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Symptom changes in patients with pre-existing psychiatric disorders in the initial phase of the COVID-19 pandemic: Vulnerability of female patients and patients with mood disorders

Shin Kurose [a,b,c,*], Michitaka Funayama [a], Taketo Takata [a], Yusuke Shimizu [a,d], Yu Mimura [a,b], Shun Kudo [a,b,e], Satoyuki Ogino [a,d], Masaru Mimura [b]

[a] Department of Neuropsychiatry, Ashikaga Red Cross Hospital, Tochigi, Japan
[b] Department of Neuropsychiatry, Keio University School of Medicine, Tokyo, Japan
[c] Department of Functional Brain Imaging, National Institutes for Quantum and Radiological Science and Technology, Chiba, Japan
[d] Department of Trauma and Critical Care Medicine, Kyorin University School of Medicine, Tokyo, Japan
[e] Department of Psychiatry, Saitama City Hospital, Saitama, Japan

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ABSTRACT

How patients with pre-existing psychiatric disorders are responding to the COVID-19 pandemic remains unclear, and no comprehensive studies have yet been performed. To elucidate (1) which psychiatric disorders were exacerbated during the initial phase of the COVID-19 pandemic and (2) the contributing factors, we prospectively assessed psychiatric symptoms of 1592 psychiatric outpatients in a single-center study using the Global Assessment of Functioning (GAF) before the state of emergency was declared in Japan and during two months under the state of emergency (study period: April 8 to June 7, 2020). We conducted a chi-squared test for the relationship between psychiatric diagnostic category (ICD-10) and exacerbation. To control for confounders, we conducted a logistic regression analysis using sex, age, diagnostic category, and pre-pandemic GAF score as independent variables. Exacerbation rates of patients with mood disorders (F3) and neurotic disorders (F4) were 4.32% and 5.37%, respectively, and were significantly higher than those for patients with organic disorders (F0) and schizophrenic disorders (F2) (X^2 (9, N = 1592) = 27.8, $p < .01$). Logistic regression analysis revealed that patients with F3 and female patients were significantly more affected than patients with other disorders or male patients, respectively (odds ratio (95% confidence interval) = 2.4 (1.2–4.6), $p < .01$ for F3; 3.1 (1.5–6.6), $p < .01$ for females). These findings suggest a need for careful management of patients with mood disorders and female psychiatric patients during a pandemic.

1. Introduction

Since December 2019, the outbreak of coronavirus disease (COVID-19) has spread quickly from China to the entire world, leading to approximately 263 million reported cases and 5.2 million deaths globally as of December 3, 2021 (https://www.who.int/emergencies/diseases/novel-coronavirus-2019). In particular, Asia and Italy were the centers of the pandemic in the initial phase (Tandon, 2020). The COVID-19 pandemic is believed to increase the risk of mental health problems not only because of the threat of an unknown and unpredictable infection, but also because of associated containment strategies such as lockdowns and social isolation as well as economic breakdown (Moreno et al., 2020; Tandon, 2021a). Several reports have pointed out the risk of exacerbation of conditions in patients with pre-existing psychiatric disorders, including major depressive disorders, anxiety disorders, schizophrenia, eating disorders, dementia, and developmental disorders (Moreno et al., 2020). However, most of these reports are based on expert opinions and a few observational studies conducted specifically for a certain psychiatric disease category, such as mood disorders or anxiety-related disorders (Asmundson et al., 2020; Hao et al., 2020). No such study has yet examined all psychiatric disorders. In addition, those studies were conducted cross-sectionally by online

Abbreviations: COVID-19, coronavirus disease; GAF, Global Assessment of Functioning; ICD-10, International Classification of Diseases 10; PTSD, post-traumatic stress disorder.

* Correspondence to: Department of Neuropsychiatry, Keio University School of Medicine, 35 Shinanomachi, Shinjuku-ku, Tokyo 160-8582, Japan.
E-mail address: skurose@keio.jp (S. Kurose).

