

The correlation between mental health status, sleep quality, and inflammatory markers, virus negative conversion time among patients confirmed with 2019-nCoV during the COVID-19 outbreak in China

An observational study

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Abstract

The 2019 coronavirus disease (COVID-19) has spread to the whole world. Psychological and sleep problems among confirmed patients have drawn extensive attention which may be highly related to immune function and inflammatory responses of people. The aim of this study is to examine the correlation of mental health status, sleep quality, and inflammatory markers, virus negative conversion time (NCT) among confirmed patients during the COVID-19 outbreak.

A cross-sectional survey was conducted in this study. Data from 66 patients assessed with demographic information, anxious symptom, depressive symptom, stress, and sleep quality were collected using a smartphone-based questionnaire platform and then clinical characteristics and laboratory indicators were collected using case review.

Nearly 30% of the participants reported depression, anxiety, perceived pressure, and poor sleep quality. Compared with the group without depression, neutrophil count, and ratio of neutrophil count to lymphocyte count (NLR) in the depression disorder group were increased ($P = .028, 0.043$). There was also a significant difference in NLR and NCT between the anxiety group and the non-anxiety group ($P = .021, .024$). Similarly, compared with the good sleep quality group, NLR in the poor sleep quality group was increased ($P = .011$). Correlation analysis indicated that Self-Rating Depression Scale score was positively related to neutrophil count and NLR ($r = 0.366, 0.330, P = .016, .031$). The total score of Pittsburgh Sleep Quality Index (PSQI) was negatively related to lymphocyte count ($r = -0.317, P = .049$), and the sleep disturbance as 1 of the 7 dimensions of PSQI scale was positively correlated with NCT and NLR ($r = 0.370, 0.340, P = .020, .034$).

In our study, confirmed patients were prone to have psychological and sleep problems. The level of inflammation in patients with psychological and sleep problems was higher than that in patients without corresponding problems. The inflammatory level increased with the increase of Self-Rating Depression Scale score, and the lymphocyte count decreased with the increase of the PSQI score. NCT was prolonged in the anxiety group and sleep disturbance was positively correlated with NCT.

Abbreviations: 2019-nCoV = 2019 Novel Coronavirus, COVID-19 = Coronavirus Disease 2019, CPSS = Chinese Perceived Stress Scale, NCT = coronavirus negative conversion time, NLR = neutrophil/lymphocyte ratio, PSQI = Pittsburgh Sleep Quality Index, SARS = Severe Acute Respiratory Syndrome, SAS = Self-Rating Anxiety Scale, SDS = Self-Rating Depression Scale.

Keywords: anxiety, coronavirus, depression, inflammation, mood disorder, sleep problem, stress

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1. Introduction

The 2019 novel coronavirus (2019-nCoV) was first reported in late December 2019, originating from Wuhan in Hubei Province, China. Then, 2019-nCoV pneumonia broke out in Hubei province and started to spread throughout China in January, 2020. On January 30, 2020, the World Health Organization declared the 2019-nCoV outbreak as a public health emergency of international concern and subsequently named 2019 coronavirus disease (COVID-19). The 2019-nCoV is a beta-coronavirus, like severe acute respiratory syndrome (SARS) and middle east respiratory syndrome, presenting as viral pneumonia with acute respiratory tract infection, which is infectious strongly.^[1] To lower the risk of further disease transmission, a range of measures have been urgently adopted in many countries such as reducing travel, closing restaurants and entertainment venues, early identification and isolation of suspected and diagnosed cases, tracing and monitoring of the persons who have contacted the infected person, and collecting biological samples from patients. However, as the infectivity and harmfulness of the virus increase, and the unpredictability of the situation and the uncertainty of when the disease can be controlled have made negative emotions spread. A large number of people feel helpless, fearful, anxious, and depressed.^[2]

Although studies on the general mental health status and sleep quality of COVID-19 patients during the novel coronavirus epidemic were not much, high detection rates of depression, anxiety, post-traumatic stress disorder, and sleep problems among COVID-19 patients have been found, the same situation that has been observed among SARS survivors during the SARS epidemic.^[3–5] Studies reported that the prevalence of COVID-19 patients with anxiety and/or depression was 10.8% to 43.1%, the prevalence of post-traumatic stress disorder was above 10%, and nearly 30% of the patients suffered from sleep problems.^[6–10] These findings indicate that the mental status and sleep quality of the confirmed patients and the impact of the virus disease to mental status should not be ignored.

