

Clinical characteristics and outcomes of psoriasis patients with COVID-19: a retrospective, multicenter cohort study in China

Yanhua Liu

Xijing Hospital, Fourth Military Medical University

Zhongrui Xu

Xijing Hospital, Fourth Military Medical University

Gang Wang

x.jwang@fmmu.edu.cn

Xijing Hospital, Fourth Military Medical University

Chen Yu

Xijing Hospital, Fourth Military Medical University

Aijun Chen

First Affiliated Hospital of Chongqing Medical University

Junling Zhang

Tianjin University of Traditional Chinese Medicine

Xiaojing Kang

People's Hospital of Xinjiang Uygur Autonomous Region

Xian Jiang

West China Hospital of Sichuan University

Chunrui Shi

First Hospital of Lanzhou University

Yuling Shi

Skin Disease Hospital of Tongji University

Xiaoming Liu

University of Hong Kong - Shenzhen Hospital

Fuqiu Li

Second Affiliated Hospital of Jilin University

Bin Yang

Dermatology Hospital of Southern Medical University

Yongmei Huang

Xining First People's Hospital

Chengzhi Lv

Dalian Dermatoses Hospital

Research Article

Keywords: COVID-19, SARS-CoV-2, psoriasis, psoriasis treatment, biologics

Posted Date: September 20th, 2023

DOI: <https://doi.org/10.21203/rs.3.rs-3352492/v1>

License:  This work is licensed under a Creative Commons Attribution 4.0 International License. [Read Full License](#)

Additional Declarations: No competing interests reported.

Version of Record: A version of this preprint was published at Chinese Medical Journal on May 6th, 2024. See the published version at <https://doi.org/10.1097/CM9.0000000000003024>.

Abstract

Objective and design

Limited information is available on the impact of SARS-CoV-2 infection in psoriasis patients, and we aim to identify clinical factors associated with the prognosis of psoriasis following SARS-CoV-2 infection.

Subjects and methods

A retrospective, multicenter study was conducted between March and May 2023. Univariable and multivariable logistic regression analysis were employed to identify factors associated with COVID-19-related psoriasis outcomes. A total of 2371 psoriasis patients from 12 clinical centers were included in the study, with 2049 of them being infected with COVID-19.

Results

Among the infected group, individuals treated with biologics exhibited lower exacerbation rates compared to those receiving traditional systemic or non-systemic treatments (26.7% vs.39.8% vs.37.5%, $P<0.001$). Multivariable logistic regression analysis revealed that psoriasis progression with lesions (adjusted odds ratio[OR]=8.197, 95% confidence interval[CI]=5.685-11.820, compared to no lesions), hypertension (adjusted OR=1.582, 95%CI=1.068-2.343), traditional systemic (adjusted OR=1.887, 95%CI=1.263-2.818), and non-systemic treatment (adjusted OR=1.602, 95%CI=1.117-2.297) were associated with exacerbation of psoriasis after SARS-CoV-2 infection but not biologics (adjusted OR=0.931, 95%CI =0.680-1.274, compared to no treatment).

Conclusions

Biologics may reduce the risk of psoriasis exacerbation after SARS-CoV-2 infection, compared to traditional systemic and non-systemic treatments. The presence of existing psoriatic lesions and hypertension have been identified as significant risk factors for exacerbation after infection.

Introduction

The coronavirus disease 2019 (COVID-19) pandemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has posed significant challenges to global public health worldwide [1, 2]. In December 2022, the Chinese Government officially announced the transition of China's dynamic zero SARS-CoV-2 infection policy towards reopening [3]. However, this move was met with a substantial surge in COVID-19 cases in China in the subsequent period, primarily driven by the highly transmissible omicron variant with an average basic reproduction number of 9.5[4]. Amidst this surge, certain populations face elevated risks of contracting SARS-CoV-2,

Patients with immune-mediated inflammatory diseases are at a higher risk of contracting SARS-CoV-2 compared to the general population, as evidenced by research studies [5]. Thus, the COVID-19 pandemic poses concerns for individuals with psoriasis, a chronic immune-mediated inflammatory skin disease that affects more than 125 million people worldwide [6]. The pathogenesis of psoriasis is believed to be primarily driven by overactivation of the adaptive immune system [7]. Many patients require immunosuppressive therapy to control disease activity, but this treatment may increase the susceptibility to SARS-CoV-2 infection, impair antiviral immunity, and exacerbate COVID-19 clinical [5]. Additionally, infection is a major contributing factor to the exacerbation of psoriasis [8], and researches has demonstrated that SARS-CoV-2 infection can act as an allergen and induce skin [9, 10]. This suggests that SARS-CoV-2 may indirectly exacerbate symptoms of psoriasis.

