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ORIGINAL ARTICLE

Clinical characteristics, management, and quality of life of psoriasis patients with coexistent lupus erythematosus: Data from the Malaysian Psoriasis Registry

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Abstract

Objective: To describe the clinical characteristics, management and quality of life of psoriasis patients with and without coexistent lupus erythematosus (LE).

Methods: This retrospective cross-sectional study uses data from the Malaysian Psoriasis Registry (MPR) from January 2007 to December 2018.

Results: Of 21 735 psoriasis patients, 34 (0.16%) had coexistent LE. The male to female ratio among psoriasis patients with coexistent LE was 1:5.8 versus 1.3:1 in patients with psoriasis but without LE. Nearly 70% presented with LE preceding psoriasis. Psoriasis patients with LE had an earlier age of psoriasis onset (27.56 ± 11.51 versus 33.31 ± 16.94 years, $P = 0.006$), a higher rate of psoriatic arthropathy (26.5% versus 13.0%, $P = 0.02$), and a significantly greater impairment of quality of life (Dermatology Quality of Life Index >10; 57.6% versus 40.3%, $P = 0.04$) compared with psoriasis

patients without LE. The majority (87.5%) had systemic LE. The incidences of lupus nephritis (72.7% versus 40%) and hematological abnormalities (50% versus 20%) were higher among patients with LE preceding psoriasis compared with those with psoriasis preceding LE. Antinuclear antibody and double-stranded DNA were positive in 59.4% and 28.1% of psoriasis patients with LE, respectively. Hydroxychloroquine triggered the onset of psoriasis in 7 (24.1%) patients. Patients with LE were more likely to receive systemic treatment for psoriasis compared with those without LE (30.3% versus 14.2%, $P = 0.008$).

Conclusions: Psoriasis patients with coexistent LE were uncommon, displayed a female preponderance, were more likely to have joint involvement, and had greater quality of life impairment than those without LE. LE preceded psoriasis in most of these patients, and systemic LE was the most common subtype.

KEYWORDS
lupus erythematosus, Malaysian Psoriasis Registry, psoriatic arthropathy

1 | INTRODUCTION

Psoriasis is an inflammatory skin disease, characterized by hyperproliferation of keratinocytes in the epidermis. Affecting 2%-3% of the general population, psoriasis can be associated with several comorbid conditions, including psoriatic arthritis, enthesopathy, uveitis, and an increased prevalence of cardiovascular comorbidities.[1] Another chronic autoimmune disorder, lupus erythematosus (LE), may be localized to the skin (cutaneous LE [CLE]) or more extensively involve almost any organ in the body (systemic LE [SLE]). The 2019 European League Against Rheumatism/American College of Rheumatology criteria require the presence of an autoimmune marker, the antinuclear antibody, along with other organ-specific criteria for a diagnosis of LE.[2] In contrast, diagnosis of CLE is usually confirmed by skin biopsy. CLE is divided into three subtypes: acute CLE, subacute CLE, and chronic CLE. Acute CLE includes the localized form, malar rash, and the generalized form which can be photodistributed or more diffuse. For subacute CLE, there are two morphological presentations, annular and papulosquamous. Chronic CLE includes discoid LE, lupus tumidus, lupus profundus, and chilblain LE.[3]

The coexistence of psoriasis and LE is uncommon, occurring together in 0.3%-0.69% of patients with psoriasis[4–6] and in 0.02%-5% of patients with LE.[7,8] The prevalence of concomitant LE and psoriasis in Malaysia has not been reported to date. Previous studies and numerous other case reports have described the clinical characteristics of such patients as well as the challenges in diagnosing coexistent LE and psoriasis.[9–13] The complexity in the management of both conditions has also been communally recognized, especially as the first-line treatments for each may aggravate the other. In particular, hydroxychloroquine and corticosteroids for LE may worsen psoriasis, and phototherapy for psoriasis may trigger LE. Varying levels of success have been reported in the management of both conditions simultaneously. For this reason, a panel of experts has recommended immunomodulating agents such as methotrexate and acitretin, and biologic agents such as ustekinumab as appropriate options for the management of concomitant psoriasis and LE.[14]

The Malaysian Psoriasis Registry (MPR) is managed by the Malaysian Ministry of Health and the Dermatological Society of Malaysia (Appendix S1). It is an ongoing prospective registry for the systematic collection of data on psoriasis patients in Malaysia with 37 participating dermatology centers (32 government, three private and two university centers). All patients with psoriasis are notified to the MPR at the first encounter, whereas those with severe disease requiring phototherapy and/or systemic therapy would have subsequent 6-monthly notifications to the MPR. The registry collects data on demographics, co-morbidities, disease severity, and the types of treatments received, among other information. For health-related quality of life (HRQoL) assessment, patients are asked to complete the Dermatology Life Quality Index (DLQI) questionnaire (or the Children's Dermatology Life Quality Index [CDLQI] questionnaire for pediatric patients).

