

Influence of Previous Neurotic Disorders on the Course of Anxiety-Depressive Disorders in Patients with COVID-19

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Abstract This study aimed to explore the progression of depression and anxiety in individuals who have recovered from COVID-19, considering their psychiatric background in comparison to individuals without such a history. The variables analyzed included psychiatric history and the duration since COVID-19 infection. The main outcomes and measures focused on the severity of depression and anxiety, assessed using the Patient Health Questionnaire-9 (PHQ-9) and Generalized Anxiety Disorder-7 (GAD-7), respectively. The results indicated that individuals with a psychiatric history who had survived COVID-19 exhibited a more pronounced trajectory of depression and anxiety when compared to those without a psychiatric history.

Keywords COVID-19, Depression, Anxiety

1. Introduction

The emergence of the novel coronavirus outbreak in the Republic of Uzbekistan is associated with multiple factors that contribute to the progression and intensification of depression, anxiety, and other mental disorders. These contemporary epidemic infectious diseases have been identified as significant triggers for severe mental health problems, which require expert assessment and therapy [1].

According to a recent study carried out in China, it was found that 73.4% of the participants suffered from anxiety disorders, 50.7% experienced depression, and 36.1% faced insomnia [2]. Furthermore, a comprehensive study involving 7236 volunteers highlighted that one-third of the individuals experienced anxiety disorders, whereas one-fifth experienced depressive disorders [3].

People who suffer from anxiety and depression are more prone to experiencing emotional reactions to the COVID-19 pandemic. This can result in the reoccurrence or deterioration of their existing conditions. The reason behind this increased vulnerability to stress is their heightened sensitivity compared to the general population [3]. Psychiatric symptoms, including depression and anxiety, continue to be significant problems during the acute, prolonged, and post-COVID periods [4]. A study showed that four months after recovering from COVID-19, 20.6% of patients experienced depression, while 31.4% experienced anxiety [2].

A meta-analysis also revealed that between 14% and 44% of individuals who had recovered from COVID-19 reported

experiencing generalized anxiety disorder, while 19.2% to 21.5% reported experiencing depression four months after their infection [5]. Moreover, at six months and twelve months after infection, depression and anxiety persisted in 23% and 26% of survivors, respectively, showing a higher prevalence compared to the control group [6]. Furthermore, patients who had contracted COVID-19 had a greater risk of developing psychiatric disorders compared to those who had influenza or other respiratory infectious diseases [7].

Depression and anxiety have a profound impact on both the quality of life and the economy as a whole [7]. However, a systematic review of the literature has produced conflicting results [8]. One study suggests that the severity of depression in COVID-19 patients returns to normal after a month of follow-up [8], while other studies indicate a poor prognosis or no change [9,10]. Similarly, there are mixed reports on the improvement, deterioration, or lack of change in anxiety, and there is no consensus on the direct impact of the coronavirus infection on anxiety [3]. The variations in psychiatric symptoms observed in different studies may be influenced by various background factors. Among these factors, a history of psychiatric illness has been identified as one of the most significant contributors to psychiatric symptoms following COVID-19.

The experience of being infected with COVID-19 is extremely painful [11], and these unpleasant experiences have a negative impact on the mental well-being of patients who have contracted the virus [2]. As a result, patients with a history of psychiatric disorders who have also contracted COVID-19 may be more susceptible to the adverse effects of the infection and are more likely to experience ongoing psychiatric symptoms. According to the neuroinflammation hypothesis, a psychiatric history contributes to

neuroinflammation during COVID-19 infection, leading to more severe depression and anxiety. Based on these psychological and biological pathways, it is believed that a psychiatric history influences the progression of psychiatric symptoms as a result of COVID-19, although it is still unclear whether the progression of psychiatric symptoms differs between COVID-19 survivors with and without a psychiatric history. A study has indicated that neurotic symptoms after 1 and 3 months in patients who have contracted COVID-19 and have a psychiatric history are worse compared to patients without a psychiatric history [3]. However, considering the available data on the prolonged persistence of neurotic symptoms even after 6 or 12 months [6], it is essential to validate this observation over a longer duration and examine the impact of interaction on a larger sample size. If depression and anxiety do not decrease in severity over time, it is crucial to initiate treatment rather than relying on the possibility of spontaneous improvement. Therefore, determining the trajectory of neurotic symptoms is of utmost importance in making informed decisions about appropriate therapeutic interventions.

The aim of this study was to ascertain whether the intensity of neurotic symptoms varies over a period of time following COVID-19 infection, contingent upon the existence or non-existence of a psychiatric history prior to COVID-19 infection.