Previous studies have primarily focused on the COVID-19 related symptoms and outcomes in patients with psoriasis or other immune system diseases [11–15]. However, limited information is available on the specific impact of SARS-CoV-2 infection on psoriasis patients undergoing different treatment types (including biologics or other systemic agents) in the context of COVID-19 epidemic. Therefore, the objective of this retrospective, multicenter study was to describe the clinical characteristics and outcomes of psoriasis patients with COVID-19 in a large cohort. Additionally, we aimed to investigate the impact of SARS-CoV-2 infection on psoriasis patients receiving different treatments while identifying risk factors associated with exacerbation of psoriasis following SARS-CoV-2 infection.

Methods

Participants and study design

The psoriasis patients were recruited from the registries of 12 specialized treatment centers for psoriasis, based on inclusion criteria that encompassed all ages and sexes, a confirmed diagnosis of psoriasis (including psoriasis vulgaris, arthritic psoriasis, pustular psoriasis, and erythrodermic psoriasis) by a dermatologist, as well as having visited one of these centers' outpatient clinics within the past year. Patients or their family members could independently complete follow-up information surveys (questionnaires, telephone interviews, etc.) and ensure data authenticity. Exclusion criteria included any conditions deemed inappropriate by the investigator for this research project. Finally, a total of 2371 patients were included in the final analysis after applying exclusion criteria, accounting for missing data and refusal to participate during the COVID-19 period.

The study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki for Medical Research Involving Human Subjects. Approval for this study (Reference number: KY-20232073-F-2) was granted by the Clinical Research Ethics Committee of the participating centers. And the protocol of this study was reviewed and approved by independent ethics committees at each study site, and all patients provided oral informed consent. The trial is registered on ClinicalTrials.gov (Identifier: NCT05961605).

Data collection

The demographic and clinical information were extracted from psoriasis registration platform. SARS-CoV-2 infection condition, status of psoriasis (in progressive or no progressive), treatments of psoriasis (biologics [TNF inhibitors: adalimumab, etanercept, infliximab; IL-17 inhibitors: ixekizumab, secukinumab; IL12/IL-23p40 or IL-23p19 inhibitors: guselkumab, ustekinumab], traditional systemic therapy [methotrexate, cyclosporine, acitretin, Chinese herbal medicine], non-systemic therapy [topical medications, phototherapy, Chinese herbal medicine bath], as well as cases with no treatment) were collected by telephone follow-up and questionnaire between March and May 2023 (following the initial surge of SARS-CoV-2 infection in China). During follow-up, if a SARS-CoV-2 infection is present, additional clinical information regarding symptoms, treatment, and outcomes of COVID-19 would be obtained. Furthermore, we collected the change of psoriasis condition (exacerbation or remission/no change) following SARS-CoV-2 infection.

Definition of SARS-CoV-2 infection and exacerbation of psoriasis: owing to limited availability of PCR and antigen testing supplies in the initial surge of SARS-CoV-2 infection, individuals displaying evident symptoms of COVID-19 or residing with confirmed SARS-CoV-2 positive cases through PCR or antigen testing were strongly suspected to be infected with the SARS-CoV-2. Consequently, we incorporated these highly suspected cases into our cohort analysis for SARS-CoV-2 infections. Exacerbation of psoriasis was defined as the following criteria[16]: increased involvement of body surface area, and patient-reported worsening. Those who did not have the above manifestations were classified into remission/no change.

Statistical analysis

Continuous variables are reported as mean with standard deviation (SD) or median with interquartile range (IQR), while categorical variables are presented as number with percentage. We performed the univariate analysis of all clinical features and features with $P < 0.2$ or with clinically significant were selected into multivariate analysis. The linearity assumption of independent variables and logit transformation of the dependent variable was evaluated through Box-Tidwell test, while multicollinearity was assessed using variance inflation factors (less than 10). Significance levels were taken as two-sided 0.05. Analyses were conducted using SPSS (version 27, IBM, Armonk, NY, U.S.A).

Results

Baseline characteristics of psoriasis patients with or without COVID-19 infection

A total of 2,371 psoriasis patients were included in this study, and their clinical and demographic characteristics are presented in Table 1. Among them, the rate of COVID-19 infection was 86.4% (2,049 cases). The infected and uninfected groups exhibited a

similar distribution of sex (female, 35.2% vs. 35.1%, $P = 0.974$) and duration of psoriasis (11.1 vs. 11.1 years, $P = 0.039$), with the COVID-19 infected group showing a slightly lower mean age than the uninfected group (41.5 vs. 44.5 years, $P < 0.001$). In addition, there was no significant difference in the types of psoriasis and rates of comorbidity between the two groups. Interestingly, in terms of treatment modalities for psoriasis, the proportion of biologics was significantly higher in infected group than in uninfected group (51.6% vs. 25.2%, $P < 0.001$) (Table 1). The patients' other comorbidities and treatment modalities for psoriasis are showed in Table 1.

