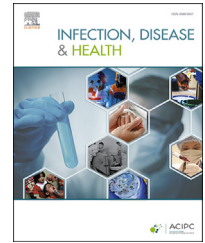ELSEVIER

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Research paper

Factors associated with the mental health status of isolated COVID-19 patients in Korea

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Abstract *Background:* The COVID-19 pandemic has a substantial impact on the physical and mental health status of patients with COVID-19. This study's objective was to evaluate the factors associated with mental health in patients isolated with COVID-19.
Methods: It is a retrospective, cross-sectional study. One hundred and two patients discharged from COVID-19 hospitalization in Korea were analyzed. The primary outcome was the correlation between psychological problems such as anxiety, depression, and fear of stigma and physical symptoms such as respiratory symptoms, gastrointestinal symptoms, headache, and fever. Mental and physical symptoms were ascertained using closed and multiple-choice questions. The secondary outcome was the correlation between mental issues, demographic factors, and disease severity. Hypoxia and the need for oxygen therapy, a need for remdesivir antiviral treatment, and indications of pneumonia progression on chest x-ray were confirmed through a review of medical records and used to measure disease severity.
Results: Patients with COVID-19 indicated feelings of depression (48.1%), anxiety (49.1%), and fear of stigma (60.45%), and some continued to experience physical symptoms even after discharge. Logistic regression revealed that gastrointestinal symptoms positively correlated with depression (p < .05) and headache positively correlated with fear of stigma (p < .05), while the other factors were not statistically significant (p > .05).
Conclusions: This study showed that psychological symptoms persisted even after discharge. Gastrointestinal symptoms and headache were influential factors in predicting depression and fear of stigma. Based on this, dedicated COVID-19 hospitals should provide mental health support and preventive management.
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Highlights

- Gastrointestinal symptoms positively correlated with depression and headache positively correlated with fear of stigma.
- COVID-19 patients showed physical and psychological symptoms even after discharge.
- Early intervention related to psychology would be needed for COVID-19 patients.

Introduction

The COVID-19 pandemic has become a global disaster, continuing unabated for more than two years [1,2]. A total of 35,701 SARS-CoV-2 infections had been reported from South Korea of Dec 03, 2020. The number of confirmed cases per 100,000 population was 69.15. Among these cases, 18,613 (52%) occurred in females. The patients who died related to COVID-19 was 529; the number of deaths per 100,000 population was 1.02. The daily number of confirmed cases is 540 as of December 3, and is gradually increasing. Similar to countries around the world, South Korea has implemented isolation policies to reduce the rates of transmission [3—5]. Isolation policies have the advantage of reducing transmission. Still, isolation causes psychological symptoms such as anxiety, depression, fear of stigma, and Posttraumatic stress disorder (PTSD) due to the disease and environmental changes [6—8]. This psychological distress is especially relevant for patients who remain in isolation for extended periods of time with limited social interactions, lack of stimulation, and loss of freedom, which may result in anger, fear, restlessness, and irritability [9]. As the number of isolated patients increases exponentially, so does the number of patients experiencing mental distress. Early intervention and preventive management are required to solve these problems [10,11].

COVID-19 is a type of viral infection that develops non-specific and broad symptoms, typically including respiratory problems such as coughing and sputum build-up, fever, headache, and gastrointestinal issues like diarrhea and constipation [12]. Most of these symptoms were only reported after discharge [13]. Some of them may be related to mental distress and could be confused with symptoms caused by the actual viral infection [14]. The more severe the physical symptoms are during isolation, the worse the depression and anxiety [15]. It is uncertain which symptoms are more commonly associated with mental distress. Early intervention can be implemented if the correlation between mental problems and physical symptoms is identified. Therefore, we investigated the correlation between mental distress and physical symptoms experienced by COVID-19 patients during and after hospitalization.

