Clin Exp Dermatol 2023; **00**:1–8
https://doi.org/10.1093/ced/llad013
Advance access publication date: 12 January 2023

CED
Clinical and Experimental Dermatology
Original Article

Liver disease among patients with psoriasis: the Malaysian Psoriasis Registry

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Abstract

Background Therapeutic options may be limited for patients with psoriasis who have concomitant liver disease (PsL).

Objectives We aimed to report the frequency of liver disease among patients with psoriasis, and describe the clinical features, treatment modalities and quality of life.

Methods This was a multicentre cross-sectional study of patients with psoriasis notified to the Malaysian Psoriasis Registry (MPR) from January 2007 to December 2018.

Results Of 21 735 patients with psoriasis, 174 (0.8%) had liver disease. The three most common liver diseases were viral hepatitis (62.1%), fatty liver (14.4%) and liver cirrhosis (10.9%). The male-to-female ratio was 3.8 : 1. Mean age (SD) of onset of psoriasis was higher in those with liver disease vs. those without [37.25 years (13.47) vs. 33.26 years (16.96), $P<0.001$]. Patients with PsL, compared with those without liver disease, had a higher rate of dyslipidaemia (27.5% vs. 16.4%, $P<0.001$), hypertension (33.9% vs. 23.7%, $P=0.002$), diabetes mellitus (22.4% vs. 15.9%, $P=0.021$) and HIV infection (5.3% vs. 0.4%, $P<0.001$). Those with PsL were also more likely than those without liver disease to have severe disease [body surface area > 10% and/or Dermatology Life Quality Index (DLQI) > 10] (59.3% vs. 49.9%, $P=0.027$), psoriatic arthropathy (21.1% vs. 13.0%, $P=0.002$) and nail involvement (78.2% vs. 56.1%, $P<0.001$). Also significantly higher in the group with PsL were the use of phototherapy (8.4% vs. 2.6%, $P<0.001$), acitretin (7.3% vs. 2.8%, $P<0.001$) and ciclosporin (3.0% vs. 0.7%, $P<0.001$). Mean DLQI was similar in both groups [9.69 (7.20) vs. 9.62 (6.75), $P=0.88$].

Conclusions The frequency of patients with PsL in the MPR was 0.8%. Patients with PsL were more likely to be male, had a higher rate of comorbidities, severe disease, and nail and joint involvement than those without liver disease.

What is already known about this topic?

- Psoriasis is a systemic inflammatory disease.
- Nonalcoholic fatty liver disease has been shown to be a risk factor for severe psoriasis.
- Challenges arise as therapeutic options for psoriasis may be limited for patients with concomitant liver disease.

What does this study add?

- Patients with psoriasis with coexistent liver diseases (PsL) displayed a male preponderance, had more severe disease, and were more likely to have nail and joint involvement than those without liver disease.
- Viral hepatitis and nonalcoholic fatty liver disease were the most frequent aetiology for liver disease among patients with psoriasis.
- Patients with PsL had a higher rate of comorbidities.

Psoriasis is a systemic inflammatory disease. Patients with psoriasis are at an increased risk of systemic issues including psychiatric disorders, malignancies and gastrointestinal diseases.[1] An increased prevalence of nonalcoholic fatty liver disease (NAFLD), viral hepatitis including hepatitis B virus (HBV), hepatitis C virus (HCV) infection, drug-induced hepatitis, alcoholic hepatitis and neutrophilic cholangitis[2,3] have also been reported among patients with psoriasis. The consequences of these liver issues range from an asymptomatic increase in serum liver enzymes to severe hepatitis or even fatal liver failure.[3]

This study intends to raise awareness of comorbidities associated with psoriasis, focusing on the relationship with various liver diseases. This is important especially for severely affected patients with psoriasis with concurrent liver disease (PsL), as determining the appropriate treatment for these patients is a challenge. Therefore, this study aimed to determine the frequency of liver diseases among patients with psoriasis, and describe the clinical features, treatment modalities and health-related quality of life (QoL) among patients with PsL.