Table 1
Baseline characteristics of psoriasis patients with or without COVID-19

	All patients (n = 2371)		Infected group (n = 2049)		Uninfected group (n = 322)		P value
Gender/Female, no. (%)	834	35.2%	721	35.2%	113	35.1%	0.974
Age/ year, mean (SD)	41.9	14.6	41.5	14.4	44.6	16.1	0.001
Duration of psoriasis/ year, mean (SD)	11.1	9.7	11.1	9.6	11.1	10.3	0.039
Type of psoriasis, no. (%)							
Psoriasis vulgaris	2201	92.8%	1900	92.7%	301	93.5%	0.355
Arthritic psoriasis	114	4.8%	102	5.0%	12	3.7%	
Erythrodermic psoriasis	30	1.3%	27	1.3%	3	0.9%	
Pustular psoriasis	26	1.1%	20	1.0%	6	1.9%	
Comorbidity, no. (%)							
Hypertension	203	8.6%	180	8.8%	23	7.1%	0.328
Diabetes	122	5.1%	104	5.1%	18	5.6%	0.698
Hyperlipidemia/Fatty liver	74	3.1%	69	3.4%	5	1.6%	0.082
Obesity	61	2.6%	53	2.6%	8	2.5%	0.914
Cardiovascular disease	38	1.6%	33	1.6%	5	1.6%	0.939
Hyperuricemia	29	1.2%	28	1.4%	1	0.3%	0.109
Malignant tumor	9	0.4%	9	0.4%	0	0.0%	0.233
Others	44	1.9%	39	1.9%	5	1.6%	0.665
Psoriasis treatment modalities, no. (%)							
Biologics	1139	48.0%	1058	51.6%	81	25.2%	0.001
TNF- α inhibitors	82	7.2%	73	6.9%	9	11.1%	
IL-17 inhibitors	891	78.2%	839	79.3%	52	64.2%	
IL-12/23 inhibitors	166	14.6%	146	13.8%	20	24.7%	
Traditional systemic therapy	253	10.7%	231	11.3%	22	6.8%	
Non-systemic therapy	394	16.6%	373	18.2%	21	6.5%	
No treatment	585	24.7%	387	18.9%	198	61.5%	
Data are presented as mean (SD) and n (%).							
Biologics: TNF inhibitors, IL-17A inhibitors, IL12/23 inhibitors; TNF- α inhibitors: etanercept, infliximab, and adalimumab; IL-17A inhibitors: secukinumab and ixekizumab; IL-12/23 inhibitors: ustekinumab and guselkumab.							
Traditional systemic therapy: methotrexate, cyclosporine, acitretin, Chinese herbal medicine.							
Non-systemic therapy: topical medications, phototherapy, Chinese herbal medicine bath.							

The impact of SARS-CoV-2 infection on psoriasis patients receiving different treatments

Firstly, we categorized COVID-19 patients based on their pre-infection psoriasis treatment into four groups and conducted a comparative analysis of their clinical characteristics. Among all infected patients, the biologic group had the highest proportion

(1058, 51.6%), followed by those who received no treatment (387, 18.9%), non-systemic therapy (373, 18.2%), and traditional systemic therapy (231, 11.3%) prior to being diagnosed with COVID-19 (Table 2). The status of psoriatic lesions in patients prior to SARS-CoV-2 infection varied among different group, we observed a higher proportion of psoriasis with progression among those receiving traditional systemic (38, 16.5%) and non-systemic therapies (74, 19.8%) compared to the biologics group (130, 12.3%).

Table 2
The impact of SARS-CoV-2 infection on patients receiving different treatment modalities of psoriasis

	Infected group (n = 2049)		Biologics (n = 1058)		Traditional systemic therapy (n = 231)		Non-systemic therapy (n = 373)		No treatment (n = 387)		P value
Gender/Female, no. (%)	721	35.2%	355	33.6%	82	35.5%	134	35.9%	150	38.8%	0.320
Age/year, mean (SD)	41.5	14.4	41.8	13.8	42.8	15.8	41.9	15.3	39.6	13.9	0.025
Duration of psoriasis/ year, mean (SD)	11.1	9.6	10.9	8.9	10.6	10.1	11.6	10.8	11.5	10.0	0.446
Types of psoriasis, no. (%)											
Psoriasis vulgaris	1900	92.7%	971	91.8%	216	93.5%	346	92.8%	367	94.8%	0.006
Psoriatic arthritis	102	5.0%	68	6.4%	9	3.9%	17	4.6%	8	2.1%	
Erythrodermic psoriasis	27	1.3%	14	1.3%	1	0.4%	7	1.9%	5	1.3%	
Pustular psoriasis	20	1.0%	5	0.5%	5	2.2%	3	0.8%	7	1.8%	
Disease activity status prior to COVID-19 diagnosis, no. (%)											
No skin lesions	551	26.9%	302	28.5%	28	12.1%	34	9.1%	187	48.3%	0.001
With lesions, no progression	1224	59.7%	626	59.2%	165	71.4%	265	71.0%	168	43.4%	
With lesions, with progression	274	13.4%	130	12.3%	38	16.5%	74	19.8%	32	8.3%	
COVID-19 treatment modalities, no. (%)											
Antivirals drugs	1271	62.0%	696	65.8%	142	61.5%	255	68.4%	178	46.0%	0.001
Chinese herbal medicine	642	31.3%	365	34.5%	72	31.2%	126	33.8%	79	20.4%	0.001
Antibiotics	183	8.9%	139	13.1%	6	2.6%	22	5.9%	16	4.1%	0.001
Hospitalization	52	2.5%	31	2.9%	6	2.6%	13	3.5%	2	0.5%	0.038
Azulfidine/Paxlovid/Baricitinib	35	1.7%	20	1.9%	5	2.2%	7	1.9%	3	0.8%	0.464
Psoriasis outcomes after SARS-CoV-2 infection, no. (%)											
Exacerbation	547	26.7%	236	22.3%	92	39.8%	140	37.5%	79	20.4%	0.001
No change/remission	1502	73.3%	822	77.7%	139	60.2%	233	62.5%	308	79.6%	
Data are presented as mean (SD) and n (%).											