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self-questionnaires. As a result, it is not yet known which clinical observations psychiatrists should pay most attention to in managing patients with pre-existing psychiatric disorders during this pandemic. More precisely, it is not yet known which psychiatric disorders are exacerbated in a pandemic or what underlying factors contribute to the risk for exacerbation. Some studies have examined how psychiatric patients responded to pandemic outbreaks such as severe acute respiratory syndrome (SARS), Middle East respiratory syndrome (MERS), and influenza (Banerjee, 2020). Other studies have investigated changes in psychiatric symptoms after natural disasters like earthquakes and hurricanes (Katz et al., 2002). Findings on post-traumatic stress disorder (PTSD) may also provide insights into the responses of psychiatric patients to disasters. Most reports indicate that patients with pre-existing mood disorders experience exacerbation of psychiatric symptoms, whereas those with pre-existing schizophrenia do not (Katz et al., 2002). However, DeLisi and colleagues (DeLisi et al., 2004) showed the opposite result following the United States World Trade Center disaster on September 11, 2001: significantly more psychiatric inpatients with schizophrenic spectrum disorders experienced a worsening of symptoms. It is possible that not only differences in the nature of the disaster but also other elements, such as demographics and psychiatric conditions before the disaster, influence these contradictory results. For example, female dominance in PTSD is well established (Christiansen and Berke, 2020; Katz et al., 2002) and severely ill psychiatric patients show almost no reaction to disasters (Funayama and Mizushima, 2013; Katz et al., 2002). The effect of age in PTSD is currently unclear (Bokszczanin, 2007; Norris et al., 2002). To elucidate how patients with pre-existing psychiatric disorders have responded to the COVID-19 pandemic, we conducted the first prospective observational study that examines (1) the exacerbation rate of symptoms in patients with pre-existing psychiatric disorders for each diagnostic category in the initial phase of the pandemic, and (2) how age, sex, and severity of illness before the pandemic influence exacerbation.

2. Material and methods

This study was conducted at Ashikaga Red Cross Hospital in Tochigi prefecture, located ~80 km (~50 miles) north of Tokyo, Japan. Ethical aspects of this study were reviewed and approved by the Ashikaga Red Cross Hospital Human Research Ethics Committee.

2.1. Study design

This was a prospective observational study. The observation period was from April 8 to June 7, 2020, corresponding to the 2-month period after a state of emergency was declared in Japan on April 7. The study period was slightly longer than the state of emergency, which lasted until May 25. We compared psychiatric conditions during the study period with those before the state of emergency was declared. In the initial phase of the COVID-19 pandemic, the number of infected individuals in Japan was small compared with Western countries (https://www.who.int/emergencies/diseases/novel-coronavirus-2019), but it had increased rapidly in the end of March (mainly in Tokyo) and spread was predicted to become similar to that in Western countries. Thus, the Japanese government declared a state of emergency from April 7 to May 25. Under the state of emergency, there was no mandatory lockdown as in other countries due to Japanese law (Yan et al., 2020). Instead, the Japanese government requested people's voluntary "self-restraint", which resulted in a practical lockdown as follows. Even without legal restriction, most Japanese citizens kept in voluntary "self-restraint" because Japan is associated with tight culture, in which they attach importance to group solidarity and orders, as result of a Confucius's legacy (Yan et al., 2020). The school was closed, restaurants were closed voluntarily, and most events such as the Tokyo Olympics were postponed.