Accepted: 11 January 2023

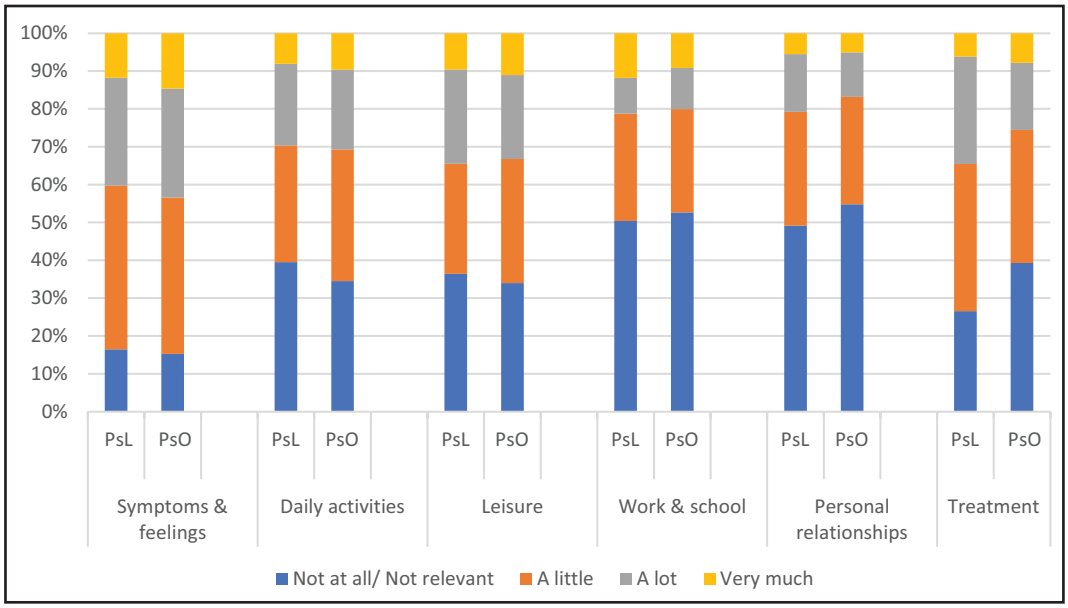

Figure 1 Dermatology Life Quality Index scores comparing patients with psoriasis with concomitant liver disease (PsL) and patients with psoriasis without liver disease (PsO).

Methods

This was a multicentre cross-sectional study of patients with PsL who were notified to the Malaysian Psoriasis Registry (MPR) from January 2007 to December 2018. The MPR collects data of patients with psoriasis prospectively nationwide from 32 public hospitals and two private hospitals. This study was approved by the Malaysian Ministry of Health Institutional Review Board and Medical Research Ethnics Committee (NMRR-21-346-58577).

Study procedures

Patients with psoriasis were entered into the MPR at first point of care and every 6 months. Study data of interest included demographics, type of liver disease, age of onset, ethnicity, comorbidities, family history of psoriasis, type of psoriasis, psoriasis severity in terms of body surface area (BSA) involvement, type of psoriasis treatment in the last 6 months, and Dermatology Life Quality Index (DLQI) scores. A diagnosis of liver disease was notified to the MPR by registered dermatologists based on blood parameters (deranged liver profile, positive serological results of viral hepatitis, autoimmune markers), imaging (ultrasound of hepatobiliary system, fibroscan) and liver biopsy. All patients were concurrently managed by hepatologists or gastroenterologists. Comorbidities present among patients with psoriasis such as hypertension, diabetes and dyslipidaemia were diagnosed based on local guidelines, namely the 5th Malaysian Hypertension Clinical Practice Guidelines (CPG), the 5th CPG on Management of Type 2 Diabetes Mellitus, and the 5th CPG on Management of Dyslipidaemia, respectively. Diagnoses of ischaemic heart disease and cerebrovascular disease were accepted if the patient had been diagnosed by a physician, cardiologist or neurologist for the corresponding diseases. Body mass index (BMI) was categorized into four groups according to the Asia-Pacific classification: underweight (< 18.5 kg m^{-2}), normal weight (18.5–22.9 kg m^{-2}), overweight (23–24.9 kg m^{-2}) and obese (≥ 30 kg m^{-2}).[4] Severe psoriasis was defined as affected body surface area (BSA) $> 10\%$ and/or DLQI score > 10.