Additionally, according to previous studies, mental health status and sleep quality may be highly related to the physiological state of people. It was well documented in animal and human researches that the immune system responds acutely to psychological stress, mental disorder, and sleep deprivation, such as lymphocyte and red blood cells decrease, number and proportion of T cell and B cell changes. In addition, the mental disorder and decreased sleep quality can also lead to inflammatory activation, such as IL-6, CRP, white blood cells, and neutrophils increasing. These changes in the physiological state may increase the susceptibility to infection and increase disease risk and shape disease course.^[11,12] Regarding the influence of physical conditions on the process of disease recovery, studies have found that the increased ratio of neutrophils and CD4+ lymphocytes among COVID-19 patients was related to the longer coronavirus negative conversion time (NCT), and the NCT of 2019-nCoV was essential in the recovery and discharge criteria.^[13] Therefore, mental disorders and sleep problems may prolong the disease recovery process by influencing immune function and level of inflammation. It seems that in addition to the efforts at various levels to prevent the spread of the disease, special attention should be given to mental disorders and sleep quality which may further affect the physiological state and recovery process.

Since January, 2020, the National Health Commission of China has published several guideline documents for people

affected by COVID-19.^[14] To date, a number of COVID-19 epidemic-related mental health studies have been published.^[2,15–18] But based on our understanding, little researches explore the correlation between psychological response and the level of inflammation, the recovery process among confirmed patients during the outbreak of severe infectious disease. Therefore, the aim of this study is to examine the correlation of mental health status, sleep quality, and inflammatory markers, NCT (1 of the essential indicators of recovery) among patients with confirmed 2019-nCoV, so as to remind healthcare professionals to pay more attention to the physical state of patients with psychological and sleep problems, and timely give further psychological intervention to promote disease recovery.

2. Methods

2.1. Study design and participants

An online cross-sectional survey was conducted among patients confirmed with 2019-nCoV during the COVID-19 pandemic from February 21 to March 6, 2020. Patients were recruited from Hong Shan Stadium Mobile Cabin Hospital, Huoshenshan Hospital, and Leishenshan Hospital in Wuhan, China, which were the designated hospitals for COVID-19, and our doctors were dispatched to take charge of 1 section in each hospital. Patients were enrolled by voluntarily adding our We Chat mini-program on a smartphone and data were collected by the smartphone-based questionnaire program. Inclusion criteria included: (1) The patients who met the diagnostic criteria of “Diagnosis and Treatment Scheme for Pneumonia Infected by Novel Coronavirus (Trial 6th Edition)” issued by the National Health and Health Commission. (2) The patients’ physical condition was relatively stable and capable of understanding the content of the assessment and providing written informed consent. Exclusion criteria included: (1) The patients who did not complete a basic socio-demographic questionnaire or any test. (2) The patients diagnosed with cancer or blood system diseases. A total of 93 confirmed patients responded, and 22 of them did not complete any test. Four of the respondents answered the questionnaire twice in a short period of time and 1 of them failed to complete the socio-demographic questionnaire, and thus only the 66 confirmed patients met the study criteria.

2.2. Ethical statement

The study was approved by the First Affiliated Hospital of China Medical University Ethics Committee and electronic informed consent was obtained from patients involved before completed the online questionnaire and test.

2.3. Measurements and data collection

Socio-demographic data were collected on age, gender, education, marital status, children, annual income, and so on.

