ORIGINAL RESEARCH

Nonadherence to Treatment and Patient-Reported Outcomes of Psoriasis During the COVID-19 Epidemic: A Web-Based Survey

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Purpose: The COVID-19 epidemic has caused difficulties in continuous treatment for patients with chronic diseases and resulted in nonadherence to treatment and adverse health outcomes. This study aimed to investigate the associations of nonadherence to treatment with patient-reported outcomes of psoriasis during the COVID-2019 epidemic.

Methods: A cross-sectional study among Chinese patients with psoriasis was conducted through a web-based questionnaire survey during 25 Feb 2020 and 6 Mar 2020. Demographic and clinical data, nonadherence to treatment, and patient-reported outcomes were collected. The outcomes included deterioration of the disease condition, perceived stress, and symptoms of anxiety and depression. Logistic regression was used to investigate the associations.

Results: A total of 926 questionnaires were collected. A total of 634 (68.5%) reported nonadherence to treatment, and worse adherence was found among patients receiving systemic treatment (adjusted odds ratio [AOR]: 2.67; 95% CI: 1.40–5.10) and topical treatment (AOR: 4.51; 95% CI: 2.66–7.65) compared to biological treatment. Nonadherence to treatment (less than two weeks and more than two weeks) was significantly associated with deterioration of psoriasis (aOR: 2.83 to 5.25), perceived stress (AOR: 1.86 to 1.57), and symptoms of anxiety (AOR: 1.42 to 1.57) and depression (AORs: 1.78). Subgroup analysis by treatment showed consistent results in general.

Conclusion: Nonadherence to treatment was associated with the aggravation of psoriasis conditions, perceived stress, and symptoms of anxiety and depression.

Keywords: psoriasis, coronavirus disease 2019, patient-reported outcome, treatment adherence

Introduction

The novel coronavirus disease 2019 (COVID-19) caused by the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) has now spread all over the world during the past few months and has brought profound impacts on people's daily life.[1] To save limited medical resources and avoid nosocomial infection, many hospitals in China closed the outpatient service during February and March 2019, which led to the difficulties and inconvenience in continuous treatment among patients with chronic conditions and resulted in nonadherence to treatment and aggravation of diseases. Psoriasis, a chronic inflammatory skin disease with prevalence rate varying from 0.5% to 11.4% globally, is affecting over 125 million people worldwide.[2–4] The prevalence of psoriasis in China has

increased from 0.12% to 0.47% during the past two decades.[5,6] Psoriasis has a significant negative impact on health-related quality of life,[7–10] and nonadherence to treatment is a pivotal risk factor for aggravation of psoriasis conditions.[11] The current study aimed to investigate the association of nonadherence to treatment with the patient-reported outcomes of psoriasis, including the aggravation of psoriasis conditions, stress, anxiety, and depression during the period of COVID-19 epidemic.

Methods
Study Design and Participants
We performed a cross-sectional study among Chinese patients with psoriasis. An online survey link was created and posted on social media platforms (teledermatology platforms and WeChat groups) for psoriatic patients who were diagnosed by one or more experienced dermatologists. The patients were introduced to the platforms by certified physicians with permissions. Each participant was allowed to submit a questionnaire once by IP address in order to avoid repeated submissions. The participants needed to complete all the questions before submitting the questionnaire successfully. The survey was conducted between 25 Feb 2020 and 6 Mar 2020. The study was reviewed and approved by the institutional research ethics boards of Xiangya Hospital, Central South University (Changsha, China); approval number: 202002024. Electronic informed consent was gathered from all patients.

Exposure Variable
We defined the adherence to the primary treatment as the exposure variable, measured by a single question "During the epidemic, were you adhere to the medication or treatment prescribed by the physician?" with the following three responses: "(1) Yes, I followed my doctor's instruction", "(2) No, I reduced the dosage of medication on my own", "(3) No, I totally stopped the treatment on my own". If a patient responded (2) or (3), a question "How long have you done this?" with two responses including "less than two weeks" and "more than two weeks" was further inquired. Those who reduced the dosage or stopped the treatment were defined as nonadherence to treatment. This question was after another question inquiring about the primary treatment they were receiving.

Patient-Reported Outcomes
The primary outcome was aggravation of psoriasis, measured by the Global Rating of Change (GRC). Patients responded to the following question "Overall, has there been any change in how your psoriasis bothers you during the past two weeks?" using the following five options: much improvement, moderate improvement, no change, moderate deterioration, much deterioration. We defined deteriorated disease condition as the reportedly moderate-to-much deterioration.