In this observational study, we aim to describe the clinical characteristics and management of psoriasis patients with coexistent LE registered in the MPR and compare them to the cohort of patients who have psoriasis and not LE. Both conditions are known to negatively affect patients' quality of life and can impose a significant burden on healthcare provision due to their severity and chronicity, so we needed to ascertain whether coexistence of LE and psoriasis may further affect patients' quality of life. This study contributes to the sparse literature regarding diagnosis and management of concomitant LE and psoriasis. In particular, we compared quality of life for psoriasis patients with and without LE to increase the awareness of clinicians in addressing the different needs of these patients. To our knowledge, this is the first cross-sectional study focusing on psoriasis with coexistent LE in an Asian population.

2 | PATIENTS AND METHODS

2.1 | Study design

This is a retrospective cross-sectional study. All patients with psoriasis notified to the MPR between January 1, 2007 and December 31, 2018 were included in this study. Data for patients with psoriasis only were obtained from the MPR at enrolment, whereas data for patients with both psoriasis and LE were captured when concomitant LE was first noted. Additional data concerning disease onset, organ involvement, autoantibodies, and systemic treatment for psoriasis patients with concomitant LE were collected at the respective participating centers. Documentation of organ involvement and/or autoantibodies before the point of registration to the MPR were gathered. The history of systemic treatment received since the diagnosis of LE until the point of registration with MPR was also recorded for analysis. During the study period, the American College of Rheumatology 1992 criteria[15] and Systemic Lupus International Collaborating Clinics (SLICC) 2012 criteria[16] were being used in clinical practice to diagnose SLE. Hence, our cohort had their SLE diagnosed based on these two criteria.

The DLQI and CDLQI by Professor Andrew Y Finlay (available at https://www.cardiff.ac.uk/medicine/resources/quality-of-life-questionnaires/dermatology-life-quality-index) were used to assess patients' quality of life (QoL) in our cohort.[17] Both DLQI and CDLQI are validated QoL assessment tools used for a wide range of dermatoses since 1994 and 1995, respectively. They are available for use in various languages. They are a dermatology-specific tool, comprising 10 multiple choice questions assessing patients' symptoms and feelings, daily activities, leisure, work and school, personal relationships, and treatment in the last 1 week. It is self-explanatory and can be completed in 1-2 minutes. The total DLQI score is calculated by summing the score of each question with a total score of 0-30. The higher the score, the more the QoL is impaired.

2.2 | Patient and public involvement

This research was performed without any formal patient involvement or patient organization involvement in the study design, development of patient-relevant outcomes, interpretation of results, or writing of the manuscript.

2.3 | Statistical analysis

Data collected were analyzed using IBM SPSS Statistics for Windows, Version 21.0 (IBM Corp, Armonk, NY, USA). Categorical data were analyzed using χ^2 tests and presented as numbers or percentages. Continuous data were analyzed using *t* tests. Descriptive analyses were used for sociodemographic characteristics, clinical pattern, treatment modalities, and their impact on HRQoL. Ethical approval for this study was obtained from the Medical Research and Ethics Committee (MREC), Ministry of Health Malaysia (NMRR-21-114-58126).

3 | RESULTS

A total of 21735 patients with psoriasis were registered to the MPR, including 12058 male (55.5%) and 9677 female (44.5%) patients. Among all psoriasis patients, 34 (0.16%) had coexistent LE. Table 1 shows the demographic data for psoriasis patients with and without LE. Their LE preceded their psoriasis in more than half of the patients (16; 65%). Psoriasis patients with LE had an earlier age of psoriasis onset (27.56 ± 11.51 versus 33.31 ± 16.94 years, $P = 0.006$) compared with those without LE. There was a significant female preponderance, with a male to female ratio of 1:5.8 ($P < 0.001$) for patients with both psoriasis and LE compared with those without LE, with the ratio of 1.3:1.

Face and neck involvement were more prevalent among psoriasis patients with LE compared with those without LE (61.8% versus 51.5%, $P = 0.23$), although the difference was not statistically significant. Psoriasis patients with LE had a higher prevalence of psoriatic arthropathy (PsA; 26.5% versus 13.0%, $P = 0.02$) compared with those without LE. Seven (58%) psoriasis patients with LE had PsA with the most common types being symmetric polyarthropathy (3; 25%) and asymmetric monoarthropathy (2; 16.7%). Among psoriasis patients with LE, plaque psoriasis was the most common subtype (29; 90.6%); others included erythrodermic (1; 3.1%), localized pustular (1; 3.1%), and palmoplantar (1; 3.1%) forms of psoriasis.