2.2. Participants

We targeted outpatients in the outpatient clinic affiliated with Ashikaga Red Cross Hospital who had been diagnosed with psychiatric disorders using International Classification of Diseases 10 (ICD-10) diagnostic criteria prior to the COVID-19 pandemic. Diagnoses included F0 (organic, including symptomatic, mental disorders), F1 (mental and behavioral disorders due to psychoactive substance use), F2 (schizophrenia, schizotypal, and delusional disorders), F3 (mood disorders), F4 (neurotic, stress-related, and somatoform disorders), F5 (behavioral syndromes associated with physiological disturbances and physical factors), F6 (disorders of adult personality and behavior), F7 (mental retardation), F8 (disorders of psychological development), and F9 (behavioral and emotional disorders with onset usually occurring in childhood and adolescence). Diagnosis of each psychiatric disorder was determined by agreement of two board-certified psychiatrists (M.F and T.T). If there were multiple diagnosis, we adopted the main diagnosis. We included subjects who attended outpatient appointments from April 8 to June 7. We excluded those who did not attend the clinic during the study period despite having scheduled appointments. Informed consent was obtained in the form of opt-out on the web-site. Those who rejected were excluded.

2.3. Variables

During ordinary outpatient treatments, we evaluated severity of illness by using the Global Assessment of Functioning (GAF) assessment based on interviews with patients and information from their caregivers or close relatives (Aas, 2011). All raters were highly experienced psychiatric attending physicians trained in evaluation of GAF scores. For each patient, a GAF score was obtained by the same attending physician at two points in time, i.e., once prior to the state of emergency and once during the study period. The GAF score measures how much a person's psychological symptoms impact their daily life. The scale ranges from 0 (worst) to 100 (best). This assessment has the advantage of evaluating psychiatric symptoms across all psychiatric diagnostic categories (F0-F9), whereas other commonly used psychiatric scales focus on a particular diagnostic category. The starting GAF score for each patient was administered and calculated before the first visit following the start of the state of emergency (i.e., on April 7). The second GAF score was conducted during a visit to the clinic during the study period. We considered a change of $\geq$ 10 points to be a significant change in symptoms based on a previous inter-rater reliability study suggesting that a change of 10 points would not be due to differences among raters (Lindström et al., 1994). As predictor variables that might be associated with changes in symptoms, we collected the following demographic data: age (Bokszczanin, 2007; Norris et al., 2002), sex (Christiansen and Berke, 2020; Katz et al., 2002), diagnostic category (Katz et al., 2002), and GAF score before the COVID-19 pandemic (Funayama and Mizushima, 2013; Katz et al., 2002).

To determine whether exacerbation of a patient's psychiatric symptoms was caused by the COVID-19 pandemic, the attending physician for each patient discussed their findings with the two staff psychiatrists, S.K. and M.F., who judged the relationship between the change in symptoms and the pandemic. A deterioration of psychiatric symptoms due to the pandemic was counted only when both staff psychiatrists assessed that the deterioration was caused by the pandemic.

2.4. Data analysis

In order to identify factors associated with exacerbation of psychiatric symptoms associated with the pandemic in the study subjects, we performed the following statistical analyses using R (R Foundation for Statistical Computing, Vienna, Austria, version 4.0.2). First, a chi-squared test of independence was employed to assess the relationship between psychiatric diagnostic categories (F0–9) and exacerbation of

psychiatric symptoms associated with the pandemic. Further, as a post hoc analysis, residual analysis was performed to investigate significant differences among diagnostic categories. For a multiple testing correction, p values were corrected by the Benjamini & Hochberg method (Benjamini and Hochberg, 1995). Second, a Student's t-test was employed to evaluate the difference in age or severity of illness (GAF score) between patients with exacerbation and those without. Finally, logistic regression analyses were performed using independent variables (sex, age, diagnostic category, and GAF score before the pandemic) and exacerbation of psychiatric symptoms as a dependent variable to account for potential cofounding factors. p values < 0.05 were considered significant.