The secondary outcomes included perceived stress and symptoms of anxiety and depression. Perceived stress during the past two weeks was assessed with a visual analogue scale (VAS), which was previously validated by the Perceived Stress Scale (PSS14) with an area under the receiver operating characteristic curve of 0.9–0.93 and a cutoff of 6.8–7.2.[12,13] We defined significant perceived stress with the cutoff ≥ 7. Anxious and depressive symptoms were measured by the two-item Generalized Anxiety Disorder (GAD-2) and the two-item Patient Health Questionnaire (PHQ-2), respectively. The cut-off points of both scales were ≥ 3 according to validation studies.[14,15]

Covariates
Clinical and demographic information including gender, age, educational level (middle school and below, high school, college and above), annual income (Chinese yuan, CNY), marital status (unmarried, married, divorced, widowed), type of psoriasis (psoriasis vulgaris, psoriatic arthritis, pustular psoriasis, erythrodermic psoriasis), course of disease (<1 year, 1–5 years, >5 years), body surface area of psoriatic lesions (self-rated palm size, <3%, 3–10%, >10%), and treatment received (biological treatment, systemic treatment, topical treatment, other) were collected and analyzed as covariates.

Statistical Analysis
The data were exported from the online survey system and analyzed with SPSS 23 (IBM, SPSS Statistics 23). Continuous variables with normal distribution were expressed as mean ± standard deviation (SD) and compared with analysis of variance (ANOVA). Categorical variables were summarized as counts (percentages) and compared using the chi-square test or Fisher's exact test. Logistic regression was used to estimate the associations of exposure and outcomes with adjustments for potential confounders. Effect size of association was presented as adjusted odds ratios (AORs) and 95% confidence intervals (CIs). P value less than 0.05 was considered statistically significant.

Results

We collected 926 valid questionnaires. The IP addresses of the respondents covered all the provinces of mainland China. One patient reported confirmed infection with SARS-CoV-2. The mean age of the patients was 39.1±12.2 years, and 584 (63.1%) were male. The characteristics of the participants by treatment adherence are shown in Table 1. The course of psoriasis and body surface area of skin lesion were significantly different across the groups.

A total of 292 (31.5%) reported adherence to treatment, while 289 (31.2%) reported nonadherence to the treatment, either stopped the medication or reduced the prescribed dosage, for less than two weeks, and 345 (37.3%) for more

than two weeks, respectively. The prevalence of single use of biological, systemic, and topical treatment was 9.0%, 9.5%, and 37.1%, respectively. Others reported phototherapy, Chinese medicine, other treatment, or no treatment. The prevalence of nonadherence was 37.3%, 63.7%, and 71.2% for biological, systemic, and topical treatment, respectively. Patients receiving systemic treatment (AOR=2.67; 95% CI: 1.40–5.10; P=0.003) or topical treatment (AOR=4.51; 95% CI: 2.66–7.65; P<0.001) reported worse adherence compared to those receiving biological treatment.

The proportions of perceived stress, anxiety, and depression were 18.4%, 66.3%, and 68.1%, respectively. As shown in Table 2, nonadherence to the treatment was

Table 1 Characteristics of the Patients, by Reported Treatment Adherence During the Period of COVID-19 Epidemic

Characteristics	Total (n=926)	Adherent to Treatment (n=292)	Nonadherent to Treatment		P
			< 2weeks (n=289)	≥ 2weeks (n=345)	
Age (mean±SD)	39.1±12.2	34.1±12.9	32.5±11.9	32.7±11.8	0.236
Female (%)	36.9	37.0	37.0	36.8	0.998
Education (%)					0.050
Primary/middle school	26.2	25.0	30.4	23.8	
High school	26.3	22.6	24.6	30.7	
College or above	47.5	52.4	45.0	45.5	
Annual income, CNY (%)					0.371
<10,000 (1500 US$)	28.4	27.7	29.4	28.1	
10,000–50,000 (1500–7500 US$)	35.6	32.9	37.0	36.8	
50,000–100,000 (7500–15,000 US$)	23.1	24.3	19.7	24.9	
>100,000 (15,000 US$)	12.9	15.1	13.9	10.2	
Marital status (%)					0.204
Unmarried	24.2	25.0	22.8	24.4	
Married	70.7	67.5	74.4	70.4	
Divorced	4.6	6.5	2.4	4.9	
Widowed	0.5	1.0	0.4	0.3	
Type of psoriasis (%)					0.233
Psoriasis vulgaris	78.4	74.3	80.0	80.6	
Psoriatic arthritis	11.8	13.4	10.7	11.3	
Pustular psoriasis	2.7	4.1	3.1	1.2	
Erythrodermic psoriasis	7.1	8.2	6.2	6.9	
Course of psoriasis, year (%)					0.012
<1	4.9	4.8	8.0	2.3	
1–5	23.0	22.9	24.9	21.5	
>5	72.1	72.3	67.1	76.2	
Body surface area of skin lesion (%)					<0.001
≤3%	45.8	58.2	46.4	34.8	
3–10%	29.8	23.3	29.4	35.7	
>10%	24.4	18.5	24.2	29.5	

Note: P value by single factor logistic regression model.