Psychiatric status was evaluated by the Self-Rating Depression Scale (SDS) and the Self-Rating Anxiety Scale (SAS) which are self-administered scales, consisting of 20 items in each scale. Each item scored from 1 to 4. The boundary values of depression are as follows: 0–52, normal; 53–62, mild; 63–72, moderate; and above 73, severe.^[19] The boundary values of anxiety are as follows: 0–49, normal; 50–59, mild; 60–69, moderate; and above 70, severe.^[20] Sleep quality was evaluated by the Pittsburgh Sleep

Quality Index (PSQI) – Chinese version.^[21] The PSQI total score ranges from 0 to 21, with the score of >7 considered as “having poor sleep quality.”^[22] Perceived stress was evaluated by the Chinese Perceived Stress Scale. There are 14 items in total and each item is rated on a 5-point Likert-type scale (0=never, 1=almost never, 2=sometimes, 3=fairly often, and 4=very often). A higher score indicates a higher level of perceived stress.^[23]

Clinical characteristics, inflammatory markers, and NCT were collected after completing the test through medical records that could be found by referring to accurate information filled by patients on the questionnaire platform. Clinical characteristics included fever, cough, shortness of breath, and pulmonary infiltration which were signs related manifestations of inflammatory. Inflammatory markers included white blood cell, neutrophil count, lymphocyte count, and neutrophil/lymphocyte ratio (NLR). Chest computed tomography and inflammatory markers were the latest results before the questionnaire survey. NCT was defined as the interval between symptom onset and the first of 2 consecutive negative virus tests.^[13]

2.4. Data analysis

The SPSS program Version 26.0 was used to analyze data. The demographic data of the respondents were summarized using descriptive statistics expressed in terms of number and percentage (%). Normal distribution of continuous variables was tested by Kolmogorov–Smirnov test. Data conforming to the normal distribution were expressed as $x \pm s$, while the measurement data not conforming to the normal distribution was expressed as median and quartile intervals. Categorical variables were expressed as the frequency (%). Clinical characteristics were categorical variables, and Chi-square tests and Fisher exact test (used to sample size <40) were used to detect group differences. Inflammatory markers and NCT were continuous variables. The Mann–Whitney *U* tests were used to analyze continuous and abnormal distributed variables of inflammatory markers and NCT between the patients with and without mental disorders and sleep problems. Independent sample *T* test was used to analyze continuous and normal distributed variables of inflammatory markers between the patients with and without mental disorders and sleep problems. Pearson correlation analysis and Spearman rank correlation analysis were utilized to examine the relationship of mental health status, sleep quality, and laboratory data in confirmed patients. Significant level was set as $P < .05$ for all tests (2-sided).

3. Results

The current sample was consisted of 66 confirmed patients, with 9 mild cases, 51 common cases, 3 severe cases, and 3 critical cases based on the admission diagnosis. Clinical characteristics and laboratory data of 48 patients were collected via medical records.

Table 1 showed sample characteristics. Among the 66 participants, 38 were women and 28 were men. The ages of the participants ranged from 17 to 79 years old, with an average age of 46.11. Most of the confirmed patients were aged ≥ 40 years old, accounting for 72.7%. The majority of the participants were with high school degree and below (51.5%), married (86.4%), had 1 child (59.1%), living with family members (92.4%), with a household size of more than 3 persons (65.2%), and in a good interpersonal relationship (92.4%). A 39.4% of the participants needed psychological counseling. There were 27.6% and 22.7% of the confirmed patients with depressive symptoms and anxious

Table 1
Sample characteristics.

Variables	Percent (%) (N=66)
Age (years) ≥ 40	48 (72.7%)
Female	38 (57.6%)
High school and below	34 (51.5%)
Married	57 (86.4%)
Children	
No children	13 (19.7%)
One child	39 (59.1%)
More than 2 children	14 (21.2%)
Annual income $\geq 50,000$ RMB	33 (50%)
Living with family	61 (92.4%)
Household size ≥ 3	43 (65.2%)
Good interpersonal relationship	61 (92.4%)
Need psychological counseling	26 (39.4%)
Current smoker	12 (18.2%)
Current drinker	16 (24.2%)
Depression (SDS measurement)	16/58 (27.6%)
Mild	13 (22.4%)
Moderate	2 (3.4%)
Severe	1 (1.7%)
Anxiety (SAS measurement)	15/66 (22.7%)
Mild	11 (16.7%)
Moderate	3 (4.5%)
Severe	1 (1.5%)
Perceived stress (CPSS measurement)	14/50 (28%)
Poor Sleep quality (PSQI measurement)	13/51 (25.5%)

The boundary values of depression are as follows: 0–52, normal; 53–62, mild; 63–72, moderate; and above 73, severe.