Material and methods

Study design and participants

This a retrospective, cross-sectional study using questionnaire data assessing discharged patients' information to improve the quality of in-hospital medical care. The patients who had been isolated in accountable care hospital in Korea due to COVID-19 infection were analyzed. Clinical symptoms (respiratory symptoms, digestive symptoms, fever, headache) and psychological symptoms (anxiety, depression, fear of social stigma) during isolation and after discharge were collected through telephone interviews. A structured questionnaire-based survey was conducted via a computer-aided telephonic interview. The study observed the correlation between physical symptoms and psychological problems such as anxiety, depression, and fear of stigma. We used the term 'stigma' instead of stress or worry to more directly investigate social isolation and discrimination status in patients who have experienced COVID-19 infection [16].

Non-specific symptoms were classified into four categories: respiratory symptoms such as dyspnea, cough, or sputum build-up; gastrointestinal symptoms such as diarrhea, abdominal pain, or constipation; headache, and fever. Secondary outcomes included the correlation between mental problems, demographic factors, and disease severity. Hypoxia and oxygen requirement, the need for remdesivir antiviral treatment, and indications of pneumonia progression on CXR were indicators of disease severity. From December 1, 2020, to December 3, 2020, the survey data and epidemiological factors were compared through an electronic medical records (EMR) review.

Methodology

The COVID-19 screening tool used for the telephone interviews was developed through peer-review and a multidisciplinary team. The participant's symptoms addressed in the screening tool were respiratory symptoms, gastrointestinal symptoms, fever, headache, and psychological problems, including depression, anxiety, and fear of stigma. The screening tool comprised seven questions administered telephonically to participants after being discharged from COVID-19 treatment. Patients were called at various times throughout the day to increase the chance of success. Informed verbal consent to proceed with telephonic consultation was obtained. The survey consisted of closed and multiple-choice questions. Fear of stigma and physical symptoms such as respiratory, gastrointestinal, headache, and fever were assessed using closed questions. The degree of depression and anxiety was evaluated on a 4-point Likert scale. The categories were "severe," "moderate," "sometimes," and "almost never."

A focused review of the medical admission records was conducted to identify demographic data, comorbidities,

oxygen requirements, antiviral treatment, and length of hospital stay.

Statistical analysis

We used SPSS version 22 for statistical analyses. Descriptive statistics were used to summarize participants' demographic characteristics. We performed a Pearson correlation analysis and logistic regression analysis to estimate the relationship between the patients' psychological symptoms such as anxiety, depression, and fear of stigma and physical symptoms such as respiratory, gastrointestinal, fever, and headache. Association between persistent symptoms, participant characteristics such as disease severity, and psychological problems was analyzed. We used ordinal logistic regression analysis of the quality of life outcomes in the ordered response category versus one or more persistent symptoms. Statistical significance was set at $p < .05$ for all analyses.

Results

Patient demographics and clinical characteristics

A total of 102 participants completed the survey, with females accounting for 53 of them (52%). The mean age of the patients was 55.5 ± 16.7 years. Hypertension was the most common comorbidity among the participants (17.6%). Fifteen patients (4.4%) were hospitalized for more than 15 days. Seventeen patients (16.75%) were transferred from the Community Treatment Center; a community-based isolation facility converted from private dormitories and state-run institutions [17]. At discharge, there were 53 patients (52%) without pneumonia on chest x-ray (CXR), 25 patients (24.5%) with improved pneumonia, and 24 patients (23.5%) with stationary pneumonia. Thirteen patients (12.7%) underwent oxygen therapy due to hypoxia, and 54 patients (54.9%) had pneumonia at hospitalization. Nine patients (8.8%) were prescribed remdesivir, a coronavirus RNA polymerase inhibitor, and treatment used for coronavirus patients with pneumonia needing oxygen therapy [18]. After discharge, the average score of psychological symptoms surveyed on a 4-point Likert scale was $3.3 \pm .9$ for anxiety, 3.2 ± 1.0 for depression, and $1.4 \pm .5$ for fear of stigma. The patients' general demographic and clinical characteristics are summarized in Table 1.