Regarding clinical outcomes on COVID-19, no fatalities were observed among the patients. Out of all patients, 35 received COVID-19-related medications (including Azulfidine, Paxlovid, and Baricitinib), while 52 patients were hospitalized due to serious comorbidities. Most patients presented with mild to moderate symptoms and received treatments, including antiviral agents (1271, 62.0%), Chinese herbal medicines (642, 31.3%), and antibiotics (183, 8.9%). Notably, antiviral drugs were the most frequently utilized among the four groups (ranging from 40.6–68.4%), while the biologics group had a higher percentage of antibiotic use (13.1% vs. 2.6% vs. 5.9% vs. 4.1%) than other groups. The impact of COVID-19 infection on psoriasis outcomes varied among four

treatment groups. Patients receiving traditional systemic therapy (92, 39.8%) had the highest proportion of exacerbation, followed by those receiving non-systemic therapy (140, 37.5%), biologics (236, 22.3%), and no treatment (79, 20.4%) (Table 2).

Clinical characteristics of psoriasis patients with different outcomes of lesions following SARS-CoV-2 infection

Subsequently, we compared the clinical characteristics between two groups of psoriasis outcomes based on exacerbation or no change/remission after SARS-CoV-2 infection (Table 3). The prevalence of most comorbidities was higher in the exacerbation group than in the no change/remission group, including hypertension (11.0% vs. 8.0%, $P = 0.035$) and hyperlipidemia/fatty liver (5.3% vs. 2.7%, $P = 0.003$). A higher proportion of patients in the exacerbation group (164, 30%) had progression psoriasis status prior to COVID-19 infection compared to the no change/remission group (110, 7.3%) (Table 3). The proportion of treatment modalities for COVID-19 were significantly higher in the exacerbation group compared to the no change/remission group, such as antipyretic drugs (66.2% vs. 60.5%, $P = 0.020$) and Chinese herbal medicine (37.3% vs. 29.2%, $P < 0.001$) (Table 3). In terms of COVID-19 symptoms, most COVID-19 symptoms such as fever (84.5% vs. 77.8%, $P < 0.001$), fatigue (29.3% vs. 18.8%, $P < 0.001$) and cough (50.8% vs. 40.9%, $P < 0.001$) were more prevalent in exacerbation group than in no change/remission group (Table 3). For psoriasis treatment modalities, biologics were further categorized into TNF- α , IL-17, and IL-12/23 inhibitors based on their different targets. The TNF- α inhibitors group exhibited a higher incidence of psoriasis exacerbation compared to the other two groups (37.0% vs. 21.1% vs. 21.9%) (Table 3).

Table 3
Clinical characteristics of different psoriasis outcome after SARS-CoV-2 infection

	Exacerbation (n = 547)		No change/remission (n = 1502)		P value
Gender/Female, no. (%)	195	27.0%	526	73.0%	0.792
Age/year, mean (SD)	40.6	14.7	41.9	14.2	0.075
Duration of psoriasis/ year, mean (SD)	11.6	10.8	11.0	9.2	0.194
Comorbidities, no. (%)					
Hypertension	60	11.0%	120	8.0%	0.035
Hyperlipidemia/Fatty liver	29	5.3%	40	2.7%	0.003
Diabetes	20	3.7%	80	5.3%	0.392
Obesity	16	2.9%	37	2.5%	0.560
Hyperuricemia	11	2.0%	17	1.1%	0.129
Cardiovascular disease	10	1.8%	23	1.5%	0.637
Malignant tumor	2	0.4%	7	0.5%	0.761
Other	17	3.1%	22	1.5%	0.016
Disease activity status prior to COVID-19 diagnosis, no. (%)					
No skin lesions	80	14.6%	471	31.4%	0.001
No progression	303	55.4%	921	61.3%	
With progression	164	30.0%	110	7.3%	
COVID-19 treatment modalities, no. (%)					
Antipyretic drugs	362	66.2%	909	60.5%	0.020
Chinese herbal medicine	204	37.3%	438	29.2%	0.001
Antibiotics	54	9.9%	129	8.6%	0.367
Hospitalization	16	2.9%	36	2.4%	0.501
Azulfidine/Paxlovid/Baricitinib	11	2.0%	24	1.6%	0.523
Common COVID-19 symptoms, no. (%)					
Fever	462	84.5%	1168	77.8%	0.001
Cough	278	50.8%	615	40.9%	< 0.001
Muscle aches and pains	246	45.0%	485	32.3%	< 0.001
Sore throat	207	37.8%	490	32.6%	0.028
Weakness	160	29.3%	283	18.8%	< 0.001
Runny nose	88	16.1%	157	10.5%	< 0.001
Decreased sense of taste	64	11.7%	132	8.8%	0.048
Data are presented as mean (SD), and n (%).					
TNF- α inhibitors: etanercept, infliximab, and adalimumab; IL-17A inhibitors: secukinumab and ixekizumab; IL-12/23 inhibitors: ustekinumab and guselkumab.					