Statistical analysis

Statistical analysis was carried out using IBM SPSS Statistics 24.0 for Windows (IBM SPSS, Armonk, NY, USA). A *P*-value of < 0.05 was considered statistically significant. Descriptive statistics were applied. Normally distributed continuous variables were summarized as mean (SD). For categorical variables, frequencies and percentages were tabulated. Pearson's χ^2-test was used to compare categorical data, and the independent samples *t*-test was used to compare means.

Results

Demographic characteristics

In total, 21 735 patients with psoriasis were registered into the MPR from January 2007 to December 2018. Of these, 138 (79.3%) men and 36 (20.7%) women, with a mean age (SD) of 37.3 years (13.5), had liver disease. The male-to-female ratio among patients with PsL was significantly higher at 3.83 : 1 as compared with those without liver disease, which was 1.2 : 1 ($P < 0.001$). In terms of ethnic distribution, 42.0% were Malay, 29.3% Chinese, 14.9% Indian and 13.8% belonged to other minority ethnic groups.

Patients with PsL had significantly more comorbidities compared with those without liver disease. Those with PsL had a higher rate of dyslipidaemia (27.5% vs. 16.4%, $P < 0.001$), hypertension (33.9% vs. 23.7%, $P = 0.002$) and diabetes mellitus (22.4% vs. 15.9%, $P = 0.021$) compared with those without liver disease. Out of the 156 patients

Table 1 Demographic data and clinical characteristics of 21 735 patients with psoriasis, with concomitant liver disease (PsL) and without liver disease (PsO)

Demographic and clinical characteristics	PsL $n=174$	PsO $n=21\,561$	*P*-value
Sex			
Male	138 (79.3)	11 920 (55.3)	**< 0.001**
Female	36 (20.7)	9641 (44.7)	
Age of onset of psoriasis (years), mean (SD)	37.25 (13.47)	33.26 (16.96)	**< 0.001**
Ethnicity		$n=21\,553$	
Malay	73 (42.0)	11 718 (54.4)	
Chinese	51 (29.3)	4097 (19.0)	
Indian	26 (14.9)	3554 (16.5)	
Others	24 (13.8)	2184 (10.1)	
Family history of psoriasis	49 (28.2)	$n=20\,980$ 4808 (22.9)	0.101
Comorbidities			
Dyslipidaemia	$n=171$ 47 (27.5)	$n=20\,554$ 3365 (16.4)	**< 0.001**
Hypertension	$n=171$ 58 (33.9)	$n=20\,788$ 4928 (23.7)	**0.002**
Diabetes mellitus	$n=170$ 38 (22.4)	$n=20\,759$ 3291 (15.9)	**0.021**
Ischaemic heart disease	$n=171$ 9 (5.3)	$n=20\,744$ 1002 (4.8)	0.793
Cerebrovascular disease	$n=170$ 2 (1.2)	$n=20\,736$ 305 (1.5)	0.751
HIV infection	$n=171$ 9 (5.3)	$n=21\,561$ 96 (0.4)	**< 0.001**
BMI (kg m^{-2})	$n=156$	$n=19\,044$	
< 18.5	11 (7.0)	1378 (7.2)	
18.5–22.9	36 (23.1)	4240 (22.3)	
23–24.9	31 (19.9)	2854 (15.0)	
≥25	78 (50.0)	10 572 (55.5)	
BSA (%)	$n=144$	$n=16\,426$	
<5	47 (32.6)	7376 (44.9)	**< 0.001**
5–10	33 (22.9)	5159 (31.4)	
11–90	57 (39.6)	3469 (21.1)	
>90	7 (4.9)	422 (2.6)	
Area of involvement			
Scalp	$n=165$ 129 (78.2)	$n=20\,477$ 16 642 (81.3)	0.311
Face and neck	$n=163$ 86 (52.8)	$n=20\,249$ 10 424 (51.5)	0.744
Nail	$n=170$ 133 (78.2)	$n=20\,932$ 11 743 (56.1)	**< 0.001**
Arthropathy	$n=171$ 36 (21.1)	$n=20\,917$ 2720 (13.0)	**0.002**
Type of psoriasis	$n=168$	$n=20\,207$	
Plaque	153 (91.1)	18 842 (93.3)	
Guttate	4 (2.4)	734 (3.6)	
Pustular	2 (1.2)	146 (0.7)	
Flexural	2 (1.2)	102 (0.5)	
Erythrodermic	7 (4.1)	383 (1.9)	
DLQI, mean (SD)	9.69 (7.20)	9.62 (6.75)	0.88
DLQI > 10	$n=170$ 69 (40.6)	$n=19\,585$ 7891 (40.3)	0.937
Severe disease (BSA > 10 & DLQI > 10)	$n=140$ 83 (59.3)	$n=15\,071$ 7521 (49.9)	**0.027**