Table 2 shows baseline clinical characteristics and quality of life data for psoriasis patients with and without LE. Although psoriasis patients with and without LE had comparable body surface area involvement and mean DLQI scores, a significantly higher percentage of the cohort with LE had a DLQI score greater than 10, indicating a very large to extremely large effect on their QoL (DLQI score of >10; 57.6% versus 40.3%, $P = 0.04$) (Figure 1). Among psoriasis patients with LE, "symptoms and feelings" was the most severely affected domain, with 43.9% indicating that their disease had "very much" and "a lot" of impact on QoL; the least affected domain was "personal relationship", as 84% reported that they were affected "a little" or "not at all." Findings for these domains were generally similar for those patients without LE (Figure 2).

Psoriasis patients with LE were more likely to receive systemic treatment, particularly methotrexate, corticosteroids, and cyclosporine, compared with those without LE (30.3% versus 14.2%, $P = 0.008$). Among those with LE on systemic treatment, 21.2% received concomitant systemic corticosteroids; however, only 0.8% ($P < 0.001$) of those without LE received systemic corticosteroids.

Table 3 compares the characteristics of LE in psoriasis patients in relation to the onset of LE. Among psoriasis patients with LE, most (87.5%) had SLE and the remainder had CLE. Psoriasis patients with SLE presented mainly with renal (78.6%), joint (50%), and hematological (46.4%) involvement, but also experienced skin and eye

TABLE 1 Demographic data of psoriasis patients with and without lupus erythematosus.

Characteristics	Psoriasis with LE n = 34	Psoriasis without LE n = 21 701	*P* value
Mean age of psoriasis onset (years)	27.56 ± 11.51	33.31 ± 16.94	0.006
Gender	n = 34	n = 21 701	<0.001
Male	5 (14.7%)	12 053 (55.5%)	
Female	29 (85.3%)	9648 (44.5%)	
Ethnicity	n = 34	n = 21 695	–
Malay	15 (44.1%)	11 776 (54.3%)	
Chinese	8 (23.5%)	4140 (19.1%)	
Indian	4 (11.8%)	3576 (16.5%)	
Others	7 (20.6%)	2201 (10.1%)	
Family history	n = 34	n = 21 122	0.46
	6 (17.6%)	4851 (23%)	
Comorbidities	n = 34	n = 21 122	
Dyslipidemia	6 (16.5%)	3406 (16.1%)	0.73
Hypertension	9 (28.1%)	4977 (23.6%)	0.56
Diabetes mellitus	0	3329 (15.8%)	0.01
IHD	0	1011 (4.8%)	0.20
CVA	0	307 (1.5%)	0.48
HIV	0	105 (0.5%)	0.68

Abbreviations: CVA, cerebrovascular accident, HIV, human immunodeficiency virus; IHD, ischemic heart disease; LE, lupus erythematosus.

manifestations, oral ulcers, deep vein thrombosis, and cardiovascular events. A quarter of the psoriasis patients with SLE presented with skin lesions such as malar rash, cutaneous vasculitis, discoid LE, annular erythema, and generalized erythema. Of the 34 psoriasis patients with LE, 9 (26.5%) had skin biopsies to confirm the diagnosis of psoriasis and 13 (38.2%) had LE confirmed by biopsy and direct immunofluorescence. Four patients had subacute CLE; however, only two were confirmed by biopsy.

The incidences of lupus nephritis and hematological abnormalities were higher among patients with LE preceding psoriasis compared with those with psoriasis preceding LE (lupus nephritis: 72.7% versus 40%; hematological abnormalities: 50% versus 20%, respectively). Antinuclear antibody was positive in 59.1%, extractable nuclear antigen antibodies were positive in 45.5%, and dsDNA was positive in 22.7% among psoriasis patients with LE. Hydroxychloroquine triggered the onset of psoriasis in 7 (24.1%) patients with LE.