The boundary values of anxiety are as follows: 0–49, normal; 50–59, mild; 60–69, moderate; and above 70, severe.

Stress was defined as the Chinese Perceived Stress Scale (CPSS) >26.

Poor sleep quality was defined as Pittsburgh Sleep Quality Index (PSQI) >7.

CPSS=Chinese Perceived Stress Scale, PSQI=Pittsburgh Sleep Quality Index, SAS=Self-Rating Anxiety Scale, SDS=Self-Rating Depression Scale.

symptoms, respectively, and most of them reported mild mental disorders. A 28% of the participants felt stressed; 25.5% of the participants were reported suffering from sleep problems. Sleep problems mainly manifested poor subjective sleep quality (90.2%), increased sleep disturbance (92.2%), and more daytime dysfunction (78.4%) (Table 2).

Table 3 showed clinical characteristics of the patients with and without mental disorders and sleep problems. Fever (62.5%) and cough (47.9%) were the common symptoms in the 48 patients for whom clinical and laboratory data were available. Shortness of breath (20.8%) was a less common symptom in these patients. Pulmonary infiltration was present in more than half of the patients (52.1%). However, there was no significant difference in these clinical manifestations of inflammation between the patients with mental disorders and sleep problems and those without mental disorders and sleep problems.

Table 4 showed a comparison of inflammatory markers and NCT between the patients with and without mental disorders and sleep problems. Independent sample *T* test and the non-parametric Mann–Whitney *U* test were used to compare the laboratory data between the patients with and without mental disorders and sleep problems from 48 patients. There was a difference in neutrophil count and NLR between the depression group and the non-depression group, and the difference was statistically significant ($P = .028, .043$). Compared with the non-depression group, neutrophil count and NLR increased in the

Table 2
Percentages and types of symptoms of sleep problems.

	Poor subjective sleep quality	Longer sleep latency	Decreased sleep continuity	Decreased sleep efficiency	Increased sleep disturbance	Usage of sleep medication	Daytime dysfunction
Yes	46 (90.2%)	9 (17.6%)	6 (11.8%)	3 (5.9%)	47 (92.2%)	9 (17.6%)	40 (78.4%)
No	5 (9.8%)	42 (82.4%)	45 (88.2%)	48 (94.1%)	4 (7.8%)	42 (82.4%)	11 (21.6%)

Table 3
Clinical characteristics of the patients with and without mental disorders and sleep problems.

Variables	Depression (N=43)					Anxiety (N=48)				Perceived stress (N=38)			Sleep quality (N=39)		
	All (N=48)	Absent (n=34)	Present (n=9)	χ^2	P	Absent (n=40)	Present (n=8)	χ^2	P	Absent (n=28)	Present (n=10)	P	Good (n=29)	Poor (n=10)	P
Fever	30 (62.5%)	21 (61.8%)	6 (66.7%)	0.000	1.000	25 (62.5%)	5 (62.5%)	0.000	1.000	19 (67.9%)	4 (40.0%)	.150	19 (65.5%)	5 (50.0%)	.463
Cough	23 (47.9%)	16 (47.1%)	4 (44.4%)	0.000	1.000	19 (47.5%)	4 (50.0%)	0.000	1.000	13 (46.4%)	6 (60.0%)	.714	14 (48.3%)	5 (50.6%)	1.000
Shortness of breath	10 (20.8%)	9 (26.5%)	0 (0.0%)	1.626	.202	9 (22.5%)	1 (12.5%)	0.025	.874	5 (17.9%)	1 (10.0%)	1.000	6 (20.7%)	0 (0.0%)	.308
Chest CT with infiltration	25 (52.1%)	17 (50.0%)	5 (55.6%)	0.000	1.000	22 (55.0%)	3 (37.5%)	0.267	.605	12 (42.9%)	7 (70.0%)	.269	14 (48.3%)	5 (50.0%)	1.000

N is the total number of patients with available data. The counting data were expressed as the frequency (%) and p values comparing patients with and without mental disorders and sleep problems were from χ^2 test, Fisher exact test (simple size <40).