All values are presented as *n* (%) unless otherwise stated. BMI, body mass index; BSA, body surface area; DLQI, Dermatology and Life Quality Index. *P*-values in **bold** are statistically significant at $P<0.05$.

with PsL whose BMI was measured, 31 (19.9%) and 78 (50%) were overweight or obese, respectively. About 5% of patients with PsL had HIV coinfection ($P<0.001$), which was significantly higher than those without liver diseases (Table 1).

Clinical presentation

Plaque psoriasis was the most frequent presentation (91%) among our patients with PsL. This was followed by erythrodermic and guttate psoriasis, seen in 4% and 2% of patients with PsL, respectively. Patients with PsL had a significantly higher rate of arthropathy and nail involvement compared with patients with psoriasis with no liver disease (21.1% vs. 13.0%, $P=0.002$ and 78.2% vs. 56.1%, $P=0.027$) (Table 1). Our registry also demonstrated that patients with PsL had a significantly higher rate of severe psoriasis vs. those with no liver disease (59.3% vs. 49.9%, $P=0.027$) (Table 1).

Mean DLQI scores were similar for patients with psoriasis with and without liver disease: 9.69 (7.20) and 9.62 (6.75) ($P=0.88$), respectively. DLQI domains that were more significantly impaired for patients with PsL compared with those without liver disease were personal relationships [1.60 (1.67) vs. 1.32 (1.55), $P=0.042$] and treatment [1.14 (0.89) vs. 0.94 (0.94), $P=0.007$] (Figure 1).

Types of liver diseases

The most common liver diseases among Malaysian patients with psoriasis were viral hepatitis whereby 59 (33.9%) had HBV infection, 47 (27.0%) had HCV infection, and two (1.1%) had concomitant HBV and HCV. We also noted that among our PsL cohort, 25 (14.4%) had fatty liver and 19 (10.9%) had liver cirrhosis (Table 2). The aetiology of the liver cirrhosis cases included alcoholic liver disease (31.6%), HBV infection (10.5%), autoimmune hepatitis (10.5%), HCV infection (5.3%), and HCV infection with alcoholic liver disease (5.3%) (Table 3).

Treatment modalities

About 8% of patients with PsL were treated with phototherapy compared with only 2% of patients with psoriasis without liver diseases ($P<0.001$) (Table 4). Approximately 18% of those with PsL were started on systemic therapy. The most frequently prescribed systemic medications among patients with PsL were methotrexate (10%), acitretin (7%) and ciclosporin (3%). None were exposed to biologics.

Table 2 Types of liver diseases in the study population of patients with psoriasis with concomitant liver disease ($n=174$)

Type of liver disease	*n* (%)
Hepatitis B[a]	59 (33.9)
Hepatitis C[a]	47 (27.0)
Fatty liver	25 (14.4)
Liver cirrhosis[a]	19 (10.9)
Chronic liver disease, indeterminate	18 (10.3)
Alcoholic liver disease[a]	8 (4.6)
Autoimmune hepatitis[a]	3 (1.7)
Hepatitis B and hepatitis C coinfection	2 (1.1)
Drug-induced hepatitis	2 (1.1)
Hepatocellular carcinoma	2 (1.1)
Congestive hepatitis	1 (0.6)

[a]A patient may present with more than one type of liver disease.