4 | DISCUSSION

The coexistence of psoriasis and LE is uncommon and the underlying pathogenesis of their association is unknown. In our study, the prevalence of psoriasis with LE (0.16%) was lower compared with other countries, such as Israel (0.37%) and the USA (5.1%).[18,19] This could be a result of under-reporting, because data are submitted to the MPR on a voluntary basis and may not reflect the true incidence. The prevalence of SLE in Malaysia is estimated to be 43 per 100 000 population or 0.043%;[20] comparatively, the prevalence of specifically SLE in the Malaysian Psoriasis Registry was higher than the estimated prevalence of SLE in the general population of Malaysia at 0.12% (28/21 735).[20] The prevalence of SLE in psoriasis patients has been reported to be higher at 0.69% in the USA.[4]

The female to male ratio was significantly higher in psoriasis patients with co-existent LE compared with those with psoriasis alone in our cohort. This corresponds to the gender predilection in SLE, which involves the female hormone estradiol and estrogen receptors.[21]

Arthritis, commonly a manifestation of both diseases, is a contributing factor to physical deformity, eventual permanent disability, and QoL impairment. Bonilla E et al[7] reported that psoriasis patients with coexistent SLE were predisposed to developing PsA. The level of interleukin-17-positive (IL-$^{+}$) CD4^{-} T cells, which reflects PsA serological and clinical disease activity, was found to be elevated in the synovial fluid of PsA patients compared with rheumatoid arthritis patients.[22] In turn, our findings were consistent with a predisposition of patients with both psoriasis and LE developing PsA. Joint involvement in psoriasis, most commonly in the hands, wrists, and knees, ranges from minor arthralgia without deformity to erosive arthropathy with functional impairment. In general, arthritis in SLE is usually non-erosive, but a small group of patients may experience a chronic course of joint disease resembling rheumatoid arthritis with or without joint deformity.[23] However, PsA is usually erosive and destructive.[24] It is a seronegative inflammatory form of arthritis with involvement of the distal interphalangeal joints representing a distinguishing clinical feature. Enthesitis, spondylitis, and sacroiliitis are also characteristic features of PsA.[25] Evaluation with the psoriasis

TABLE 2 Clinical characteristics & quality of life of psoriasis patients with & without lupus erythematosus.

Characteristics	Psoriasis with LE n (%)	Psoriasis without LE n (%)	*P*-value
Psoriasis affected sites			
Scalp	n = 34 31 (91.2%)	n = 20610 16740 (81.2%)	0.14
Face & neck	n = 34 21 (61.8%)	n = 20380 10489 (51.5%)	0.23
Nail	n = 34 21 (61.8%)	n = 21070 11855 (56.3%)	0.52
Psoriatic arthropathy	n = 34 9 (26.5%)	n = 21056 2747 (13.0%)	0.02
Distal hand joint arthropathy	1 (12.2)	832 (36.6)	
Asymmetrical polyarthritis	2 (28.6)	1098 (45.4)	
Symmetrical polyarthritis	3 (32.9)	777 (42.9)	
Spondylitis/ sacroiliitis	0 (0)	227 (9.9)	
Arthritis mutilans	1 (14.3)	88 (3.8)	
Types of psoriasis	n = 32	n = 20440	
Plaque	29 (90.6%)	18966 (92.8%)	
Erythrodermic	1 (3.1%)	389 (1.9%)	
Pustular	1 (3.1%)	147(0.72%)	
Guttate	0 (0%)	738 (3.6%)	
Flexural	0 (0%)	104 (0.5%)	
PNP	1 (3.1%)	86 (0.42%)	
Extent of psoriasis in terms of BSA of involvement	n = 28	n = 16542	-
<5%	17 (60.7%)	7406 (44.8%)	
5%-10%	7 (25%)	5185 (31.3%)	
10%-90%	3 (10.7%)	3523 (21.3%)	
>90%	1 (3.6%)	428 (2.6%)	
BSA >10	6 (20%)	3949 (23.9%)	0.62
Mean DLQI	10.45 ± 6.25	9.61 ± 6.76	0.44
DLQI >10	19 (57.6%)	7941 (40.3%)	0.04
DLQI domain (mean score ± SD)			
Symptoms and feelings	n = 33 2.81 ± 1.38	n = 19664 2.86 ± 1.55	0.88
Daily activities	n = 31 2.43 ± 1.52	n = 18802 2.12 ± 1.74	0.15
Leisure	n = 31 2.31 ± 1.56	n = 17193 2.26 ± 1.86	0.83
Work and school	n = 27 1.00 ± 1.12	n = 15660 0.77 ± 0.97	0.21
Personal relationship	n = 18 1.50 ± 1.47	n = 14645 1.32 ± 1.55	0.69
Treatment	n = 32 1.00 ± 0.98	n = 18662 0.94 ± 0.94	0.51
Systemic therapy	n = 33 10 (30.3%)	n = 20747 2950 (14.2%)	0.008
Acitretin	1 (3%)	580 (2.8%)	0.94
Methotrexate	8 (24.2%)	2285 (11.0%)	0.02
Corticosteroids	7 (21.2%)	172 (0.8%)	<0.001
Cyclosporine	2 (6.1%)	142 (0.7%)	<0.001
Hydroxyurea	0 (0%)	23 (0.1%)	0.85
Phototherapy	0 (0%)	552 (2.7%)	0.33
Biologics	0 (0%)	78 (0.4%)	0.72