Prevalence of physical and psychological symptoms

The most frequent symptoms occurring during isolation recalled by the participants were fever (50, 47.2%), respiratory symptoms (47, 44.3%), headaches (31, 29.2%), gastrointestinal symptoms (24, 22.6%). At the time of survey after discharge, physical symptoms of participants were respiratory (21, 19.8%), gastrointestinal (11, 10.4%), fever (11, 10.4%), and headache (12, 11.3%). Majority of the patients also had the following psychological symptoms after discharge: fear of stigma (64, 60.45%), anxiety (52, 49.1%), and depression (51, 48.1%) (Table 2).

Psychological variables and factors

Correlations between physical symptoms and psychological variables are presented in Table 3. Pulmonary symptoms did not correlate with psychological symptoms. Gastrointestinal symptoms correlated with anxiety ($p < .001$),

Table 1 Demographic data and clinical characteristics of patients.

		COVID-19 Patients (N = 102) N (%)
Age, median (SD)		55.5 (16.7)
Gender (N of Female)		53 (52.0)
Comorbidity	Hypertension	18 (17.6)
	DM	8 (7.8)
	CAD	2 (2.0)
	CVD	2 (2.0)
HD, median (SD)		15.0 (4.4)
Transfer Hx[a]		17 (16.7)
CXR at discharge[b]	Normal	53 (52.0)
	Improved pneumonia	25 (24.5)
	Stationary pneumonia	24 (23.5)
Clinical finding	Hypoxia (Sat ≤95%)	13 (12.7)
	O2 therapy	13 (12.7)
	Pneumonia[c]	54 (54.9)
	Remdesivir[d] use	9 (8.8)

Abbreviations: DM, diabetes mellitus; CAD, coronary artery disease; CVD, cerebrovascular disease; HD, hospital day for admission; CXR, chest X-ray; Sat, saturation.
  [a] Transferred from the Community Treatment Center to hospital due to disease progression.
  [b] Findings at discharge compared with lesions observed on CXR during hospitalization. According to the quarantine principle in Korea, an immobilized pneumonic infiltrate in the CXR of an asymptomatic patient 10 days after diagnosis is interpreted as non-infectious.
  [c] Pneumonia was observed in CXR by a radiologist's reading.
  [d] Anti-viral therapy using Remdesivir due to disease progression, including pneumonia.

Table 2 Prevalence of physical and psychological symptoms (N = 102).

	Symptom	N (%)
During isolation	The presence of respiratory symptoms during inpatient treatment	47 (44.3)
	The presence of gastrointestinal symptoms during inpatient treatment	24 (22.6)
	The presence of fever[a] during inpatient treatment	50 (47.2)
	The presence of headache during inpatient treatment	31 (29.2)
After discharge	The presence of respiratory symptoms after discharge	21 (19.8)
	The presence of gastrointestinal symptoms after discharge	11 (10.4)
	The presence of fever[a] after discharge	11 (10.4)
	The presence of headache after discharge	12 (11.3)
	Depression, N (%)	51 (48.1)
	Median (SD)[b]	3.3 (.9)
	Anxiety, N (%)	52 (49.1)
	Median (SD)[b]	3.2 (1.0)
	Fear of stigma, N (%)	64 (60.4)

[a] Fever was determined when the body temperature was 37.5 °C or higher.
[b] The severity of depression and anxiety were evaluated using a 4-point Likert scale.

depression (p < .001), and fear of stigma (p < .05). Fever correlated with depression (p < .05). Headache correlated with anxiety (p < .001), depression (p < .001), and fear of stigma (p < .001). There was no correlation between demographic and psychological variables (Table 4).

Table 5 shows the impact of physical symptoms on mental problems. Gastrointestinal symptoms were positively associated with depression (OR = 3.857, 95% CI [1.178, 12.629]). Headache was positively associated with fear of stigma (OR = 4.178, 95% CI [1.213, 14.399]). The other factors were not statistically significant (p > .05).

Discussion

Our study is the first on the association between mental problems and COVID-19 related symptoms in South Korea to the best of our knowledge. According to our study, patients with gastrointestinal symptoms were more likely to suffer from depression (OR = 3.857, 95% CI [1.178, 12.629], p = .026) and anxiety symptoms (OR = 2.779; 95% CI,.893—8.649; p = .078). Depressive symptoms were statistically significantly higher. This agrees with previous studies that the degree of gastrointestinal symptoms correlates with depressive and anxiety symptoms [19—21].