Depressive disorder was defined as Self-Rating Depression Scale (SDS) ≥ 53 ; anxiety disorder was defined as Self-Rating Anxiety Scale (SAS) ≥ 50 ; stress was defined as Chinese Perceived Stress Scale (CPSS) >26 . Poor sleep quality was defined as Pittsburgh Sleep Quality Index (PSQI) >7 .

depression group. There was a difference in NCT and NLR between the anxiety group and the non-anxiety group, and the difference was statistically significant ($P = .024, .021$). Compared with the non-anxiety group, NLR increased and NCT was prolonged in the anxiety group. Compared with the good sleep quality group, NLR also increased in the poor sleep quality group, and the difference was statistically significant ($P = .011$). There was no significant difference between the 2 groups with and without perceived stress.

The correlation analysis results of the mental health status score, sleep quality score, inflammation markers, and NCT were shown in Tables 5 and 6. SDS score was positively associated with neutrophil count and NLR ($r = 0.366, 0.330, P = .016, .031$). The total score of PSQI was negatively related to lymphocyte count ($r = -0.317, P = .049$), and the sleep disturbance as 1 of the 7 dimensions of the PSQI scale was positively correlated with NCT and NLR ($r = 0.370, 0.340, P = .020, .034$).

Table 4
Comparison of laboratory parameters between the patients with and without mental disorders and sleep problems.

Variables	Depression			Anxiety			Perceived stress			Sleep quality		
	Absent $X \pm s$	Present $X \pm s$	P	Absent $X \pm s$	Present $X \pm s$	P	Absent $X \pm s$	Present $X \pm s$	P	Good $X \pm s$	Poor $X \pm s$	P
NCT [*]	12.50 (0.00–20.25)	15.00 (5.00–25.00)	.355	11.50 (0.00–17.00)	18.00 (15.00–24.0)	.024	13.00 (0.00–21.00)	12.5 (0.00–17.75)	.638	12 (0.00–20.50)	17.00 (9.75–23.75)	.157
WBC $\times 10^9/L$	5.14 \pm 1.18	6.02 \pm 1.22	.054	5.41 \pm 1.41	5.39 \pm 1.10	.967	5.30 \pm 1.27	5.24 \pm 1.42	.907	5.27 \pm 1.22	5.30 \pm 1.49	.951
NE [†] $\times 10^9/L$	2.91 (2.36–3.44) [†]	3.34 (3.22–4.69) [†]	.028	3.08 \pm 0.93	3.44 \pm 0.99	.326	3.07 \pm 0.89	3.09 \pm 1.06	.940	2.98 \pm 0.77	3.36 \pm 1.25	.263
LY [‡] $\times 10^9/L$	1.61 (1.39–2.02)	1.67 (1.33–2.21)	.777	1.79 (1.40–2.33)	1.49 (1.31–1.80)	.154	1.64 (1.38–2.06)	1.62 (1.37–2.07)	.987	1.63 (1.40–2.17)	1.41 (1.24–1.78)	.074
NLR [§]	1.74 \pm 0.52	2.22 \pm 0.91	.043	1.63 (1.35–2.04) [§]	2.01 (1.85–2.30) [§]	.021	1.83 \pm 0.66	1.84 \pm 0.62	.962	1.69 \pm 0.51	2.28 \pm 0.81	.011

Data conforming to the normal distribution were expressed as $x \pm s$, while the measurement data not conforming to the normal distribution was expressed as median and quartile intervals. The Mann–Whitney U tests were used to analyze abnormal distributed variables. Independent sample T test was used to analyze normal distributed variables.

Depressive disorder was defined as Self-Rating Depression Scale (SDS) ≥ 53 ; anxiety disorder was defined as Self-Rating Anxiety Scale (SAS) ≥ 50 ; stress was defined as Chinese Perceived Stress Scale (CPSS) >26 . Poor sleep quality was defined as Pittsburgh Sleep Quality Index (PSQI) >7 .

LY=lymphocyte, NCT=virus negative conversion time, NE=neutrophile, NLR=ratio of neutrophile count to lymphocyte count, WBC=white blood cell.