2. Materials and Methods

During the period of 2021-2022, a research study was carried out to examine the occurrence of anxiety and depression in individuals who had a history of anxiety and depressive disorders and had contracted COVID-19, as well as those who developed these disorders after recovering from the illness. The study enrolled a total of 128 participants from two medical facilities in Tashkent, namely the 2nd City Psychoneurological Dispensary and the 5th Family Outpatient Clinic. Among the participants, 68 patients had a clinically confirmed diagnosis of neurotic disorder (diagnosis with group code F40-F48 according to the International Classification of Diseases of the 10th revision (ICD-10)) that existed prior to contracting COVID-19, while 60 patients developed neurotic disorders after recovering from COVID-19. The study population consisted of 93 women and 35 men, with an average age of 39.5 ± 7.2 years. Both groups were similar in terms of gender and age.

The severity of depressive states was assessed using the PHQ-9 (Patient Health Questionnaire-9) scale, which is known for its high validity and reliability. This scale consists of nine items that are evaluated on a 4-point scale, ranging from "not at all" to "almost every day". Similarly, the level of anxiety and symptoms of anxiety disorders, particularly generalized anxiety disorder, were assessed using the GAD-7 (Generalized Anxiety Disorder-7) scale, which also has high validity and reliability [12]. The GAD-7 scale consists of seven items that are evaluated on the same 4-point scale as the PHQ-9. A higher total score on both scales

indicates a greater severity of symptoms. The dates of response to the questionnaires were categorized into four periods (<1 month, ≥ 1 month, ≥ 3 months, ≥ 6 months) from the time of contracting COVID-19. These periods were classified as "acute" for symptoms occurring within the first month after COVID-19, "long-lasting" for symptoms between 1 and 3 months, and "post-COVID" for symptoms older than 3 months [9].

Statistical analysis. The mean and standard deviation were computed for continuous variables, while the count and percentage were computed for categorical variables. For each group categorized by psychiatric history and time since COVID-19 infection, the mean and standard error were calculated. The significance level was established at $p < 0.05$. All statistical analyses were conducted using IBM SPSS Statistics version 25 (Chicago, IL, USA).

3. Results

On average, the Patient Health Questionnaire-9 (PHQ-9) yielded scores of 5.19 ± 5.91 , while the Generalized Anxiety Disorder-7 (GAD-7) resulted in scores of 3.34 ± 4.71 . Notably, individuals with a previous history of neurotic disorders displayed significantly higher levels of depression and anxiety compared to those without such a history (PHQ-9 – 9.74 ± 7.02 vs. 4.21 ± 5.14 , $p < 0.001$; GAD-7, 7.09 ± 5.85 vs. 2.54 ± 4.0 , $p < 0.001$). The median duration following COVID-19 infection was 4.5 ± 4.37 months, which was notably longer in patients with a history of neurotic disorders than in participants without such a history (4.44 ± 4.36 vs. 4.79 ± 4.42 , $p = 0.018$).

Individuals with a previous record of neurotic disorders had an average PHQ-9 score of 8.95 ± 0.40 within a month, 8.42 ± 0.36 at or beyond 1 month, 9.69 ± 0.33 at or beyond 3 months, and 9.23 ± 0.27 at or beyond 6 months. On the other hand, participants without any history of neurotic disorders displayed a mean score of 5.02 ± 0.17 within a month, 4.44 ± 0.15 at or beyond 1 month, 4.01 ± 0.16 at or beyond 3 months, and 4.10 ± 0.13 at or beyond 6 months.

Participants who had a documented history of neurotic disorders had an average GAD-7 score of 5.80 ± 0.32 within a period of less than 1 month, 5.78 ± 0.28 after 1 month or more, 7.27 ± 0.27 after 3 months or more, and 7.02 ± 0.12 after 6 months or more. On the other hand, participants without a history of neurotic disorders had a mean score of 2.76 ± 0.14 within a period of less than 1 month, 2.65 ± 0.12 after 1 month or more, 2.61 ± 0.13 after 3 months or more, and 2.56 ± 0.11 after 6 months or more.

The GAD-7 test results revealed a significant distinction between individuals with and without a psychiatric history after being infected with COVID-19. This distinction was observed across all time periods ($p < 0.001$). Specifically, participants with a history of neurotic disorders had lower scores at less than 1 month compared to scores at 3 months or more, as well as at 6 months or more ($p < 0.001$ for 3 months or more; $p = 0.002$ for 6 months or more). Furthermore, these participants also had lower scores at 1 month or more

compared to scores at 3 months or more, as well as at 6 months or more ($p=0.001$ for 3 months or more; $p=0.005$ for 6 months or more). On the other hand, no significant differences were observed among participants without a history of neurotic disorders.