Abbreviations: BSA, body surface area; DLQI, Dermatology Life Quality Index; LE, lupus erythematosus; PNP, palmoplantar non-pustular; SD, standard deviation.

epidemiology screening tool (PEST) questionnaire and radiographic imaging in patients with a high index of suspicion may facilitate the diagnosis of PsA and early treatment.

The onset of both psoriasis and LE may be variable; either may precede the other, or they may occur simultaneously. Cutaneous LE may often resemble other conditions; specifically, the papulosquamous variant of subacute cutaneous lupus erythematosus (SCLE) may be confused with the photosensitive variant of psoriasis.[26] Therefore, thorough history taking, adequate knowledge of cutaneous manifestations of LE, and a high index of suspicion are crucial for early detection and effective management of patients with both diseases. Lupus erythematosus preceded psoriasis in two-thirds of the patients in our cohort. They tended to present with earlier disease onset of LE and had a higher prevalence of renal and joint involvement compared with patients with psoriasis preceding LE. Millns reported that half of the patients (eight out of 16) with psoriasis preceding LE and concomitant LE in their cohort had discoid LE. Patients with psoriasis and concomitant LE were found to have widespread psoriasis and significant photosensitivity, and to be treatment resistant.[27] In our cohort, subacute and chronic cutaneous LE appeared to be more frequent among those who had LE concurrently or psoriasis preceding LE.

The utility of autoantibodies, such as antinuclear antibodies, extractable nuclear antigen, and dsDNA, to predict the onset of LE in psoriasis patients is not well established. In our cohort, the presence of autoantibodies was comparable among patients regardless of the pattern of onset of LE in relation to psoriasis. Anti-Sjögren syndrome-related antigen A (anti-SSA; Ro) antibody was detected in 64% of patients with SLE in a study by Agarwal et al, but it was not detected in psoriasis.[28,29] Anti-SSA (Ro) antibody screening is recommended for psoriasis patients with a history of photosensitivity before the initiation of phototherapy, given the association between anti-SSA antibodies and photosensitivity.[30] In our cohort, six patients (18.8%) were positive for anti-SSA (Ro) antibodies.

Autoantibodies against the Ro/La autoantigen complex are involved in the regulation of interferon responses and innate immune system mechanisms that result in the sequestration of Ro52 and Ro60.[25] The presence of anti-Ro60 antibodies was found to be associated with SLE, and more specifically CLE.[31]

Both IL-17 and IL-23, which are known to be associated with both psoriasis and LE, play an important role in the induction of both diseases.[32] Psoriasis is an IL-23-driven T helper type 17 (Th17) cell-mediated disease with overproduction of IL-17 and IL-22, which promotes neutrophil chemotaxis and induces keratinocyte hyperproliferation, respectively.[33] Wong, et al[34] found that IL-12- and IL-23-mediated activation of Th1 and Th17 cells induces Th1 chemokines, CXCL10 and IL-17 in SLE. Therapeutic antibodies targeting IL-17 and IL-23, which are commonly prescribed for patients with moderate to severe psoriasis, have been used in the treatment of SLE following advances in research into the importance of the IL-23/

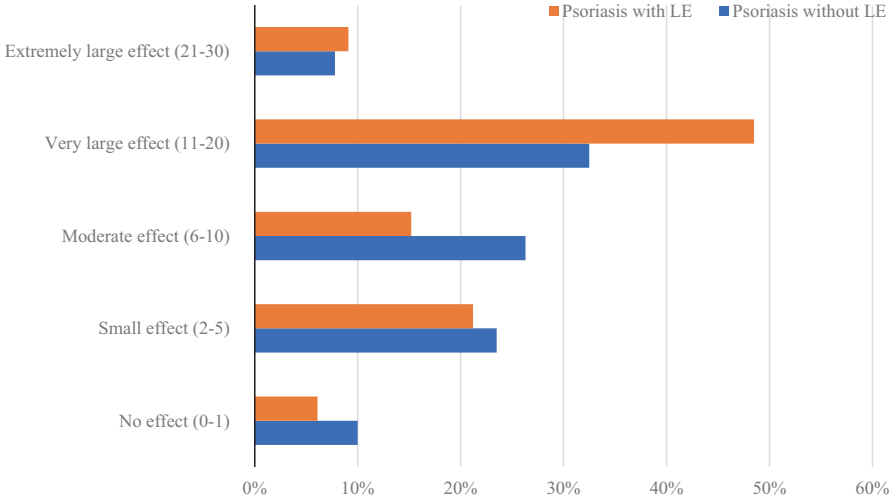

FIGURE 1 Baseline Dermatology Life Quality Index score for psoriasis patients with and without lupus erythematosus (LE).