^{*} NCT was defined as the interval between symptom onset and the first of 2 consecutive negative virus tests. It did not conform to the normal distribution.

[†] The neutrophile of depressive and non-depressive groups did not conform to the normal distribution.

[‡] The lymphocyte count did not conform to the normal distribution.

[§] The NLR of anxious and non-anxious groups did not conform to the normal distribution.

Table 5**Correlation analysis between mental health scores and laboratory parameters.**

Variables	NCT		WBC × 10 ⁹ /L		NE × 10 ⁹ /L		LY × 10 ⁹ /L		NLR	
	r	P	r	P	r	P	r	P	r	P
SDS	-0.007	.963	0.245	.113	0.366	.016	-0.018	.907	0.330	.031
SAS	0.193	.189	0.103	.487	0.207	.158	-0.138	.351	0.283	.052
CPSS	-0.084	.617	0.202	.223	0.235	.155	0.094	.576	0.108	.518
Mean	11.92		5.41		3.14		1.82		1.81	
SD	-		1.355		0.937		-		0.622	
Minimum	0		3.27		1.43		0.97		0.76	
Maximum	29		8.96		5.54		3.44		4.23	

NCT, lymphocyte count and SAS did not conform to the normal distribution. Spearman correlation tests were used to analyze abnormal distributed variables and Pearson correlation analysis were used to analyze normal distributed variables.

CPSS = Chinese Perceived Stress Scale, LY = lymphocyte, NCT = virus negative conversion time, NE = neutrophile, NLR = ratio of neutrophile count to lymphocyte count, SAS = Self-Rating Anxiety Scale, SDS = Self-Rating Depression Scale, WBC = white blood cell.

4. Discussion

In relation to the recent global outbreak of COVID-19, most of the researches mainly focus on identifying the epidemiology and clinical characteristics of infected patients and the genomic characterization of the virus.^[1,24,25] Little research data has been obtained about the mental health status and sleep quality of those confirmed with 2019-nCoV, especially the relationship of mental health, sleep quality, and physiological state is still unclear.^[26] In our study, the main results are as follows: (1) Nearly one-third of the participants reported depressive symptoms, anxious symptoms, perceived pressure, and poor sleep quality. (2) Fever, cough, and pulmonary infiltration were the common symptoms and signs in the confirmed patients. (3) The level of inflammation in patients with mood disorders and poor sleep quality was higher than that in patients without corresponding problems. Compared with the non-anxiety group, NCT was prolonged in the anxiety group. (4) SDS score was positively related to neutrophil count and NLR. The total score of PSQI was negatively related to lymphocyte count and the sleep disturbance score as 1 of the 7 dimensions of the PSQI scale was positively correlated with NCT and NLR.

Our findings suggested that nearly 30% of the participants reported depressive symptoms, anxious symptoms, perceived pressure, and poor sleep quality. Nearly 40% of the patients needed psychological counseling. Our results are similar to those in previous studies about COVID-19. During the SARS epidemic, 10%–35% of SARS survivors continued to suffer from anxiety,

depression, and post-traumatic stress disorder 1 month or more after discharge.^[27–30] A 4-years follow-up study has shown that mental health problems in SARS survivors, such as post-traumatic stress disorder could still be detected even after a long time.^[31] Therefore, we can predict that the outbreak of COVID-19 may also cause persistent psychological impact among confirmed patients. Based on the above findings, confirmed COVID-19 patients are prone to have mood and sleep quality problems, which may exist for a long time, and many confirmed patients have psychological counseling needs. Thus, timely and appropriate psychological intervention is very necessary for COVID-19 patients.

In our study, we collected clinical and laboratory data related to inflammation. Consistent with previous findings, we also found that fever, cough, and pulmonary infiltration were the common symptoms and signs in the confirmed patients.^[1,24] Shortness of breath was a less common symptom, which may be due to the fact that most of the patients in our study were mild and common cases. There was no significant difference in these clinical manifestations of inflammation between the patients with and without mental disorders and sleep problems. This may be because most of the patients with psychological problems reported mild mental disorders. But we found some significant results in the laboratory indicators.