	Exacerbation (n = 547)		No change/remission (n = 1502)		P value
Loss of sense of smell	59	10.8%	97	6.5%	< 0.001
Headache	30	5.5%	96	6.4%	0.450
Diarrhea	19	3.5%	31	2.1%	0.070
Nausea and/or vomiting	14	2.6%	18	1.2%	0.032
Biologics (n = 1058, 236 patients with exacerbation), no. (%)					
TNF- α inhibitors	27	37.0%	46	63.0%	0.007
IL-17 inhibitors	177	21.1%	662	78.9%	
IL-12/23 inhibitors	32	21.9%	114	78.1%	
Data are presented as mean (SD), and n (%).					
TNF- α inhibitors: etanercept, infliximab, and adalimumab; IL-17A inhibitors: secukinumab and ixekizumab; IL-12/23 inhibitors: ustekinumab and guselkumab.					

Univariate and multivariate analyses identified risk factors associated with psoriasis exacerbation after SARS-CoV-2 infection

In the univariable analyses, the presence of pre-existing skin lesions, particularly those in stage of progression (OR = 8.778, 95%CI = 6.258–12.313), was significantly associated with exacerbation of psoriasis. Regarding comorbidities, hypertension (OR = 1.419, 95%CI = 1.023–1.967) and hyperlipidemia/fatty liver (OR = 2.046, 95%CI = 1.256–3.335) exhibited significant associations with psoriasis exacerbation (Table 4). Except for headache and diarrhea, all COVID-19 symptoms demonstrated a correlation with psoriasis exacerbation (Table 4). The therapies for psoriasis including traditional systemic therapy (OR = 2.580, 95%CI = 1.798–3.703) and non-systemic therapy (OR = 2.343, 95%CI = 1.694–3.239) also exhibited a significant association with the exacerbation of psoriasis compared with no treatment (Table 4).

Table 4

Univariate and multivariate analyses identify risk factors associated with psoriasis exacerbation after SARS-CoV-2 infection.

	Univariate analysis			Multivariate analysis		
	OR	95%CI	<i>P</i> value	adjusted OR	95%CI	<i>P</i> value
Gender/ female	1.028	0.838–1.261	0.792	0.933	0.743–1.173	0.554
Age > 65 years	0.939	0.649–1.358	0.736	0.615	0.396–0.955	0.030
Disease activity prior to COVID-19 diagnosis						
No skin lesions				Ref		
With lesions, no progression	1.937	1.478–2.538	< 0.001	1.699	1.268–2.276	< 0.001
With lesions, with progression	8.778	6.258–12.313	< 0.001	8.197	5.685–11.820	< 0.001
Co-morbidities						
Hypertension	1.419	1.023–1.967	0.036	1.582	1.068–2.343	0.022
Hyperlipidemia/fatty liver	2.046	1.256–3.335	0.004	1.395	0.790–2.465	0.251
Hyperuricemia	1.793	0.834–3.852	0.135	1.317	0.567–3.060	0.521
Common COVID-19 symptoms						
Fever	1.554	1.197–2.018	0.001	1.297	0.959–1.754	0.091
Cough	1.491	1.224–1.814	< 0.001	1.345	1.064–1.702	0.013
Muscle aches and pains	1.714	1.403–2.094	< 0.001	1.349	1.052–1.729	0.018
Sore throat	1.257	1.026–1.541	0.028	0.900	0.702–1.152	0.402
Weakness	1.781	1.422–2.230	< 0.001	1.638	1.233–2.175	< 0.001
Runny nose	1.642	1.239–2.177	< 0.001	1.292	0.917–1.818	0.142
Decreased sense of taste	1.375	1.003–1.886	0.048	0.910	0.579–1.428	0.681
Loss of sense of smell	1.751	1.247–2.459	< 0.001	1.466	0.906–2.372	0.119
Headache	0.850	0.557–1.296	0.450	0.685	0.419–1.119	0.131
Diarrhea	1.708	0.956–3.049	0.070	1.296	0.661–2.54	0.450
Nausea and/or vomiting	2.166	1.070–4.384	0.032	1.641	0.730–3.690	0.230
Treatment of psoriasis prior to COVID-19 diagnosis						
No treatment				Ref		
Biologics	1.119	0.841–1.491	0.440	0.931	0.680–1.274	0.656
Traditional systemic treatment	2.580	1.798–3.703	< 0.001	1.887	1.263–2.818	0.002
Non-systemic treatment	2.343	1.694–3.239	< 0.001	1.602	1.117–2.297	0.010
OR, odds ratio; 95% CI, 95% confidence interval.						
Biologics: TNF inhibitors, IL-17 inhibitors, IL12/23 inhibitors.						
Traditional systemic therapy: methotrexate, cyclosporine, acitretin, and Chinese herbal medicine.						
Non-systemic therapy: topical medications, phototherapy, and Chinese herbal medicine bath.						