Table 3 Causes of liver cirrhosis in the study population ($n=19$)

Causes of liver cirrhosis	*n* (%)
Indeterminate[a]	7 (36.8)
Alcoholic liver disease	6 (31.6)
Hepatitis B	2 (10.5)
Autoimmune	2 (10.5)
Hepatitis C	1 (5.3)
Hepatitis C and alcoholic liver disease	1 (5.3)

[a]No data available/cause of liver cirrhosis was under investigation at the time of writing.

Discussion

Psoriasis has been known to affect approximately 3% of the population in the USA, affecting both sexes equally.[5] Prior studies have reported an increased prevalence of liver diseases, especially fatty liver disease, among patients with psoriasis.[6] The pathophysiology of the liver's response to chronic inflammation associated with psoriasis and how the liver may be impacted by the severity of psoriasis is not well understood. Furthermore, challenges arise when dermatologists need to determine optimal and safe treatment in patients with PsL.

Tsai *et al.* reported an overall higher psoriasis prevalence rate of 2.35% from their national database in Taiwan. Male sex and advancing age were generally associated with a higher prevalence rate in their study.[7] Similarly, Ogdie *et al.* reported a lifetime prevalence rate of liver disease of 3–4% among patients with psoriasis but with a female predominance. Their study also demonstrated that among patients with psoriasis without liver disease at baseline, the incidence of newly diagnosed liver diseases was approximately 1% during their 6-year follow-up.[8] The lower prevalence rate of liver disease among our study cohort might be explained by under-reporting or even underdetection of liver diseases among our patients with psoriasis. Screening for the presence of liver diseases is not mandatory for all patients with psoriasis unless they present with severe disease and are planned for systemic treatment or biologic therapy.

The epidemiological study by Tsai *et al.* in Taiwan showed that their psoriasis population had an adjusted relative risk of 1.73 and 2.02 for HBV and HCV infection, respectively, compared with patients without psoriasis.[7] Tula and coworkers from Turkey went a step further to analyse the presence of liver enzyme abnormalities among their psoriasis cohort. They found that the most common associations of pathological liver enzymes were medications (57%) and NAFLD (22%). At the same time, they detected chronic HBV and HCV infection in 2% and 3% of their patients with psoriasis, respectively, who all had mild elevation of their liver enzymes.[2] In the latest national health survey conducted in 2020, Malaysia's Ministry of Health reported a yearly incidence rate of 12.64 per 100 000 and 10.13 per 100 000 population for HBV and HCV infection among the Malaysian general population, respectively.[9] Analysis from our MPR showed that viral hepatitis infection (62%) was the predominant cause of concomitant liver disease among people with PsL. The prevalence rates of HBV and HCV infection among patients with PsL were recorded at 35% and 28%, respectively.

As 60% of our patients with PsL presented with severe psoriasis, they would be considered as candidates for conventional systemic therapy/biologics. Screening tests that include full blood count, liver and renal function tests, fasting serum glucose, fasting serum cholesterol, and screening for viral hepatitis, human immunodeficiency virus and tuberculosis, are routinely carried out prior to commencement of conventional systemic therapy/biologics. With screening done, the prevalence of viral hepatitis and other comorbidities can be ascertained. However, the duration of the comorbidities among our psoriasis cohort could not be determined as these data were not captured.

The epidemiology of liver cirrhosis appears to be related to sex, ethnic group and geographic region.[10] In the USA, alcohol and chronic HCV infection were the leading causes of liver cirrhosis.[11] This differs from the Asia-Pacific region, where chronic HBV infection is endemic and is the most common cause of liver cirrhosis.[12] Qua and Goh found that the major determinants for liver cirrhosis among the Malaysian general population were chronic HBV infection (46.1%) and chronic HCV infection (18.5%), followed by alcoholic liver cirrhosis (12.6%).[10] Our registry echoed similar findings whereby the majority of liver cirrhosis cases were secondary to alcoholic liver disease (31.6%) and viral hepatitis (21.1%).