4. Discussion

Our study reveals that individuals who have previously experienced neurotic disorders and contract COVID-19 tend to experience a prolonged persistence of depression severity. On the other hand, individuals without a history of neurotic disorders show a gradual decrease in depression severity over time. Furthermore, those with a history of neurotic disorders who contract COVID-19 also experience a gradual increase in anxiety severity, while individuals without such a history do not exhibit this increase.

The study findings indicated that patients who had no previous neurotic disorders and contracted COVID-19 experienced a positive trajectory in terms of depression and anxiety over time. However, this was not the case for patients with a history of neurotic disorders. These results are consistent with the conclusions drawn by Taquet *et al.* and Matalon *et al.* [14,15], who also suggested that individuals without a psychiatric history are vulnerable to developing symptoms such as depression and anxiety. In COVID-19 patients, the symptoms of depression remained stable after one month, while the symptoms of anxiety worsened. This pattern was observed in both patients with and without a history of neurotic disorders, which aligns with the findings of Iqbal *et al.* and Lorenzo *et al.* [16,17]. These findings indicate that psychological symptoms do not improve over time [6]. In our study, we discovered that the level of depression experienced during the initial 3 months was similar to the findings of the Mazza study [18]. Expanding on this similarity, our study aimed to explore a longer timeframe, enabling us to identify differences in the severity of depression between individuals with and without a history of psychiatric disorders. Therefore, it is crucial to extend the observation period for depression and anxiety in individuals with a psychiatric history, potentially up to 6 months or more, to ensure early detection and appropriate care. The relationship between COVID-19 symptoms and psychiatric disorders has been clarified, with COVID-19 infection increasing the susceptibility to psychiatric disorders [13]. Additionally, the presence of neurotic disorders acts as a risk factor for the development of subacute consequences following COVID-19 infection [12].

The results of our research can be explained from both psychological and biological perspectives. From a psychological standpoint, individuals who have survived COVID-19 may frequently face various psychological stressors, such as stigma [11], guilt [17], and anxiety about the return of symptoms and reinfection [12]. These psychological factors have a significant impact on the mental well-being of COVID-19 patients [5]. At the same time, an

increase in resilience levels helps alleviate neurotic symptoms. As a result, individuals with a preexisting history of neurotic disorders who have contracted COVID-19 may need a longer period to recover mentally due to reduced resistance to adverse effects, including the infection itself [4].

Biological factors present an extra possible impact. Specifically, some research suggests a connection between increased inflammation associated with COVID-19 and the subsequent emergence of depressive and anxiety symptoms [8]. It is widely recognized that inflammation is one of the contributing factors to mental disorders. As a result, individuals with a history of psychiatric conditions may have a greater likelihood of intensifying or prolonging neurotic symptoms, such as depression and anxiety.

5. Conclusions

Our study's findings suggest that the severity of depression and anxiety caused by COVID-19 might gradually decrease or remain at a minimal level in individuals without pre-existing neurotic disorders. However, for patients with a previous history of neurotic disorders who have contracted COVID-19, these symptoms do not resolve naturally and may even persist or worsen as time goes on. Therefore, it is essential to be cautious and closely observe individuals with a psychiatric background who have been affected by COVID-19, ensuring they receive specialized care and attention.

REFERENCES

- [1] Tucci V, Moukaddam N, Meadows J, Shah S, Galwankar SC, Kapur GB. The Forgotten Plague: Psychiatric Manifestations of Ebola, Zika, and Emerging Infectious Diseases. *J Glob Infect Dis.* 2017 Oct-Dec; 9(4): 151-156.
- [2] Morin, L.; Savale, L.; Pham, T.; Colle, R.; Figueiredo, S.; Harrois, A.; *et al.* Four-Month Clinical Status of a Cohort of Patients after Hospitalization for COVID-19. *JAMA* 2021, 325, 1525–1534.
- [3] Liu S., Yang L., Zhang C., *et al.* Online mental health services in China during the COVID-19 outbreak. *Lancet Psychiatry*, 2020; 7(4): 17-18.
- [4] Kroenke, K.; Spitzer, R.L.; Williams, J.B.W. The PHQ-9: Validity of a Brief Depression Severity Measure. *J. Gen. Intern. Med.* 2001, 16, 606–613.
- [5] Heiberg, K.E.; Heggstad, A.K.T.; Jøranson, N.; Lausund, H.; Breivne, G.; Myrstad, M.; *et al.* 'Brain Fog', Guilt, and Gratitude: Experiences of Symptoms and Life Changes in Older Survivors 6 Months after Hospitalisation for COVID-19. *Eur. Geriatr. Med.* 2022, 13, 695–703.
- [6] Iqbal, A.; Iqbal, K.; Arshad Ali, S.; Azim, D.; Farid, E.; Baig, M.D.; *et al.* The COVID-19 Sequelae: A Cross-Sectional Evaluation of Post-Recovery Symptoms and the Need for Rehabilitation of COVID-19 Survivors. *Cureus* 2021, 13, e13080.

