to −1.662)	< 0.001
PGA (0–100)	0.028	(0.013–0.043)	< 0.001			
SF-36 MH (0–100)				0.594	(0.480–0.709)	< 0.001

Variables included in the model were age, gender, ethnicity, education level, BMI, duration of PsA, swollen joint count, clinically damaged joints, LEI, PASI, ESR, PGA, BASDAI-axial pain, BASDAI-peripheral joint pain, HAQ-DI and SF-36 MH

BMI body mass index; *LEI* Leeds Enthesitis Index; *PASI* Psoriasis Area and Severity Index; *ESR* erythrocyte sedimentation rate; *PGA* patient global assessment; *BASDAI* Bath Ankylosing Spondylitis disease activity index; *HAQ-DI* Health Assessment Questionnaire disability index; *SF-36* Medical Outcome Short Form-36; *VT* vitality; *MH* mental health

The association of severity of skin psoriasis with fatigue was observed in some studies [12, 13]. In our study, PASI was clustered to the first variable cluster in the PCA and associated with fatigue, but statistical significance was lost in the regression models. This could be related to the relatively low severity of psoriasis in our PsA cohort (median PASI 1.5/72). Effective treatments for PsA like biologics generally reduce but do not completely eliminate fatigue, and the magnitudes of improvement of fatigue are generally lower than that for pain following biological treatments [37], which echoes our findings that 14% of patients who achieved MDA still experienced severe fatigue. This may indicate the existence of factors in addition to inflammation in the pathophysiology of fatigue, for which other dedicated treatment, such as cognitive behavioural therapy, may be required.

While the reason for the persistence of fatigue in PsA was not entirely clear [38], multiple factors, including disability [33], and psychological distress were thought to have important contributions [32, 33]. Variables clustered to central pain sensitization were also shown to be

associated with fatigue in PsA [26]. Some studies postulate that along with chronic pain from joint symptoms and reduced physical fitness [5], elevated cytokine levels, such as IL-1β, in systemic inflammatory conditions exert central nervous system effects which contribute to fatigue [39, 40]. Psychological conditions, such as depression and anxiety, significantly exacerbate fatigue [32, 33], highlighting the central alteration of fatigue perceptions and the need to address these comorbidities of many chronic inflammatory diseases. We explored psychological status using the MH domain of SF-36 in the current study. The SF-36 MH clustered with the first component in the PCA with other variables of disease activity and impact. In the univariable analysis, statistically significant association of SF-36 MH with both BASDAI-F and SF-36 VT was shown; while in the multivariable analysis, SF-36 MH was only associated with SF-36 VT, but not with BASDAI-F. This may suggest the association of fatigue with mental health in our patients. However, this association may need to be interpreted with caution. Studies done in general populations in Asia or among Asian dependents have found that the SF-36 VT and MH had stronger correlations with each other than that reported by the western literature, casting doubts on whether SF-36 VT and MH are measuring distinct concepts [41, 42]. Furthermore, unlike BASDAI-F which enquires patients of fatigue attributable to their disease, SF-36 VT is a general measure of patients' perceived energy. These reasons may explain the slight differences in variables associated with fatigue measured by these two different measures. Other patient-related factors, such as gender [12, 21–24], education level [12, 43] and comorbidities, such as sleeping disorders [44–46] and fibromyalgia [47], were found to be associated with fatigue in previous studies. In our study, ethnicity, age and BMI were associated with fatigue in the univariable analysis but became insignificant in the multivariable analysis.

Information of fatigue in PsA is scant in Asia, and to the best of our knowledge, variables associated with fatigue in PsA have not been explored before in Asia. Fatigue may be influenced by culture and geographical location [16]. Previous studies were all conducted mainly in Caucasian countries and the generalizability of their results to Asian populations is limited. A cohort study conducted within a multi-ethnic population has allowed us to study the effects of ethnicity, even though only Chinese and non-Chinese groups could be compared owing to the small sample size. The dataset comprised consecutive and all cases seen in a designated PsA clinic, minimizing selection bias. Furthermore, we were able to analyse a large set of variables, both clinical and PROs, for associations with fatigue. In this study, we used two fatigue measurements which have provided generally consistent perspectives on the variables associated with the concept of fatigue.

There are several limitations of our study. First, the cohort studied patients from a tertiary referral centre with results that may not be generalizable to milder PsA cases seen in general practices or dermatology settings. Second, the cross-sectional nature of the study does not allow for causality inferences regarding the determinants of fatigue to be made and for longitudinal changes in fatigue to be assessed. Third, we used a single item BASDAI-F to measure fatigue which may be vulnerable to misinterpretation and measurement error. The SF-36 VT, therefore, served as a surrogate and similar results were demonstrated with an additional contribution by SF-36 MH. Notably, the SF-36 VT reflects a reverse concept of fatigue that may not necessarily have a specific attribution to PsA per se. We did not utilize other specific fatigue measures like the Functional Assessment of Chronic Illness Therapy Fatigue Scale (FACIT-F) as they have not been translated and adapted for use in our population. Lastly, we did not include other psychological variables like central sensitization, fibromyalgia, anxiety and depression which may greatly impact fatigue, possibly accounting for the large unexplained variance in our PCA.

In conclusion, fatigue is a prevalent and important complaint among Asian patients with PsA even in those with minimal disease activity. Its association with disease activity and chronicity supports an inflammatory component which is amenable to treatment but does not fully explain its existence. PsA-associated fatigue has negative impact on physical disability and quality of life. Clinicians need to be mindful of this and identify potential patient-related factors to address this important domain.

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Author contributions YYL and WF conceptualized the study design. YYL acquired the data. JSQT and YYL performed the data analysis. All authors performed the data interpretation. JSQT and YYL wrote the first draft of the manuscript and all authors revised it critically for important intellectual content. All authors approved the final version of the manuscript to be published and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Code availability Not applicable.

Compliance with ethical standards

Conflicts of interest YYL has received speaking fee from Novartis, Janssen, Eli Lilly and AbbVie (all under US$10,000).

Ethics approval The SingHealth Centralized Institutional Review Board approved the study protocol (CIRB Ref: 2012/498/E).

Informed consent Informed consent was obtained from all individual participants included in the study.

Consent for publication Not applicable.

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