Previous studies conducted among the general population in Malaysia reported prevalence rates of NAFLD as 23–38%.[13] In our study, we noted that NAFLD constituted about 15% of our study population with liver disease. Interestingly, Abedini *et al.* reported a higher prevalence rate of NAFLD, which was about 65% among their patients with psoriasis compared with their healthy controls (35%) ($P<0.01$, odds ratio 3.53).[6]

The link between psoriasis and its comorbidities is thought to be associated with insulin resistance and the effect of inflammatory cytokines.[14,15] Studies have hypothesized the connection of the 'hepatodermal axis', which implies that lymphocytes and keratinocytes from psoriasis skin produce

Table 4 Treatment modalities of the study population of patients with psoriasis, with concomitant liver disease (PsL) and without liver disease (PsO)

Treatment modalities	PsL	PsO	*P*-value
Topical therapy	$n=166$ 162 (97.6)	$n=20\,741$ 19 676 (94.9)	0.112
Phototherapy	$n=166$ 14 (8.4)	$n=20\,409$ 538 (2.6)	< **0.001**
Systemic therapy	$n=164$ 30 (18.3)	$n=20\,614$ 2930 (14.2)	0.137
Methotrexate	$n=164$ 16 (9.8)	$n=20\,614$ 2277 (11.0)	0.60
Acitretin	$n=164$ 12 (7.3)	$n=20\,614$ 569 (2.8)	< **0.001**
Ciclosporin	$n=164$ 5 (3.0)	$n=20\,614$ 139 (0.7)	< **0.001**
Systemic corticosteroids	$n=164$ 1 (0.6)	$n=20\,614$ 178 (0.9)	0.726
Hydroxyurea	$n=164$ 0	$n=20\,614$ 23 (0.1)	0.669
Biologics	$n=164$ 0	$n=20\,614$ 78 (0.4)	0.43

All values are presented as *n* (%).

inflammatory cytokines [interleukin (IL)-6, IL-17 and tumour necrosis factor alpha (TNF-α)], which act on the liver and produce metabolic abnormalities. Similarly, secretion of proinflammatory, pro-oxidant and proatherogenic mediators from a fatty and inflamed liver (C-reactive protein, fibrinogen, IL-6, plasminogen activator inhibitor-1, transforming growth factor beta) in NAFLD can worsen psoriasis.[16–18] The end result is increased keratinocyte proliferation, inflammation and upregulation of vascular adhesion molecules caused by these inflammatory mediators.[17,18] Identification of the pathophysiological mechanisms underlying these two diseases is of clinical importance, as it can uncover new therapeutic approaches.

Patients with PsL in our study cohort had a significantly higher prevalence of joint and nail involvement. This further increases the inflammatory burden and risk of systemic involvement compared with isolated psoriasis. These findings were similarly reflected in studies done by Ogdie *et al.*, which concluded that psoriasis and psoriatic arthropathy were associated with liver diseases even for patients without systemic therapy exposure.[8] Similarly, Candia *et al.* supported a strong association of psoriasis and psoriatic arthritis with NAFLD.[19]

Our study did not show any significant difference in mean DLQI scores between patients with psoriasis with and without liver diseases. Patients with psoriasis from both arms had at least moderately impaired quality of life due to their skin disease, highlighting the importance of effective treatment options. Results shown were not surprising as DLQI reflects only the impact of cutaneous lesions on quality of life. Generic QoL assessment tools such as the Medical Outcomes Study 36-Item Short Form Survey or Health Assessment Questionnaire would be better to assess the effect of PsL on the quality of life.