Then, a total of 23 features were selected into the multivariate logistic regression model, and 9 of them were independently associated with exacerbation of psoriasis after adjusted. Psoriasis patients aged over 65 have a lower risk of exacerbation after infection compared to patients under 65 years old (adjusted OR = 0.615, 95%CI = 0.396–0.955). Both no progression (adjusted OR = 1.699, 95%CI = 1.268–2.276) and progression with lesions (adjusted OR = 8.197, 95%CI = 5.685–11.820), as well as hypertension (adjusted OR = 1.582, 95%CI = 1.068–2.343) remained significantly associated with exacerbation of psoriasis (Table 4). After adjustment, for COVID-19 symptoms, only fatigue (adjusted OR = 1.638, 95%CI = 1.233–2.175), muscle aches (adjusted OR = 1.349, 95%CI = 1.052–1.729), and cough (adjusted OR = 1.345, 95%CI = 1.064–1.702) were found to be associated with psoriasis exacerbation in this study population. Baseline therapies for psoriasis including traditional systemic treatment (adjusted OR = 1.887, 95%CI = 1.263–2.818) and non-systemic treatment (adjusted OR = 1.602, 95%CI = 1.117–2.297) were still significantly associated with exacerbation of psoriasis but not biologics (adjusted OR = 0.931, 95%CI = 0.680–1.274) compared with no treatment (Table 4).

Discussion

In this study, we presented clinical data from a large cohort of psoriasis patients with COVID-19 and observed that those treated with biologics or receiving no treatment for psoriasis had the lowest rates of exacerbation following SARS-CoV-2 infection. The presence of psoriatic lesions prior to SARS-CoV-2 infection was significantly associated with an increased risk of exacerbation in psoriasis. Moreover, we have also identified certain factors associated with the exacerbation of psoriasis during COVID-19 infection, including hypertension and common COVID-19 symptoms such as fatigue, muscle aches, and cough.

Previous case reports and small sample studies of case series have indicated that psoriasis exacerbation occurs following SARS-CoV-2 infection [17, 18]. Our study initially revealed a significant association between SARS-CoV-2 infection and the exacerbation of psoriasis in a large cohort. In the subgroup analysis, significant differences were observed in the impact of treatment types on psoriasis outcomes. Notably, patients treated with biologics exhibited a significantly lower likelihood of experiencing exacerbation of psoriasis lesions following SARS-CoV-2 infection. Blocking the cytokine-mediated inflammatory cell death pathway may offer potential benefits for COVID-19 and autoinflammatory disease patients by mitigating tissue damage and inflammation[19]. Interestingly, patients who did not receive any treatment for psoriasis also exhibited a decreased rate of exacerbation. This may be related to the psoriasis stability before SARS-CoV-2 infection, as individuals who have not undergone any psoriasis treatment are likely in a stable phase of the disease.

In the multivariate analysis, we observed a higher risk of psoriasis exacerbation following SARS-CoV-2 infection in patients with coexisting hypertension. This association may be attributed to the utilization of antihypertensive medications commonly prescribed for hypertensive individuals, such as angiotensin-converting enzyme inhibitors (ACEIs), angiotensin receptor blockers (ARBs), and beta-blockers, which are known to potentially worsen psoriasis symptoms[20]. Nevertheless, the precise mechanisms underlying this aggravating effect of these drugs on psoriasis remain largely elusive and necessitate further investigation.

In a further analysis of the impact of various target biologics on psoriasis outcomes, it was observed that patients who were treated with IL-17A inhibitors had the lower proportion of exacerbations of psoriasis. This may be attributed to the involvement of IL-17 in COVID-19 pathogenesis, as evidenced by previous studies demonstrating its active role in cytokine storm and disease severity [21, 22]. Studies also presumed that targeting IL-17 is immunologically plausible as a strategy in COVID-19 [23, 24]. Therefore, it is hypothesized that the utilization of IL-17A inhibitors may potentially mitigate the severity of COVID-19 by attenuating the inflammatory cytokine storm in vivo after infection with SARS-CoV-2. Consequently, patients who employ IL-17A inhibitors may experience a reduction in psoriasis exacerbation due to decreased levels of inflammation.