3. Results

A total of 1610 outpatients with pre-existing psychiatric disorders were scheduled to visit our hospital in the first 2 months after the start of the state of emergency. Among those outpatients, 18 did not consult us during the 2-month study period. 15 of those 18 outpatients finally consulted us within six months after the observation period with no change of symptoms during the period and the remaining 3 did not consult us within six months after the observation period. Therefore, 1592 psychiatric outpatients (711 males, 881 females; age = 55.6 (37.3–73.9) years, mean ± standard deviation) were included in the analysis. Demographic and clinical characteristics are summarized in Table 1. There were more females than males in all but three groups (F0, F1, and F8). There was a significant association between sex and diagnostic category (X^2 (9, N = 1592) = 73.6, $p < .01$), with male dominance among F0, F1, and F8 patients, and female dominance among F2, F3, F4, F5, F6, F7, and F9 patients. There was also a significant association between age and diagnostic category (one-way ANOVA: $F(9, 1582) = 32.5$, $p < .01$), with F0, F1, F2, and F3 patients being on average over 50, and F5, F6, F7, F8, and F9 patients being on average under 50. Likewise, there was a significant association between mean GAF score before the study period and diagnostic category (one-way ANOVA: $F(9, 1582) = 40.0$, $p < .01$), with mean scores of > 70 for F4, F5, and F9, but < 60 for F0, F2, F5, F6, and F7.

Table 1
Demographics and characteristics of outpatients with pre-existing psychiatric disorders.

Diagnosis	Male (N = 711)	Female (N = 881)	Total (N = 1592)	Age (mean ± SD)	GAF score (mean, SD) before study	GAF score (mean, SD) during study
F0 (organic, including symptomatic, mental disorders)	201 (58.8%)	141 (41.2%)	342	62.0 (18.7)	57.5 (17.0)	57.1 (17.8)
F1 (mental and behavioral disorders due to psychoactive substance use)	17 (81.0%)	4 (19.0%)	21	57.2 (10.2)	60.0 (15.7)	60.0 (15.4)
F2 (schizophrenia, schizotypal and delusional disorders)	137 (40.7%)	200 (59.3%)	337	50.2 (15.4)	55.0 (15.6)	54.4 (16.2)
F3 (mood disorders)	219 (39.4%)	337 (60.6%)	556	60.1 (16.2)	70.2 (14.8)	69.2 (15.5)
F4 (neurotic, stress-related and somatoform disorders)	80 (39.0%)	125 (61.0%)	205	52.3 (19.5)	71.1 (11.0)	69.9 (12.7)
F5 (behavioral syndromes associated with physiological disturbances and physical factors)	0 (0%)	19 (100%)	19	41.4 (12.4)	55.3 (14.7)	54.2 (15.7)
F6 (disorders of adult personality and behavior)	4 (30.8%)	9 (69.2%)	13	44.7 (14.0)	58.8 (12.1)	58.8 (12.1)
F7 (mental retardation)	17 (42.5%)	23 (57.5%)	40	46.7 (14.6)	52.3 (14.3)	50.8 (15.1)
F8 (disorders of psychological development)	35 (62.5%)	21 (37.5%)	56	31.3 (14.2)	66.3 (13.2)	64.1 (16.7)
F9 (behavioral and emotional disorders with onset usually occurring in childhood and adolescence)	1 (33.3%)	2 (66.7%)	3	20.3 (6.7)	73.3 (17.6)	73.3 (17.6)

Table 2a
Relationship between diagnostic category and exacerbation of psychiatric symptoms associated with COVID-19 pandemic.

Diagnosis	N with exacerbation	Rate*	R_{adj}**	p value***
F0 (organic, including symptomatic, mental disorders)	1	0.29%	–3.14	0.017
F1 (mental and behavioral disorders due to psychoactive substance use)	1	4.76%	0.56	0.638
F2 (schizophrenia, schizotypal and delusional disorders)	2	0.59%	–2.73	0.021
F3 (mood disorders)	24	4.32%	2.76	0.021
F4 (neurotic, stress-related and somatoform disorders)	11	5.37%	2.43	0.037
F5 (behavioral syndromes associated with physiological disturbances and physical factors)	0	0.00%	–0.73	0.638
F6 (disorders of adult personality and behavior)	0	0.00%	–0.61	0.638
F7 (mental retardation)	2	5.00%	0.87	0.638
F8 (disorders of psychological development)	3	5.36%	1.2	0.456
F9 (behavioral and emotional disorders with onset usually occurring in childhood and adolescence)	0	0.00%	–0.29	0.77