In our study, although about 60% of patients with liver disease had severe psoriasis, the majority were maintained with topical therapy. Less than 10% were treated with phototherapy, less than 20% were on conventional systemic therapy and none were exposed to biologic treatment. The first-line treatment in localized psoriasis is topical therapy +/− ultraviolet therapy. However, deciding on the most effective and safe therapy is an arduous task for the clinician treating patients with PsL whose psoriasis is moderate-to-severe or recalcitrant. Topical treatment and phototherapy are generally considered safer treatment options, as it is known that conventional systemic therapy may negatively influence metabolic comorbidities or interact with drugs that are commonly used to treat them.[20]

Methotrexate, acitretin and ciclosporin have been widely used as systemic drugs in treating psoriasis. Nonetheless, hepatotoxicity that may result from systemic treatment due to either direct liver damage or immunosuppression, or both, is a cause for concern.[21] Gisondi *et al.* reported that the risk of methotrexate-induced liver toxicity is increased in the presence of NAFLD, excessive alcohol consumption, obesity or diabetes.[22] Elevation of serum lipid and glucose levels along with arterial hypertension have been described with ciclosporin.[15,23] Acitretin is a risk factor for steatohepatitis as it can lead to dyslipidaemia.[24] On the other hand, systemic treatments that reduce systemic inflammation may have a good impact and lessen the likelihood of progressing to NAFLD.[25] Looking back into our 12-year registry data and clinical records, we noted that 16 patients with PsL had methotrexate treatment. Of these, two developed drug-induced hepatitis secondary to methotrexate, proven by liver biopsy. Among the 21 561 patients with psoriasis with no liver disease, 2277 individuals tolerated methotrexate with no adverse effects from the drug.

Established treatments for psoriasis have not fully met the needs of patients, and while there has been remarkable progress in the development of new, highly effective targeted therapies, there are still many challenges. From a clinical perspective, awareness of the underlying comorbidities in psoriatic patients is important to ensure that the treatment prescribed is safe.[26] Low calorie diet, exercise and alcohol abstinence have been advocated[27] but poor patient compliance undermines these efforts. Treatment of concomitant diseases such as diabetes mellitus, hypertension and dyslipidaemia are recommended to reduce overall systemic inflammation.[22,24]

Another aspect that needs to be taken into consideration for patients with PsL is the high prevalence of viral hepatitis infection, as this would influence the choice of therapy. Generally, it is advisable that dermatologists co-manage these patients with hepatologists, and consider monitoring viral loads during treatment. Worsening of psoriasis has been seen in patients on interferon treatment for viral hepatitis.[28] Bonifati *et al.* and Piaserico *et al.* reviewed existing clinical data on the safety and efficacy of therapies in patients with psoriasis with concomitant HBV and HCV infections and provided practical considerations on how to manage such patients.[20,29] According to the consensus, patients who are seropositive for HBV core antibody or HCV infection do not require antiviral prophylaxis as the risk for viral reactivation is low. However, risk–benefit assessment is required in chronic HBV carriers who are being considered for systemic or biologic therapy prior to commencement of antiviral prophylaxis (given 2–4 weeks before starting immunosuppressive therapy and until 6–12 months after cessation of immunosuppressive therapy), whereas for patients with active HBV infection, antiviral treatment should be given to suppress the infection before prescribing systemic immunosuppressive medication for psoriasis.[20,26,29]

For patients with psoriasis with concurrent HCV infection, acitretin and ciclosporin are the favoured treatment choices.[30] As acitretin does not cause immunosuppression and its noxious effects are reversible upon cessation, it is the safer treatment option.[20,30] Ciclosporin is able to diminish inflammation, and stop HCV replication especially in HCV genotypes 1 and 4.[31,32] Furthermore, several case series have reported that in patients with psoriasis with HCV infections, ciclosporin treatment did not cause worsening of HCV infection.[31,32]

Due to its immunosuppressive activity and potential hepatotoxicity, methotrexate should be used with caution[30,33–34] especially among patients with PsL. There have been concerns regarding methotrexate-induced liver cirrhosis after long-term administration.[34] Tang *et al.* investigated the impact of long-term methotrexate usage on the risk of chronic viral hepatitis-related cirrhosis in Taiwan.[35] They analysed 3544 patients with psoriasis with chronic HBV and chronic HCV infection and followed them up for more than 9 years after the diagnosis of chronic viral hepatitis. The study concluded that there was no increased risk of liver

cirrhosis despite the prolonged use of methotrexate among patients with psoriasis with chronic HBV or HCV infection.