In our study, there was a difference in neutrophil count and/or NLR between the mental disorder group and those without corresponding problems. SDS score was positively related to neutrophil count and NLR. The correlation coefficient between

Table 6**Correlation analysis between Pittsburgh Sleep Quality Index score and laboratory parameters.**

Variables	NCT		WBC × 10 ⁹ /L		NE × 10 ⁹ /L		LY × 10 ⁹ /L		NLR	
	r	P	r	P	r	P	r	P	r	P
Total score	0.076	.644	-0.110	.504	-0.014	.934	-0.317	.049	0.310	.055
Subjective sleep quality	0.112	.498	0.026	.876	0.054	.743	-0.219	.180	0.287	.076
Sleep latency	0.104	.528	0.088	.594	0.162	.326	-0.045	.785	0.225	.169
Sleep continuity	-0.265	.103	-0.159	.333	-0.163	.321	-0.010	.950	-0.022	.892
Sleep efficiency	-0.248	.128	-0.228	.163	-0.239	.143	-0.107	.515	-0.004	.983
Sleep disturbance	0.370	.020	0.104	.530	0.204	.213	-0.197	.229	0.340	.034
Using sleep medication	0.003	.983	0.100	.544	0.068	.683	0.097	.559	-0.105	.526
Daytime dysfunction	0.295	.068	-0.159	.334	-0.008	.962	-0.308	.057	0.222	.175

Pittsburgh Sleep Quality Index score did not conform to the normal distribution. Spearman correlation tests were used to analyze variables.

LY = lymphocyte, NCT = virus negative conversion time, NE = neutrophile, NLR = ratio of neutrophile count to lymphocyte count, WBC = white blood cell.

SAS and NLR was 0.283, with a *P* value of .052, which was close to .05. Regarding the relationship between mental health status and laboratory parameters, as early as 1981, Ader reviewed the evidence for a complex interaction between the brain and the immune system. Numerous studies have supported the idea that emotional, psychological, or physical stress can impair immune function and trigger inflammatory responses, and that a large proportion of patients with depression or anxiety-related disorders (eg, generalized anxiety disorder and panic disorder) exhibit elevated inflammatory markers.^[32–36] The mechanism may be that the inflammatory changes are linked to the activation of the hypothalamic-corticotropin-releasing hormone system. Activation of the hypothalamic-corticotropin-releasing hormone system leads to the release of norepinephrine, which in turn stimulates the production of IL-6 and stimulates the acute phase reactive protein to produce a significant pro-inflammatory effect.^[37,38] Neutrophils are known to be the most abundant type of leukocytes and the first cells responding to inflammation. Neutrophils play an important role in the pathogenesis of inflammatory diseases. Elevated neutrophils secreted large amounts of cytokines to modulate immune responses. In patients with severe infections, the neutrophil level was significantly elevated, inducing a cytokine storm, which ultimately led to organ injury.^[39,40,13] NLR is the ratio of the neutrophil count to lymphocyte count, and is considered to be a marker for assessing progression and prognosis in patients with inflammation and tumor, while increased NLR indicates a poor prognosis.^[41,42] Recent studies reported that NLR was an independent risk factor for mortality of COVID-19 patients.^[43] Xia et al used multivariate logistic regression analysis to show that NLR was an independent risk factor for severe COVID-19.^[44] During the COVID-19 outbreak, there was a sudden and rapid deterioration in some patients. Virus infection leads to the imbalance of the immune regulation network of the body, and the cytokine storm will lead to the deterioration of the disease.^[1] Therefore, neutrophils and NLR are expected to be important biomarkers for effective diagnosis and prediction of clinical outcomes in COVID-19 patients. As previously mentioned, the emotional disorder itself can induce an inflammatory response. In addition, current studies believe that there is a bidirectional interaction between inflammation and mood disorders. The positive correlation between inflammation and mood symptoms has been consistently replicated. In that case, emotional disorders may worsen the COVID-19 patient's state, aggravate the inflammatory response, and have a negative impact on the clinical prognosis.^[38,45,46] Therefore, special attention should be given to patients diagnosed with high SDS scores and/or SAS score accompanied by increased neutrophils and NLR, which may indicate adverse clinical outcomes.