In addition to SARS-CoV-2 infections, a multitude of other factors can contribute to the onset and exacerbation of psoriasis. The COVID-19 outbreak in China, characterized by a significant surge in infections[3], coincides with the winter season when psoriasis tends to exacerbate. During this time, if the patients suffer from mental stress because of COVID-19 infection[25], this may affect the progression of psoriasis. Additionally, there have been reports indicating that COVID-19 vaccination may exacerbate in psoriasis patients[26, 27]. The COVID-19 vaccines utilize adenovirus vectors, mRNA, or virus-related proteins to elicit Th1 and Th17 immune responses, which may further exacerbate psoriasis [28].

One of the strengths of our study is that it is the first comprehensive analysis of the psoriasis outcome condition in patients with COVID-19 conducted on a large cohort. Furthermore, we included patients who received different types of treatment for psoriasis and specifically ensured the inclusion of individuals with stable disease activity and those not currently undergoing any form of treatment to minimize potential selection bias. A potential limitation of our study is the retrospective telephone follow-up, which may introduce recall bias. Additionally, this study may lack some relevant details such as COVID-19 vaccination status and other factors exacerbating psoriasis or COVID-19 related laboratory tests.

SARS-CoV-2 infection may potentially exacerbate psoriasis, while the impact of different treatment modalities on psoriasis outcomes following SARS-CoV-2 infection varies. The utilization of biologics has the potential to reduce the incidence of psoriasis exacerbation during COVID-19 persistence. Notably, pre-existing psoriatic lesions and hypertension have been identified as significant risk factors for exacerbation post-infection. These findings offer valuable insights for the management and treatment of psoriasis patients during the COVID-19 pandemic and future outbreaks. Moreover, the results support the recommendation that discontinuation of biologic therapy should not be considered in psoriasis patients during the COVID-19 pandemic. However, further validation across larger cohorts of immunosuppressed patients is warranted.

Declarations

Conflict of interest

The authors have declared that no conflict of interest exists.

Funding

This study was supported by the Clinical Research Project on COVID-19 infection at the Xijing hospital. (Grant number: XJZT23XG29).

Ethics approval statement

This study was approved by the ethics committees of Xijing Hospital (KY-20232073-F-2). Consent to use the data from this study for scientific research was obtained from all patients by oral during telephone follow-ups.

Data availability: The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Author contributions

Gang Wang and Chen Yu designed the study. Aijun Chen, Junling Zhang, Xiaojing Kang, Xian Jiang, Chengzhi Lv, Chunrui Shi, Yuling Shi, Xiaoming Liu, Fuqiu Li, Bin Yang, Yongmei Huang, contributed to the data acquisition. Yanhua Liu, Zhongrui Xu, and Jian Zhou conducted the data analysis. Yanhua Liu and Zhongrui Xu drafted the manuscript. All authors read and approved the final manuscript.

References

1. Safiabadi Tali SH, LeBlanc JJ, Sadiq Z, Oyewunmi OD, Camargo C, Nikpour B, et al. Tools and Techniques for Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2)/COVID-19 Detection. *Clin Microbiol Rev.* 2021;34:e00228-20.
2. Guan W, Ni Z, Hu Y, Liang W, Ou C, He J, et al. Clinical Characteristics of Coronavirus Disease 2019 in China. *N Engl J Med.* 2020;382:1708–20.
3. Huang S, Gao Z, Wang S. China's COVID-19 reopening measures—warriors and weapons. *The Lancet.* 2023;401:643–4.
4. Liu Y, Rocklöv J. The effective reproductive number of the Omicron variant of SARS-CoV-2 is several times relative to Delta. *J Travel Med.* 2022;29:taac037.
5. Williamson EJ, Walker AJ, Bhaskaran K, Bacon S, Bates C, Morton CE, et al. Factors associated with COVID-19-related death using OpenSAFELY. *Nature.* 2020;584:430–6.
6. Armstrong AW, Read C. Pathophysiology, Clinical Presentation, and Treatment of Psoriasis: A Review. *JAMA.* 2020;323:1945.

