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-19 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.\textsuperscript{5,6} Psoriasis has a significant negative impact on health-related quality of life,\textsuperscript{7–10} and nonadherence to treatment is a pivotal risk factor for aggravation of psoriasis conditions.\textsuperscript{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.\textsuperscript{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.\textsuperscript{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

| Characteristics | Total (n=926) | Adherent to Treatment (n=292) | Nonadherent to Treatment | P |
|-----------------|--------------|-------------------------------|--------------------------|---|
| Age (mean±SD)   | 39.1±12.2    | 34.1±12.9                     | 32.5±11.9                | 0.236 |
| Female (%)      | 36.9         | 37.0                          | 36.8                     | 0.998 |
| Education (%)   |              |                               |                          | 0.050 |
| Primary/middle school | 26.2 | 25.0                       | 30.4                    | 0.371 |
| High school     | 26.3         | 22.6                          | 24.6                    | 0.024 |
| College or above| 47.5         | 52.4                          | 45.0                    | 0.233 |
| Annual income, CNY (%) |         |                               |                          | 0.012 |
| <10,000 (1500 US$) | 28.4   | 27.7                         | 29.4                    | 0.003 |
| 10,000–50,000 (1500–7500 US$) | 35.6 | 32.9                         | 37.0                    | 0.001 |
| 50,000–100,000 (7500–15,000 US$) | 23.1 | 24.3                         | 19.7                    | 0.003 |
| >100,000 (15,000 US$) | 12.9 | 15.1                         | 13.9                    | 0.001 |
| Marital status (%) |            |                               |                          | 0.001 |
| Unmarried       | 24.2         | 25.0                          | 22.8                    | 0.204 |
| Married         | 70.7         | 67.5                          | 74.4                    | 0.012 |
| Divorced        | 4.6          | 6.5                           | 2.4                     | 0.003 |
| Widowed         | 0.5          | 1.0                           | 0.4                     | 0.001 |
| Type of psoriasis (%) |       |                               |                          | 0.001 |
| Psoriasis vulgaris | 78.4   | 74.3                         | 80.0                    | 0.233 |
| Psoriatic arthritis | 11.8   | 13.4                         | 10.7                    | 0.012 |
| Pustular psoriasis | 2.7    | 4.1                           | 3.1                     | 0.001 |
| Erythrodermic psoriasis | 7.1 | 8.2                           | 6.2                     | 0.001 |
| Course of psoriasis, year (%) |             |                               |                          | 0.001 |
| <1              | 4.9          | 4.8                           | 8.0                     | 0.001 |
| 1–5             | 23.0         | 22.9                          | 24.9                    | 0.001 |
| >5              | 72.1         | 72.3                          | 76.1                    | 0.001 |
| Body surface area of skin lesion (%) |         |                               |                          | 0.001 |
| ≤3%             | 45.8         | 58.2                          | 46.4                    | 0.001 |
| 3–10%           | 29.8         | 23.3                          | 29.4                    | 0.001 |
| >10%            | 24.4         | 18.5                          | 24.2                    | 0.001 |

Note: P value by single factor logistic regression model.
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. 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. 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%). Esposito et al conducted an observational study among

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

| Adherence to Treatment | Nonadherence to Treatment ≥ 2 Weeks | Nonadherence to Treatment < 2 Weeks |
|------------------------|-------------------------------------|-------------------------------------|
| n (%)                  | P                                   | AOR (95% CI)                       |
| Deteriorated psoriasis | 64 (21.9)                           | 1.96 (1.09, 3.52)                  |
| (VAS ≥ 27)             |                                     |                                     |
| Perceived stress (VAS | 23 (8.1)                            | 1.96 (1.09, 3.52)                  |
| ≥ 3)                  |                                     |                                     |
| Anxiety (GAD-2)        | 49 (16.6)                           | 1.96 (1.09, 3.52)                  |
| (≥ 23)                |                                     |                                     |
| Depression (PHQ-2 ≥ 3)| 49 (16.6)                           | 1.96 (1.09, 3.52)                  |

**Note:** 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.
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 |<2 Weeks | ≥2 Weeks |
| AOR* (95% CI)             | P        | AOR* (95% CI) | P        | AOR* (95% CI) | P        | AOR* (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 |
| 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 |
| 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) | 0.555 |
| 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 |

Notes: *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.
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
The authors would like to thank the Psoriatic Patient Blog (URL: https://www.yxb365.com/portal.php) and the Psoriasis Blog New Media (WeChat Official Account ID: yxbnpnx8) for their assistance in the online survey. We would also like to thank Professor Jin Zhang and Dr. Xin Guan for their contribution to the data collection.

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.

Funding
This work was supported by the National Natural Science Foundation of China (62041208, 81974479, 81573049, 81830096), the Ministry of Science and Technology of the People’s Republic of China (2016YFC0900802, 2018YFC0117004, 2016YFC0901705), the Emergency Project of Prevention and Control for COVID-19 of Central South University (502701002), and the Department of Science and Technology of Hunan Province (2018SK2082, 2018SK2086).

Disclosure
The authors report no conflicts of interest for this work.

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