* X2 (9, N = 1592) = 27.8, p < .01
** Adjusted standardized residual
*** Multiple correction by Benjamini & Hochberg method

Table 2b
Age, sex, and GAF Score in groups with and without exacerbation of psychiatric symptoms

	Groups with exacerbation (N = 44)	Groups without exacerbation (N = 1548)	p value
Age, y *	52.6 (18.8)	55.7 (18.3)	.26
Sex (male), %**	20.5	45.3	< 0.01
GAF score at start of study*	65.8 (11.9)	63.3 (16.7)	.33

Data presented as mean (SD) unless otherwise indicated;
* Student's t-test
** chi-squared test

3.1. Exacerbation rates and factors that influence psychiatric conditions associated with the COVID-19 pandemic

As shown in Table 2a, there was a significant relationship between diagnostic category and exacerbation of psychiatric symptoms associated with the COVID-19 pandemic (X^2 (9, N = 1592) = 27.8, $p < .01$). F3 and F4 patients had exacerbation rates of 4.32% and 5.37%, respectively; these were significantly higher than the exacerbation rates for F0 and F2 patients.

As shown in Table 2b, there was a significantly higher exacerbation risk in female patients than in male patients (X^2 (1, N = 1592) = 9.74, $p < .01$), but no significant difference in exacerbation risk associated with age or severity of illness (GAF scores at start of study).

Based on the above findings, we performed logistic analyses for exacerbation of psychiatric symptoms associated with the COVID-19 pandemic in F3 and F4, the results of which are summarized in Table 3. There was a significantly higher exacerbation risk in patients with F3 (mood disorders) and in female patients compared with patients with other than F3 and male patients, respectively (odds ratio [OR] (95% confidence interval [CI]) = 2.4 (1.2–4.6), $p < .01$ for F3; 3.1 (1.5–6.6), $p < .01$ for female patients). This was not the case when using F4 as a diagnostic independent variable, where no significant exacerbation risk was found (OR (95% CI) = 2.0 (0.97–4.1), $p = .06$ for F4; 3.2 (1.5–6.7), $p < .01$ for female patients). However, the p value for F4 was 0.06, suggesting that a tendency for exacerbation risk among F4 patients.

3.2. Clinical features of patients with exacerbated psychiatric disorders

Among the 24 mood disorder (F3) patients whose conditions worsened, the overwhelming majority (N = 23) exhibited depression, while only 1 exhibited mania. The same was true of bipolar disorder, with 4 out of 5 patients having depression and 1 having mania. Among the 11 neurotic disorder (F4) patients whose conditions worsened, 6 had increased anxiety, 3 developed depression, 2 exhibited a heightened washing compulsion due to fear of infection, and 1 had dissociative stupor.

Among patients with schizophrenic disorders (F2), 2 had worsened conditions and developed psychosis. Interestingly, the exacerbation of mood disorders may be relevant to these patients, as both had schizoaffective disorder, which is more similar to mood disorders than to schizophrenia itself. The 2 patients with mental retardation (F7) who experienced exacerbation exhibited sudden agitation after hearing that one of the most popular Japanese comedians died from COVID-19, which made headlines in Japan for several days. Two pediatric patients with autism spectrum disorders (F8) frequently threw tantrums after environmental changes such as school closure and isolation at home. A patient with alcoholism (F1) and a patient with an autism spectrum disorder (F8) increased their consumption of alcohol because they were bored in isolation.