Table 3 Pearson correlations matrix for physical symptoms and psychological variables.

	1	2	3	4	5	6	7
1. Pulmonary sx	—	.473**	.372**	.301**	.136	.193	.186
2. GI sx		—	.335**	.488**	.288**	.346**	.199*
3. Fever			—	.461**	.176	.235*	.126
4. Headache				—	.290**	.303**	.301**
5. Anxiety					—	.470**	.489**
6. Depression						—	.312**
7. Fear of stigma							—

Abbreviations: sx, symptoms; GI, gastrointestinal. *p < .05, **p < .001.

Gastrointestinal symptoms increase the risk of depressive, anxiety, sleep, and bipolar disorders and significantly reduce the quality of life due to recurrent symptoms [22,23]. Patients with depressive tendencies (PHQ-9 score ≥15) had presented with one or more gastrointestinal symptoms for at least four weeks. Moreover, patients with depression reported more gastrointestinal symptoms, with higher Gastrointestinal Symptom Rating Scale (GSRS) scores, contributing to greater depression severity [24,25]. Bidirectional communication has been proposed as a theory that supports this phenomenon [26]. According to the study, gastrointestinal symptoms can overlap with depression and relatively affect each other. Similarly, increased activation of brain regions such as the anterior cingulate cortex, thalamus, and prefrontal cortex in response to visceral stimuli in patients with non-organic abdominal pain has been reported [27]. These brain regions overlap considerably with regions involved in emotion regulation, forming a theoretical basis for the coexistence of gastrointestinal symptoms and depression [28,29]. However, COVID-19 is a viral infection, and various non-specific symptoms are expressed. Diarrhea, constipation, and abdominal pain are among the most commonly observed gastrointestinal symptoms associated with COVID-19 infection [30]. Therefore, doctors have tended to treat the gastrointestinal symptoms as manifestations of the viral infection. Based on the results of this study, we believe that it is necessary to consider the possibility of symptoms related to depressive mood, not just of viral infection. According to the brain-gut bidirectional correlation theory, it is hypothesized that treating gastrointestinal symptoms can reduce depression, while managing these psychological factors can conversely help treat gastrointestinal symptoms. Therefore, it is necessary to provide additional interventions for patients with gastrointestinal symptoms by performing a screening evaluation on mood change and symptomatic therapy to relieve symptoms in patients with gastrointestinal symptoms.

Headache was associated with fear of stigma (OR = 4.178, 95% CI [1.213, 14.399], p = .023), anxiety (OR = 2.511, 95% CI [.392, 6.888], p = .074), and

Table 4 Pearson correlations matrix for demographic factors and psychological variables.

	1	2	3	4	5	6	7	8	9	10	11
1. Gender	—	.242*	-.061	.052	.280**	.254**	-.027	.070	.038	-.100	-.132
2. Age		—	.203*	-.223*	-.237*	-.204*	-.369**	-.367**	.129	-.069	.022
3. Transfer Hx[a]			—	.063	-.171	-.139	-.171	.091	-.018	-.061	.027
4. Prolonged HD[b]				—	.346**	.238*	.153	.406**	.156	.052	.110
5. O2 Tx					—	.814**	.300**	.419**	.037	.044	-.123
6. Remdesivir Tx[c]						—	.257**	.402**	.041	.047	-.040
7. Comorbidity							—	.153	-.085	-.075	-.127
8. CXR at discharge[d]								—	.077	.094	-.002
9. Anxiety									—	.470**	.489**
10. Depression											.312**
11. Fear of stigma											—

Abbreviations: Hx, history; Tx, treatment; HD, hospital day for admission, *p < .05, **p < .001.
[a] Transferred from the Community Treatment Center to hospital due to disease progression.
[b] Prolonged hospitalization due to disease progression.
[c] Anti-viral therapy using Remdesivir due to disease progression, including pneumonia.
[d] Findings at discharge compared with lesions observed on CXR during hospitalization.