- [7] Konnopka, A.; König, H. Economic Burden of Anxiety Disorders: A Systematic Review and Meta-Analysis. *Pharmacoeconomics* 2020, 38, 25–37.
- [8] Schou, T.M.; Joca, S.; Wegener, G.; Bay-Richter, C. Psychiatric and Neuropsychiatric Sequelae of COVID-19 — A Systematic Review. *Brain. Behav. Immun.* 2021, 97, 328–348.
- [9] De Lorenzo, R.; Cinel, E.; Cilla, M.; Compagnone, N.; Ferrante, M.; Falbo, E.; et al. Physical and Psychological Sequelae at Three Months after Acute Illness in COVID-19 Survivors. *Panminerva Med.* 2021.
- [10] Mazza, M.G.; Palladini, M.; De Lorenzo, R.; Magnaghi, C.; Poletti, S.; Furlan, R.; Persistent Psychopathology and Neurocognitive Impairment in COVID-19 Survivors: Effect of Inflammatory Biomarkers at Three-Month Follow-Up. *Brain. Behav. Immun.* 2021, 94, 138–147.
- [11] Mahmoudi, H.; Saffari, M.; Movahedi, M.; Sanaeinasab, H.; Rashidi-Jahan, H.; Pourgholami, M.; Poorebrahim, A.; et al. A Mediating Role for Mental Health in Associations between COVID-19-Related Self-Stigma, PTSD, Quality of Life, and Insomnia among Patients Recovered from COVID-19. *Brain Behav.* 2021, 11, 1–8.
- [12] Spitzer, R.L.; Kroenke, K.; Williams, J.B.W.; Lo, B. A Brief Measure for Assessing Generalized Anxiety Disorder. *Arch. Intern. Med.* 2013, 166, 1092–1097.
- [13] Gramaglia, C.; Gambaro, E.; Bellan, M.; Balbo, P.E.; Baricich, A.; et al. Mid-Term Psychiatric Outcomes of Patients Recovered From COVID-19 From an Italian Cohort of Hospitalized Patients. *Front. Psychiatry* 2021, 12, 839.
- [14] Taquet, M.; Luciano, S.; Geddes, J.R.; Harrison, P.J. Bidirectional Associations between COVID-19 and Psychiatric Disorder: Retrospective Cohort Studies of 62 354 COVID-19 Cases in the USA. *Lancet Psychiatry* 2021, 8, 130–140.
- [15] Matalon, N.; Dorman-Ilan, S.; Hasson-Ohayon, I.; Hertz-Palmor, N.; Shani, S.; Basel, D.; et al. Trajectories of Post-Traumatic Stress Symptoms, Anxiety, and Depression in Hospitalized COVID-19 Patients: A One-Month Follow-Up. *J. Psychosom. Res.* 2021, 143, 110399.
- [16] Iqbal, A.; Iqbal, K.; Arshad Ali, S.; Azim, D.; Farid, E.; Baig, M.D.; Bin Arif, T.; Raza, M. The COVID-19 Sequelae: A Cross-Sectional Evaluation of Post-Recovery Symptoms and the Need for Rehabilitation of COVID-19 Survivors. *Cureus* 2021, 13, e13080.
- [17] De Lorenzo, R.; Cinel, E.; Cilla, M.; Compagnone, N.; Ferrante, M.; Falbo, E.; Patrizi, A.; Castellani, J.; Magnaghi, C.; Calvisi, S.L.; et al. Physical and Psychological Sequelae at Three Months after Acute Illness in COVID-19 Survivors. *Panminerva Med.* 2021.
- [18] Mazza, M.G.; De Lorenzo, R.; Conte, C.; Poletti, S.; Vai, B.; Bollettini, I.; Melloni, E.M.T.; Furlan, R.; Ciceri, F.; Rovere-Querini, P.; et al. Anxiety and Depression in COVID-19 Survivors: Role of Inflammatory and Clinical Predictors. *Brain. Behav. Immun.* 2020, 89, 594–600.