Among the 44 patients whose conditions declined, 39 showed significant improvement with adjustments to psychotropic drugs in outpatient treatment, whereas 5 required hospitalization. Table 4 summarizes the clinical course of the hospitalized cases. Two female patients presented with depression in major depressive disorder, 1 male patient with mania in bipolar disorder, 1 female patient with stupor in dissociative disorder, and 1 female patient with agitation in mental retardation.

4. Discussion

The most remarkable observations to emerge from the data were that patients with mood disorders and female patients were more affected by the COVID-19 pandemic than patients with other psychiatric disorders and male patients, respectively, even after controlling for age and the severity of symptoms before the pandemic as covariates. Our study offers several advantages compared with previous studies that have investigated symptom changes in patients with pre-existing psychiatric disorders after disasters including the COVID-19 pandemic (Asmundson et al., 2020; Hao et al., 2020): (1) it is a longitudinal study that controls for potential confounding factors (age, severity of disorder); (2) it targets all mental disorders; (3) it has the largest sample size (1592 vs. 76, 1068); (4) it investigates factors influencing exacerbation; and (5) it evaluates psychiatric symptoms as reported by psychiatrists rather than online self-questionnaires.

From the viewpoint of stress reactions, our results are consistent with various previous findings. As discussed above, pre-existing mood disorders are believed to be risk factors for further deterioration after a disaster and are related to PTSD (Katz et al., 2002). Furthermore, sex is a well-established factor in response to disasters, with women being twice

Table 3
Logistic regression analyses for exacerbation of psychiatric symptoms in F3 and F4 patients.

	Independent variables	Estimate	SE	z value	p value	OR (95% CI)
F3 (mood disorders)	Prior F3 diagnosis	0.87	0.33	2.6	0.0088	2.4 (1.2–4.6)
	Age	–0.016	0.0088	–1.8	0.066	0.98 (0.97–1.0)
	Sex (female)	1.1	0.38	3	0.0026	3.1 (1.5–6.6)
	GAF score at start of study	0.0022	0.01	0.21	0.83	1.0 (0.98–1.02)
F4 (neurotic, stress-related and somatoform disorders)	Prior F4 diagnosis	0.69	0.37	1.9	0.06	2.0 (0.97–4.1)
	Age	–0.0092	0.0084	–1.1	0.27	0.99 (0.97–1.0)
	Sex (female)	1.2	0.38	3.1	0.0023	3.2 (1.5–6.7)
	GAF score at start of study	0.0061	0.01	0.61	0.54	1.0 (0.99–1.02)

Abbreviations: CI, confidence interval; OR, odds ratio; SE, standard error.

Table 4
Characteristics and psychiatric symptoms of hospitalized patients.

	Age	Sex	Diagnosis	Observations
Case 1	54	Female	Major depressive disorder	Fearful of becoming infected with COVID-19, she was isolated at home. She became depressed with agitation and was hospitalized. She received electroconvulsive therapy.
Case 2	64	Male	Bipolar disorder	Due to the COVID-19 pandemic, he took a leave of absence. He relapsed into mania and talked constantly about the pandemic.
Case 3	29	Female	Dissociative disorder	Fearful of becoming infected with COVID-19, she lapsed into a dissociative stupor.
Case 4	36	Female	Mental retardation	After hearing that a popular comedian died from COVID-19, she became agitated.
Case 5	40	Female	Major depressive disorder	Due to the COVID-19 pandemic, she was isolated at home. She relapsed into depression and took an overdose (100 tablets or more) of psychotropic drugs.