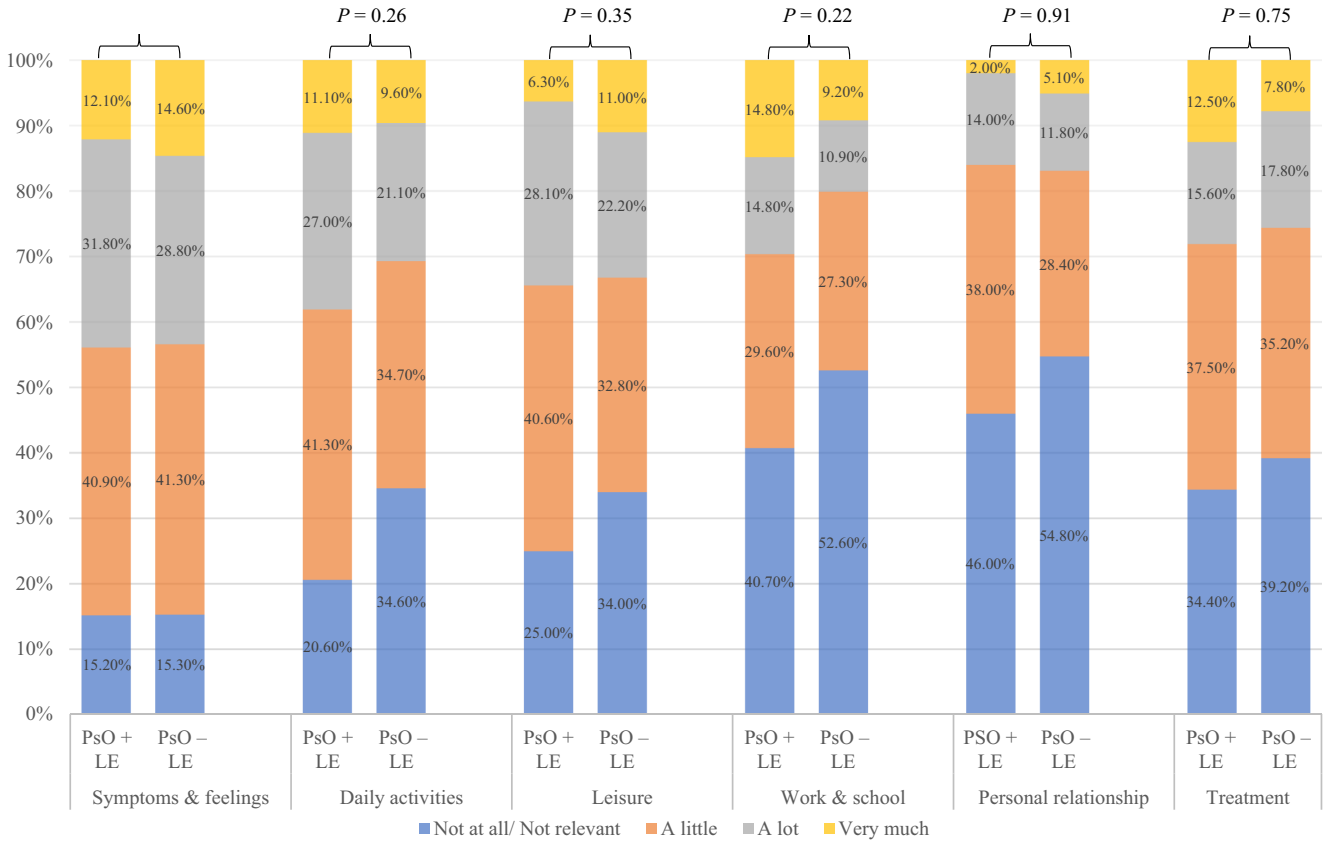

FIGURE 2 Comparison of baseline quality of life impairment in psoriasis (PsO) patients with and without lupus erythematosus (LE) based-on Dermatology Life Quality Index.

TABLE 3 Comparison of characteristics of lupus erythematosus (LE) in psoriasis patients with regards to the onset of lupus erythematosus.