7. Griffiths CEM, Armstrong AW, Gudjonsson JE, Barker JNWN. Psoriasis. *The Lancet*. 2021;397:1301–15.
8. Sbidian E, Madrange M, Viguier M, Salmona M, Duchatelet S, Hovnanian A, et al. Respiratory virus infection triggers acute psoriasis flares across different clinical subtypes and genetic backgrounds. *Br J Dermatol*. 2019;181:1304–6.
9. Novak N, Peng W, Naegeli MC, Galvan C, Kolm-Djamei I, Brügger C, et al. SARS-CoV-2, COVID-19, skin and immunology – What do we know so far? *Allergy*. 2021;76:698–713.
10. Patrick MT, Zhang H, Wasikowski R, Prens EP, Weidinger S, Gudjonsson JE, et al. Associations between COVID-19 and skin conditions identified through epidemiology and genomic studies. *Journal of Allergy and Clinical Immunology*. 2021;147:857–869.e7.
11. Lima XT, Cueva MA, Lopes EM, Alora MB. Severe COVID-19 outcomes in patients with psoriasis. *J Eur Acad Dermatol Venereol*. 2020;34:e776–8.
12. Wu JJ, Liu J, Thatiparthi A, Martin A, Egeberg A. The risk of COVID-19 in patients with psoriasis: A retrospective cohort study. *J Am Acad Dermatol*. 2022;87:1395–8.
13. Singh S, Khan A, Chowdhry M, Bilal M, Kochhar GS, Clarke K. Risk of Severe Coronavirus Disease 2019 in Patients With Inflammatory Bowel Disease in the United States: A Multicenter Research Network Study. *Gastroenterology*. 2020;159:1575–1578.e4.
14. Gianfrancesco M, Hyrich KL, Al-Adely S, Carmona L, Danila MI, Gossec L, et al. Characteristics associated with hospitalisation for COVID-19 in people with rheumatic disease: data from the COVID-19 Global Rheumatology Alliance physician-reported registry. *Ann Rheum Dis*. 2020;79:859–66.
15. Gu X, Chen X, Shen M. Association of psoriasis with risk of COVID-19: A 2-sample Mendelian randomization study. *J Am Acad Dermatol*. 2022;87:715–7.
16. Balak DMW, Perez-Chada LM, Guo LN, Mita C, Armstrong AW, Bell SJ, et al. Definitions of remission in psoriasis: a systematic literature review from the National Psoriasis Foundation. *Acad Dermatol Venereol*. 2022;36:2291–300.
17. Kutlu Ö, Metin A. A case of exacerbation of psoriasis after oseltamivir and hydroxychloroquine in a patient with COVID-19: Will cases of psoriasis increase after COVID-19 pandemic? *Dermatol Ther*. 2020;33:e13383.
18. Ozaras R, Berk A, Ucar DH, Duman H, Kaya F, Mutlu H. Covid-19 and exacerbation of psoriasis. *Dermatologic Therapy [Internet]*. 2020 [cited 2023 Jul 7];33. Available from: <https://onlinelibrary.wiley.com/doi/10.1111/dth.13632>
19. Karki R, Sharma BR, Tuladhar S, Williams EP, Zalduondo L, Samir P, et al. Synergism of TNF- α and IFN- γ Triggers Inflammatory Cell Death, Tissue Damage, and Mortality in SARS-CoV-2 Infection and Cytokine Shock Syndromes. *Cell*. 2021;184:149–168.e17.
20. Brauchli YB, Jick SS, Curtin F, Meier CR. Association between beta-blockers, other antihypertensive drugs and psoriasis: population-based case–control study. *Br J Dermatol*. 2008;158:1299–307.
21. Maione F, Casillo GM, Raucci F, Salvatore C, Ambrosini G, Costa L, et al. Interleukin-17A (IL-17A): A silent amplifier of COVID-19. *Biomed Pharmacother*. 2021;142:111980.
22. Wang J, Jiang M, Chen X, Montaner LJ. Cytokine storm and leukocyte changes in mild versus severe SARS-CoV-2 infection: Review of 3939 COVID-19 patients in China and emerging pathogenesis and therapy concepts. *J Leukoc Biol*. 2020;108:17–41.
23. Xu Q, Chen L, Li X, Zheng J. If skin is a potential host of SARS-CoV-2, IL-17 antibody could reduce the risk of COVID-19. *J Am Acad Dermatol*. 2021;84:e173.
24. Pacha O, Sallman MA, Evans SE. COVID-19: a case for inhibiting IL-17? *Nat Rev Immunol*. 2020;20:345–6.
25. Marek-Jozefowicz L, Czajkowski R, Borkowska A, Nedoszytko B, Żmijewski MA, Cubała WJ, et al. The Brain–Skin Axis in Psoriasis—Psychological, Psychiatric, Hormonal, and Dermatological Aspects. *IJMS*. 2022;23:669.
26. Wu P-C, Huang I-H, Wang C-W, Tsai C-C, Chung W-H, Chen C-B. New Onset and Exacerbations of Psoriasis Following COVID-19 Vaccines: A Systematic Review. *Am J Clin Dermatol*. 2022;23:775–99.
27. Krajewski PK, Matusiak Ł, Szepietowski JC. Psoriasis flare-up associated with second dose of Pfizer-BioNTech BNT16B2b2.pdf. *J Eur Acad Dermatol Venereol*. 2021;35:e632–4.
28. Niebel D, Novak N, Wilhelmi J, Ziob J, Wilsman-Theis D, Bieber T, et al. Cutaneous Adverse Reactions to COVID-19 Vaccines: Insights from an Immuno-Dermatological Perspective. *Vaccines*. 2021;9:944.