as likely as men to develop PTSD (Christiansen and Berke, 2020). During the COVID-19 pandemic, a population-based study based on online self-questionnaires reported that patients with pre-existing mood disorders had higher scores of traumatic stress symptoms than healthy subjects (Asmundson et al., 2020). Although pre-existing anxiety disorder (F4) has been considered a risk factor for exacerbation after a disaster (Katz et al., 2002), our study did not show a statistical significance, but only a tendency. In neurotic disorders (F4), exacerbation of obsessions and hand-washing compulsion was observed in two cases in our study. This was also reported in previous outbreaks of SARS, MERS, and influenza (Banerjee, 2020), and may be more directly related to the nature of infectious diseases. Our results also supported previous findings that patients with schizophrenia show less reaction to a disaster (Katz et al., 2002). There were only a few cases that presented with mania in our study, which was inconsistent with a previous report in which patients with bipolar disorder got worse and were more likely to exhibit manic switches than depression one month after the Great East Japan Earthquake and the subsequent Fukushima nuclear disaster (Matsumoto et al., 2014). This suggests that the response of patients with bipolar disorder may depend on the nature of the disaster.

This study did not confirm earlier findings that psychiatric patients with severe symptoms do not respond to a disaster (Funayama and Mizushima, 2013; Katz et al., 2002). This may in part be because our study targeted outpatients with milder conditions compared with the participants of previous studies targeting hospitalized patients and patients with severe mental illness (Katz et al., 2002). Our study also did not find an association between age and exacerbation of pre-existing psychiatric disorders as reported in previous studies (Bokszczanin, 2007; Norris et al., 2002). This might be due to the selection bias that our sample was relatively older (age = 55.6 (37.3–73.9) years, mean ± standard deviation).

There are several debates about suicide during the COVID-19 pandemic (Tandon, 2021b). Our samples did not include a case with a completed suicide but included an attempted case. In addition, a patient with severe depression and suicidal ideation required electroconvulsive therapy. Even though there were no definite findings on increased rates of suicide among the general population during the COVID-19 pandemic, our results suggested that psychiatrists should beware of suicide in treating with female patients with pre-existing mood disorders.

A number of factors and limitations should be considered in interpreting the results of this study. First, the social situation under the state of emergency in Japan may be different from that in other countries because there was no mandatory lockdown in Japan. Furthermore, even in countries with mandatory lockdown, social situations have varied from country to country (Yan et al., 2020). Second, because this is a single-center study targeting outpatients, there may be selection bias. Moreover, although the number of study patients was substantial, the sample size in some diagnostic categories was smaller than in others (compare F1,5–9 to F0,2–4). Although not statistically significant, we did observe cases of exacerbation in F1, F7, and F8 patients, as reported in previous studies (Moreno et al., 2020). Third, we administered the GAF assessment, for which reliability and validity are a matter of debate (Aas, 2011). Some researchers have reported high inter-rater reliability while others have not (Grootenboer et al., 2012; Hilsenroth et al., 2000; Söderberg et al., 2005). To minimize the influence of differences in raters, we considered a change of ≥ 10 points as a significant change in symptoms, because this threshold was confirmed to have high inter-rater reliability in a previous study (Lindström et al., 1994). Fourth, there is a subjective bias as to whether exacerbation is related to the COVID-19 pandemic. To reduce the effect of subjective bias, each rater discussed their findings with two staff psychiatrists (S.K. and M.F.) and an assessment of exacerbation due to the pandemic was limited to cases confirmed by both psychiatrists.

In conclusion, this prospective observational study examined psychiatric symptom changes in 1592 outpatients with pre-existing psychiatric disorders in the initial phase of the COVID-19 pandemic. The two main findings were that (1) patients with mood disorders (F3) were significantly more likely to show a deterioration in symptoms than patients with other disorders; and (2) female patients were more likely to show a worsening of psychiatric symptoms than male patients. These findings provide clinical implications for better management of psychiatric disorders during a pandemic.

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Author Contributions

M.F. conceived the original idea. S.K., M.F., T.T., Y.S., Y.M., S.K., and S.O. assessed symptoms. S.K. analyzed the data and wrote the first draft. S.K. and M.F. contributed to the interpretation of the results. M.M. supervised the project. All authors have made substantial intellectual contributions to the work and approved the final manuscript.

Data Availability

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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Declaration of Conflict of Interest

The authors declare there are no conflicts of interest.

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