Characteristics	LE preceded psoriasis n = 24 (%)	LE diagnosed concurrently with psoriasis n = 5 (%)	Psoriasis preceded LE n = 5 (%)	Total n = 34
Mean age of onset for psoriasis (years + SD)	28.41 ± 11.68	25.00 ± 12.31	23.40 ± 9.56	27.56 ± 11.51
Mean age of onset for LE (years + SD)	(n = 21)[a] 20.14 ± 7.62	25.00 ± 12.31	41.60 ± 12.68	(n = 31) 24.39 ± 11.93
Male: Female	1:4.5	0:5	1:4	1:5.8
Type of LE				
SLE	22 (91.7)	5 (100)	3 (60)	28
Acute CLE	1 (9.1)	0 (0)	1 (20)	3
Subacute CLE	1 (4.5)	0 (0)	3 (60)	4
Chronic CLE	0 (0)	4 (80)	1 (20)	5
Organ involved				
Renal	16 (72.7)	5 (100)	2 (40)	23
Joint	10 (45.5)	2 (40)	2 (40)	14
Hematology	11 (50)	2 (40)	1 (20)	14
Musculoskeletal	1 (4.5)	0 (0)	0 (0)	1
Ophthalmic	2 (9.1)	1 (20)	0 (0)	3
Autoantibodies detected				
ANA	13 (59.1)	3 (60)	3 (60)	19
ENA	10 (45.5)	2 (40)	1 (20)	13
dsDNA	5 (22.7)	3 (60)	1 (20)	9
Systemic treatment used for LE				
Corticosteroids	15 (68.2)	5 (100)	4 (80)	24
Hydroxychloroquine	13 (59.1)	2 (40)	0 (0)	15
MMF	7 (31.8)	0 (0)	1 (20)	8
Methotrexate	5 (22.7)	0 (0)	1 (20)	6
Azathioprine	5 (22.7)	3 (60)	0 (0)	8
Cyclosporine	3 (13.6)	1 (20)	0 (0)	4

[a]Three missing data on the age of onset for lupus erythematosus.

Abbreviations: ANA, antinuclear antibody; CLE, cutaneous lupus erythematosus; dsDNA, double-stranded DNA; ENA, extractable nuclear antigen antibodies; LE, lupus erythematosus; MMF, mycophenolate mofetil; SD, standard deviation; SLE, systemic lupus erythematosus.

IL-17 axis in the pathogenesis of SLE. Ustekinumab, a monoclonal antibody targeting the p40 subunit of both IL-12 and IL-23, has been reported in the treatment of psoriasis with coexistent LE. Inhibition of IL-23 may decrease the proliferation and survival of Th17 cells, which leads to the attenuation of IL-17-related manifestations in psoriasis or SLE.[35] Although there may be some scientific rationale for targeting IL-17 for treating SLE, the precise role of IL-17 inhibition in SLE is yet to be established.[36]

Phototherapy, such as narrow-band UVB (NBUVB) or psoralen UVA (PUVA), is a highly effective treatment option for psoriasis and is routinely used in cases of poorly controlled disease. NBUVB is a safer treatment modality with similar therapeutic efficacy compared with PUVA, as acute adverse effects and carcinogenic risk are significantly lower with NBUVB.[37] The mechanism of action of NBUVB includes suppression of type I and II interferon signaling, downregulation of the Th17 pathway, and modulation of epidermal differentiation.[38] Psoriasis patients with coexistent LE are at a higher risk of photosensitivity, because UV irradiation induces clinical lesions in patients with LE. UVB irradiation may induce inflammatory skin reactions with increased formation of apoptotic keratinocytes, which may trigger recruitment of inflammatory cells and autoantibody formation. Therefore, UVB phototherapy is contraindicated in LE. In contrast, UVA irradiation results in mitochondrial oxidative damage through generation of excess reactive oxygen species caused by deeper penetration into the dermis as a result of its longer wavelength.[39] UVA irradiation, particularly UVA1 (wavelength 340-400 nm), may be an effective therapeutic option for patients with LE. UVA1 exerts its effect through the release of tumor necrosis factor-α (TNF-α), cell-mediated immunosuppression, activation of immediate apoptosis, and reduction of IL-12 levels.[40] UVA1 phototherapy may be beneficial in patients with SLE because it suppresses B-cell activity and induces apoptosis of circulating activated B lymphocytes.[41] However, the efficacy of medium-dose UVA1 phototherapy in moderate to severe plaque psoriasis was found to be inferior to NBUVB

and PUVA.[42] None of the LE patients in our cohort had lesions precipitated or aggravated by phototherapy because only a minority had psoriasis extensive enough to require phototherapy.