Table 2 Associations of Nonadherence to Treatment with Patient-Reported Outcomes of Psoriasis

Patient-Reported Outcomes	Adherence to Treatment		Nonadherence to Treatment < 2 Weeks				Nonadherence to Treatment ≥ 2 Weeks			
	n (%)	OR	n (%)	OR (95% CI)	AOR (95% CI)[a]	P	n (%)	OR (95% CI)	AOR (95% CI)[a]	P
Deteriorated psoriasis	64 (21.9)	1	129 (44.6)	2.87 (2.00, 4.12)	2.83 (1.94, 4.09)	<0.001	212 (61.4)	5.68 (3.99, 8.07)	5.25 (3.66, 7.53)	<0.001
Perceived stress (VAS ≥7)	27 (9.2)	1	45 (15.6)	1.81 (1.09, 3.01)	1.86 (1.11, 3.12)	0.018	52 (15.1)	1.74 (1.06, 2.85)	1.57 (0.95, 2.59)	0.082
Anxiety (GAD-2 ≥3)	48 (16.4)	1	65 (22.5)	1.48 (0.98, 2.23)	1.42 (0.93, 2.16)	0.108	86 (24.9)	1.69 (1.14, 2.50)	1.57 (1.05, 2.35)	0.029
Depression (PHQ-2 ≥3)	49 (16.8)	1	78 (27.0)	1.83 (1.23, 2.74)	1.78 (1.18, 2.69)	0.006	95 (27.5)	1.88 (1.28, 2.78)	1.78 (1.20, 2.65)	0.004

Note: [a]Adjusted for education, course of psoriasis and body surface area of skin lesion.
Abbreviations: OR, unadjusted odds ratio; AOR, adjusted odds ratio; CI, confidence interval; VAS, visual analogue scale; GAD-2, two-item Generalized Anxiety Disorder; PHQ-2, two-item Patient Health Questionnaire.

significantly associated with the deterioration of psoriasis determined by the self-reported GRC (AORs: 2.83 to 5.25) in a clear dose–response manner. Nonadherence was also associated with the secondary outcomes, including perceived stress (AOR: 1.86 to 1.57), and symptoms of anxiety (AORs: 1.42 to 1.57) and depression (AORs: 1.78).

Subgroup analysis for nonadherence by the type of treatment is shown in Table 3. The associations remained consistent in general. Perceived stress was positively associated with nonadherence to biological treatment (AORs: 3.26 to 10.31). Symptom of depression was associated with nonadherence to systemic treatment (AORs: 3.26 to 9.18) and topical treatment (AORs: 2.18 to 2.64).

Discussion

Through the analysis of 926 valid questionnaires, we found that nonadherence to treatment was found prevalent during the outbreak of COVID-19. Patients receiving systemic or topical treatment reported worse adherence than those receiving biological treatment. The prevalence rates of perceived stress, anxiety, and depression were high among the patients, and nonadherence to treatment was significantly associated with the deterioration of psoriasis and other patient-reported outcomes including stress, anxiety, and depression.

Among our participants, the proportion of male patients was substantially higher (63%), and this was consistent with a previous study reporting that the prevalence of psoriasis in males (0.54%) was higher than females (0.44%) in China.[5] The increase in the prevalence of psoriasis in China in recent three decades might be attributable to behavioral factors and the increase of comorbid noncommunicable diseases. And the male predilection may be explained by smoking behavior, stress, and unobserved factors. As a result, the high proportion of male patients should not be regarded as a consequence of selection bias.

We reported an overall nonadherence rate of 68.5%. Patients receiving biological treatment reported less nonadherence compared to those receiving systemic or topical treatment, and this was consistent with previous reports.[11,16,17] Studies reported varied prevalence of nonadherence to treatment among psoriatic patients owing to differences in inclusion criteria, sample size, tools to assess adherence, etc. The study by Thorneloe et al suggested that prevalence of nonadherence among the patients using a conventional systemic was 29.2%, higher than those using adalimumab or etanercept (16.4%).[18] Esposito et al conducted an observational study among

Table 3 Subgroup Analysis of Associations of Nonadherence with Patient-Reported Outcomes of Psoriasis by Main Treatment