The advent of biologics has brought about a paradigm shift in psoriasis treatment as well as our comprehension of the pathogenesis of psoriasis. Although biologics have shown excellent efficacy, their safety has been of concern.[36] Some biologic treatments have been shown to reduce levels of inflammatory markers such as C-reactive protein and erythrocyte sedimentation rate.[37] This reinforces the hypothesis that biological agents which target proinflammatory cytokines involved in psoriasis may lessen the risk of cardiometabolic diseases in patients with psoriasis.[38] However, the impact of biological agents on metabolic and liver parameters is more diverse.[39] Weight gain has been seen in patients with psoriasis and psoriatic arthritis treated with TNF-α antagonists.[40–41] Additionally, there were reports suggesting that TNF-α inhibitors may cause drug-induced liver injury (DILI)[42,43] and acute liver failure[44] although the risk of developing such conditions is low. DILI encompasses elevation of liver enzymes (which is usually temporary and self-limiting) and cholestatic hepatitis. The prognosis is usually good after drug discontinuation, although some patients require systemic corticosteroids.[42,43] Kok *et al.*[44] identified nine cases of anti-TNF-α-associated acute liver failure. Six cases required emergency liver transplant and the most common anti-TNF-α agent associated with acute liver failure was infliximab. Additionally, Gerdes *et al.*[45] analysed the effects of secukinumab (IL-17 inhibitor) on metabolic and liver parameters among 3010 patients with plaque psoriasis and found that secukinumab showed a neutral effect on fasting plasma glucose, lipid parameters and liver enzymes.

Patients with psoriasis and concomitant viral hepatitis may benefit from biologic agents due to their immunomodulatory properties.[46] Safety data for patients with psoriasis with HBV or HCV infections treated with biologics are retrieved almost entirely from case reports and small retrospective cohort studies as these patients are usually excluded from clinical trials. Some biologics such as TNF-α inhibitors were associated with reactivation of viral infections[29,47] but more recent studies found no increased risk.[46,48,49] Thus far, there are no compelling safety data on IL-17 and IL-23 inhibitors used in the treatment of patients with psoriasis with viral hepatitis.[29] Overall, it is recommended that before biological agents are initiated, consultation with a hepatologist and close monitoring be carried out to minimize the risk of viral reactivation.

Liver fibrosis and cirrhosis are the final consequences of chronic liver disease.[50] The gold standard for the evaluation of liver fibrosis remains liver biopsy, which is invasive, costly and may be affected by sampling and observer bias.[50] Thus alternative methods have become available, which include numerous serological tests and radiological imaging (ultrasound-based elastography, magnetic resonance elastography, acoustic radiation force impulse imaging and cross-sectional imaging).[50] These tests are safer, noninvasive, more permissible and cost-effective despite varying sensitivity and specificity. Application of noninvasive methods for liver assessment in our clinical care will help to manage patients with PsL in a more holistic way. These methods permit not only identification of patients at high risk of adverse outcomes but also enable us to monitor disease progression and therapeutic responses.

Limitations of the study are as follows. Firstly, there are inadequate data on the onset of liver disease with its associated comorbidities in relation to psoriasis. Another limitation is that we did not assess the role of DILI. This could be another factor contributing to liver diseases among patients with psoriasis due to a myriad of potentially hepatotoxic drugs used in clinical practice along with our population's usage of available herbs and dietary supplements.

In conclusion, the frequency of liver diseases among patients with psoriasis notified to the MPR was 0.8%, with viral hepatitis being the most frequent aetiology. Patients with PsL were more likely to be male, and had a higher rate of comorbidities, with more severe disease, nail and joint involvement than those without liver disease. Longitudinal studies should be carried out to better extrapolate data on liver disease among patients with psoriasis, its associated comorbidities, and the impact on quality of life.

Acknowledgments

The authors would like to thank the Director General of Health, Malaysia, for permission to publish this article.

Funding sources

None.

Conflicts of interest

The authors declare they have no conflicts of interest.

Data availability

The data underlying this article were accessed from the Malaysian Psoriasis Registry. The derived data generated in this research will be shared on reasonable request to the corresponding author.

Ethics statement

This study was approved by the Malaysian Ministry of Health Institutional Review Board and Medical Research Ethnics Committee (NMRR-21-346-58577).

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