Management of psoriasis patients with coexistent LE is challenging; treatment options for SLE, such as antimalarial agents, may precipitate a flare of psoriasis, whereas therapies for psoriasis, such as anti-TNF-α agents, may cause a lupus-like syndrome. Hydroxychloroquine, an antimalarial agent, has been shown to reduce titers of autoantibodies, which contributes to achieving clinical remission, delaying onset of systemic LE, and lowering risk of fatal complications.[43] However, hydroxychloroquine may induce or exacerbate psoriasis, because it promotes the production of IL-17 via p38-dependent IL-23 release.[44] Apart from that, inhibition of epidermal transglutaminase activity by hydroxychloroquine may disrupt the epidermal barrier function. The resulting physiological response of epidermal proliferation may trigger psoriasis in genetically predisposed patients.[45] Seven (31.8%) of 22 patients in our cohort with pre-existing LE had their psoriasis precipitated by hydroxychloroquine.

Anti-TNF-α therapy, which is approved for the treatment of psoriasis, is associated with drug-induced LE as a result of formation of autoantibodies, such as antinuclear antibodies, anti-dsDNA antibodies, and anticardiolipin antibodies. The mechanism of TNF-α-induced LE is related to the increased release of antigens from apoptotic cells, which results in the presence of nuclear debris that triggers ANA production.[46] However, no cases of anti-TNF-α-induced lupus were captured in our registry because of the lack of psoriasis patients treated with infliximab, which accounts for most of the anti-TNF-α-induced LE cases.[47]

Psoriasis patients with LE had greater impairment of their quality of life compared with patients with psoriasis alone in our cohort. Factors possibly contributing to the poor quality of life include high disease activity of SLE, cutaneous and extracutaneous manifestations of SLE and psoriasis, and adverse effects of systemic therapies. Etchegaray-Morales et al[48] found that greater disease activity, depression, and fibromyalgia were associated with poorer HRQoL in SLE patients. Quality of life is significantly compromised in patients with cutaneous LE because of its chronic course, the visibility of the lesions, and the disfiguring scars it produces.[49] The most severely affected domain among psoriasis patients with LE in our cohort was "symptoms and feelings", owing to the visibility of both psoriasis and LE lesions leading to poor self-esteem and poor self-perception.

5 | LIMITATIONS AND RECOMMENDATIONS

The number of patients with both LE and psoriasis was too small for meaningful statistical analysis. The disease activity of SLE was only assessed by comprehensively evaluating symptoms and organ damage without the use of disease activity index. The incidence of psoriasis with coexistent LE may be underreported because of its rarity and failure of clinicians to recognize it. In addition, patients with limited psoriasis who developed LE after enrollment to the MPR, would not have been discovered in this study because follow-up notifications were not mandatory if the patients did not require phototherapy and/or systemic treatment.

Cutaneous lupus erythematosus, particularly the papulosquamous variant of subacute CLE, may mimic psoriasis, making diagnosis of both conditions in the same patient challenging. A low threshold for skin biopsy for histopathological examination and immunofluorescence study, together with autoantibody testing, are recommended to improve the diagnostic accuracy. Distinguishing PsA from arthritis in SLE can also be challenging. All the patients who were registered to the MPR must have typical psoriasis lesions on the skin. An arthritis without psoriasis skin lesions is not psoriatic arthritis. Although there was a possibility of SLE-related arthritis being falsely labeled as PsA in our cohort, we reckon it is rare. Future research opportunities in this area include further studies on the family background and genetic predisposition of psoriasis patients with concomitant LE, together with longitudinal measurement of SLE Disease Activity Index, Cutaneous LE Disease Area and Severity Index, and Psoriasis Area Severity Index, as well as determining the differentiating features between PsA and arthritis related to SLE.

6 | CONCLUSION

Psoriasis patients with coexistent LE in the MPR were uncommon (0.16%), displayed a female preponderance, and were more likely to have joint involvement, an earlier age of psoriasis onset and to suffer greater impairment to their quality of life compared with psoriasis patients without LE. Lupus erythematosus preceded psoriasis in more than half of the patients in our cohort, and SLE was the most common subtype of LE reported. Psoriasis patients with LE were more likely to receive systemic treatment compared with those without LE, but the use of systemic corticosteroids among the latter was rare. Although it is rare for patients to develop both psoriasis and LE, it is important that such patients be diagnosed to ensure appropriate management.

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CONFLICT OF INTEREST

The authors have no conflicts of interest to declare.

ETHICAL APPROVAL

Ethical approval for this study was obtained from the Medical Research and Ethics Committee (MREC), Ministry of Health Malaysia.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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