Patient-Reported Outcomes	Nonadherence to Biological Treatment				Nonadherence to Systemic Treatment				Nonadherence to Topical Treatment			
	<2 Weeks		≥2 Weeks		<2 Weeks		≥2 Weeks		<2 Weeks		≥2 Weeks	
	AOR[a] (95% CI)	P	AOR[a] (95% CI)	P	AOR[a] (95% CI)	P	AOR[a] (95% CI)	P	AOR[a] (95% CI)	P	AOR[a] (95% CI)	P
Deteriorated psoriasis	3.22 (0.89, 11.63)	0.074	11.50 (2.30, 57.55)	0.003	3.03 (0.89, 10.30)	0.075	19.43 (3.99, 94.56)	<0.001	2.34 (1.30, 4.23)	0.005	5.19 (2.77, 9.73)	<0.001
Perceived stress (VAS ≥7)	3.26 (0.69, 15.43)	0.136	10.31 (1.49, 71.27)	0.018	2.26 (0.35, 14.57)	0.393	1.80 (0.29, 11.25)	0.531	1.34 (0.59, 3.06)	0.481	1.06 (0.43, 2.61)	0.900
Anxiety (GAD-2 ≥3)	2.31 (0.51, 10.37)	0.275	1.04 (0.22, 4.92)	0.957	1.02 (0.27, 3.91)	0.974	3.61 (0.97, 13.04)	0.055	1.39 (0.66, 2.91)	0.387	1.09 (0.49, 2.43)	0.842
Depression (PHQ-2 ≥3)	1.62 (0.38, 6.88)	0.511	1.08 (0.23, 5.06)	0.923	3.26 (0.58, 18.41)	0.181	9.18 (1.72, 48.98)	0.009	2.18 (1.06, 4.50)	0.035	2.64 (1.25, 5.58)	0.011

Notes: [a]Compared with adherence to biological, systemic and topical treatment respectively; adjusted for education, course of psoriasis and body surface area of skin lesion.
Abbreviations: AOR, adjusted odds ratio; CI, confidence interval; VAS, visual analogue scale; GAD-2, two-item Generalized Anxiety Disorder; PHQ-2, two-item Patient Health Questionnaire.

650 adult psoriatic patients and found that the global adherence to anti-TNF-α blockers was 73% after 28.9 months.[19] Adherence reported by Zaghloul et al was 46% with systemic treatment and 71.9% with topical treatment.[20] Rates of nonadherence among psoriatic patients treated with topical corticosteroids in western dermatology outpatient clinics varied from 8% to 88%.[21] The rate of adherence among psoriatic patients in China was reported as 41.5%.[22] Non-adherence to topical treatments was the highest in our study, consistent with many previous studies.[23,24] Low efficiency, time consumption, and visibility of topical agents were the most frequently mentioned reasons for nonadherence.[25,26] Besides, contradiction between quick consumption and insufficient supplement of topical agents might be another reason during the pandemic. In summary, we identified a higher prevalence of nonadherence compared to the data reported by many previous studies, indicating that the epidemic might have adverse impacts on patients' adherence to treatment.

Mental health problems were prevalent during the epidemic, and early mental health intervention was suggested.[27–31] However, no study investigated the associations of nonadherence to treatment with mental well-being status among psoriatic patients during the COVID-19 pandemic yet. It is well known that patients with psoriasis have higher risks of mental disorders and suicidal behaviors. In addition, many studies indicated the importance of adherence to treatment for alleviating psoriasis conditions,[11,32] while few studies investigated the impact of nonadherence on the symptoms of anxiety and depression. In addition, many hospitals in China temporarily closed their outpatient service to avoid nosocomial infection and save limited medical resources during the pandemic. This may lead to the inconvenience and difficulties in healthcare utilization for patients with psoriasis. Moreover, many people underwent income loss or even unemployment. This further placed psoriatic patients at risks of poverty and poor health.[33] These may help explain the association between nonadherence and deterioration of psoriasis in addition to stress, anxiety, and depression. To prevent the deterioration and adverse outcomes of the disease, accessibility to medication and healthcare service as well as enhancement of adherence to treatment are critical for patients with psoriasis during the pandemic, in addition to mental health interventions. Dermatologists, primary care practitioners, and decision-makers could help improve the patients' health outcomes through telemedicine, health education, and maintained

drug supply at the individual, community, and regional levels.

The limitations of the study included selection bias of online survey, recall bias of patient-reported outcome, a lack of generalizability to pediatric or geriatric patients who were less accessible to the internet or social media.

Conclusion

Nonadherence to treatment was prevalent among Chinese patients with psoriasis during the COVID-19 epidemic and was associated with the aggravation of psoriasis conditions, perceived stress, and symptoms of anxiety and depression. Nonadherence in biologics was lower than systemic and topical treatment. Strategies targeting the adherence to treatment, including but not limited to telemedicine, health education, and drug supplies, are necessary for patients with psoriasis, in addition to mental health interventions.

Ethics Approval

Reviewed and approved by the institutional research ethics boards of Xiangya Hospital, Central South University (Changsha, China); approval #202002024.

Acknowledgments

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors report no conflicts of interest for this work.

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