Table 5 Logistic regression analysis between persistent psychological problem and various clinical symptoms.

	Variables	β	Exp(B)	95% CI	p-value
Anxiety	GI sx	1.022	2.779	(.893−8.649)	.078
	Headache	.921	2.511	(3915−6.888)	.074
Depression	GI sx	1.350	3.857	(1.178−12.629)	**.026***
	Fever	.390	1.477	(.592−3.683)	.403
	Headache	.704	2.023	(.687−5.951)	.201
Fear of stigma	GI sx	.433	1.542	(.449−5.297)	.492
	Fever	-.095	.909	(.362−2.283)	.839
	Headache	1.430	4.178	(1.213−14.399)	**.023***

Abbreviations: Sx, symptom. *p < .05, **p < .001.

depression (OR = 2.033, 95% CI [.687, 5.951], p = .201). A significantly high correlation between headache and fear of social stigma was observed. In previous studies, the association between headache and psychiatric comorbidity was high. High significance was observed in guilt, anxiety, and depression [31,32]. According to a review article by Heckman and Holroyd [31], the number of patients complaining of a negative affective state was significantly increased in the patient group complaining of headache—tension-type headache (TTH) in particular. In addition, it was found that stressful events often accompany TTH as a maladaptive process to avoid catastrophic events. Participants enrolled in this study were exposed to the catastrophic event of COVID-19 and were sometimes socially criticized. Considering that Korea's isolation system exposes individual movement and privacy, exposing patients to societal criticism can be seen as a limitation. Thus, headaches can be caused not only by viruses, but also by social guilt or hysterical tendencies. It would be desirable to consider cognitive behavioral and drug therapy by conducting psychosocial evaluations using the appropriate screening tool. In particular, considering the contagiousness of COVID-19, Internet-based cognitive behavioral therapy can be performed remotely, which can be an effective treatment [33].

Previous studies have reported that COVID-19 patients complain of psycho-emotional distress such as anxiety, depression, insomnia, and social stigma when hospitalized [25,34]. In our study, about 50% of all our participants complained of psychological symptoms such as depression (48.1%), anxiety (49.1%), and fear of social stigma (60.45%) even after discharge (Table 2). The symptoms persisted even after being released from isolation at the hospital after diagnosis. Psychosocial distress and related physical symptoms may persist even after COVID-19 infection has improved. This could be explained by the chain mediation model of COVID-19 introduced by Wang et al. According to a chain mediation model, physical symptoms are positively correlated with mental distress [35]. There was a sequential mediating effect in which physical symptoms were associated with the need for health information, which in turn was associated with adverse mental health outcomes (i.e., anxiety, depression, and stress). Therefore, interventions that can provide emotional support to isolated COVID-19 patients by performing psycho-emotional evaluation of at-risk groups from the time of hospitalization are necessary.

Several factors limited this study. The results are based on a cross-sectional analysis and correlations; therefore, causation cannot be inferred. A standardized scale for mental distress was not available due to the limitations of the telephone questionnaire, and thus the degree of correlation between disease severity and clinical status could not be precisely investigated. The survey was obtained via self-report after discharge, which can be subject to recall bias and retrospective response bias. The sample size was small, and social risk factors such as loss of income and social and family support problems were not considered. We did not study the association with cognitive dysfunction, which has been found to be closely related to mental distress [36]. Therefore, further complementary studies should be conducted.

Nevertheless, the following conclusions can be drawn from this study. Psychological symptoms were present in isolated patients with COVID-19 during and after hospitalization. Gastrointestinal symptoms and headache correlated with depression and fear of stigma, respectively. Based on these findings, psychological screening, and appropriate preventive management for patients with isolated COVID-19 are necessary.

Ethics

The Institutional Review Board approved the study (B-2106-688-107).

Authorship statement

Conceptualization: Jae Hyu Jung, Jin Young Ko.
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Methodology: Jae Hyu Jung, Jin Young Ko.
Project administration: Jin Young Ko.
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Conflict of interest

No commercial party having a direct financial interest in the results of the research supporting this article has or will confer any benefit upon the authors or upon any organization with which the authors are associated.

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