Regarding the relationship between sleep quality score and laboratory parameters, our study showed that NLR was increased in the low sleep quality group compared with the high sleep quality group. The correlation coefficient between the total score of PSQI and NLR was 0.310, and *P* value was .055, which was close to .05. And our study also found a positive correlation between sleep disturbance score and NLR. The NLR has already been used to reflect the relationship between sleep deprivation or poor sleep quality and levels of systemic inflammation. The NLR level was significantly increased in the sleep-deprived or low-sleep quality group in previous studies.^[47,48] Our study is consistent with previous research results. The mechanism may be linked to the sympathetic nervous system

and hypothalamus–pituitary–adrenal axis, which together shift the gene expression toward an increased pro-inflammatory state.^[49] Similarly, more attention has also been paid to the relationship between the sleep state and the immune system. Previous studies have demonstrated that the lymphocyte counts and T cell subsets were significantly reduced in the sleep disturbance or sleep deprivation group.^[50–53] Our study also found that the total score of PSQI was negatively correlated with lymphocyte count. Thus, these results indicate that sleep quality is related to inflammatory response and the immune system. In our study, compared with the non-anxiety group, NCT was prolonged in the anxiety group and with the increase of sleep disturbance score, NCT was also prolonged. Extended time for virus clearance may be related to the reduction of lymphocytes and increased inflammation in patients with mood disorders and poor sleep quality, which may have an adverse impact on the rehabilitation of the confirmed patients and would prolong the hospital stay.

However, we did not find the same correlation between stress and inflammation indicators as in previous studies, which may be related to the small sample size of this study. Mental health status, sleep quality, and inflammatory markers have a certain relevance but did not reach a significant level, due to that the patients with psychological problems in this study mainly had mild mood disorders. One reason is that most of the participants in this study were not severe cases, and the second reason is that a series of relief policies were issued to ease the mood disorders during the outbreak.

Based on the relationship of the emotional state, the sleep quality, and inflammatory markers, NCT in confirmed patients, early intervention should be considered for patients with mental disorders, poor sleep quality, and abnormal tendency of laboratory data. Regarding the relationship between mental disorder and inflammation, besides conventional antipsychotic drugs and psychotherapy, some studies have suggested that non-steroidal anti-inflammatory drugs, physical activity, probiotics, and other immunotherapy methods can be used.^[35] For sleep problems, sleep medications and cognitive-behavioral treatment for insomnia may be considered.^[54] In conclusion, it is necessary to maintain a relaxed state of mind and good sleep quality for patients confirmed with COVID-19 while treating the primary disease and strengthening against the disease.

This study presents several limitations. Our study is restricted by a low response rate and a small sample size of participants. Some patients had limited access to internet services and smartphones, and the actual number of participants was low compared to the total number of patients. Another limitation of this survey is that there are few kinds of laboratory indicators in this study. Though having more inflammatory markers would better illuminate the relationship between mental health status, sleep quality, and inflammation, most of the inflammatory markers such as ESR, CRP, pro-inflammatory factors, and T-cell subsets were not tested due to the urgency of the COVID-19 outbreak and the limitation of testing conditions in mobile cabin hospital. Therefore, the analysis of the impact on physiological indicators by mental health status and sleep quality is restricted. Further improvements will be needed in the future. Lastly, this study is a cross-sectional survey. It would be ideal to conduct a prospective study on the same group of participants that would provide a further finding to support the need for those patients. Despite these limitations, our findings may assist or remind government agencies and healthcare professionals in China and

different parts of the world to provide psychological interventions that can minimize psychological and sleeping impacts.

5. Conclusion

Patients confirmed with 2019-nCoV are prone to have some problems in mental health and sleep quality. With the aggravation of depression, anxiety, and the deterioration of sleep quality, patients may have systemic inflammation activation and decreased immune status, which may further aggravate psychological and sleep problems, thus delaying disease recovery and even leading to adverse events. If there are emotional and sleep problems, especially with the abnormal inflammatory and immune indicators, we should take active and effective comprehensive prevention and intervention measures, so as to better improve the psychological and physiological state of confirmed patients.

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