

Mental health in COVID-19 survivors from a general hospital: association with sociodemographic, clinical, and inflammatory variables

Jeff Huarcaya-Victoria (✉ jhuarcayav@unmsm.edu.pe)

Hospital Nacional Guillermo Almenara Irigoyen <https://orcid.org/0000-0003-4525-9545>

Jesica Barreto

Hospital Nacional Guillermo Almenara Irigoyen <https://orcid.org/0000-0002-3433-9411>

Lucia Aire

Hospital Nacional Guillermo Almenara Irigoyen <https://orcid.org/0000-0003-3961-2373>

Angela Podestá

Hospital Nacional Guillermo Almenara Irigoyen <https://orcid.org/0000-0002-6318-202X>

Mónica Caqui

Hospital Nacional Guillermo Almenara Irigoyen <https://orcid.org/0000-0002-0194-6987>

Rosa Guija-Igreda

Hospital Nacional Guillermo Almenara Irigoyen <https://orcid.org/0000-0001-7171-704X>

Claudia Castillo

Hospital Nacional Guillermo Almenara Irigoyen <https://orcid.org/0000-0002-6277-7152>

Christoper A. Alarcon-Ruiz

Universidad Científica del Sur <https://orcid.org/0000-0003-3907-2784>

Research Article

Keywords: COVID-19, COVID-19 survivors, Depression, Anxiety, Somatic symptoms, Distress, Mental health, Inflammation, Peru

Posted Date: January 25th, 2021

DOI: <https://doi.org/10.21203/rs.3.rs-146200/v1>

License: © ⓘ This work is licensed under a Creative Commons Attribution 4.0 International License. [Read Full License](#)

Abstract

Background: The current COVID-19 (coronavirus disease 2019) pandemic constitutes a significant problem for the world's public health and generates mental health problems.

Objective: To describe the characteristics of mental health in survivors of COVID-19 and the main sociodemographic, clinical, and immune factors related.

Method: A Cross-sectional and correlational study was conducted on 318 patients (196 women, mean age 54.4 ± 15.1 years) surviving COVID-19 from one hospital in Peru in which sociodemographic, clinical, and immune characteristics were explored. Through telephone interviews, an evaluation of the presence of depressive, anxious, somatic, and distress symptoms was carried out using standardized scales. Adjusted prevalence ratios (PRa) were estimated.

Results: A significant proportion of the patients have depressive (30.3%), anxious (29.9%), somatic (33.7%), and distress (28.7%) symptoms. In the regression analysis, the variables associated with a higher frequency of clinically relevant mental symptoms were female sex (depression: aPR = 2.29; anxiety: PRa = 2.71; somatic symptoms: PRa = 2.04; distress: PRa = 2.11), proceeding outside the capital (depression: PRa = 1.61; anxiety: PRa = 1.53), the self-perception of a greater severity of the infection (depression: PRa = 5.53; anxiety: PRa = 2.29; distress: PRa = 14.78), the presence of persistent COVID-19 symptoms (depression: PRa = 8.55; anxiety: PRa = 11.38; somatic symptoms: PRa = 5.46; distress: PRa = 20.55), a history of psychiatric treatment (depression: PRa = 2.29; somatic symptoms: PRa = 2.90; distress: PRa = 3.80), the history of a family member infected by COVID-19 (anxiety: PRa = 4.71; somatic symptoms: PRa = 1.99), and a neutrophil-lymphocyte index greater than 6.5 (depression: PRa = 1.67; anxiety: PRa = 1.82).

Conclusion: COVID-19 survivors show a high prevalence of negative mental symptoms. Some useful variables have been found when identifying vulnerable patients requiring psychiatric care.

1. Introduction

The current pandemic of the novel coronavirus disease (COVID-19), caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), represents a significant problem for world mental health (1). Until January 12, 2021, worldwide, more than 89 million cases and 1,940,352 deaths were reported (2). In Peru, during the same period, more than a million confirmed cases and 38,335 deaths were reported, with lethality of 3.70% (3). The great infectivity, the harmfulness of the virus, the daily increase in the number of confirmed cases and deaths, and the consequences of the pandemic, in general, have generated negative emotions and thoughts. Therefore, this situation also threatens the mental health of the population, patients, and health personnel (4).

Previous studies have reported that patients with viral respiratory infections similar to COVID-19 showed varying degrees of mental health problems such as depression, anxiety, adjustment disorder, acute stress-related disorder, and post-traumatic stress disorder (PTSD), even after their recovery from the disease (5). Hence, research in different countries has documented that COVID-19 patients also experienced the onset or exacerbation of diverse problems in their mental health (5-7). This could be due to diverse factors, from psychosocial problems caused by quarantine and hospitalization (8). An invasion of SARS-CoV-2 to the central nervous system or the consequence of the systemic immune response in the form of a "cytokine storm" has even been proposed (9). Soluble cytokines that reach the brain, or their altered levels on a local level, may influence the synthesis, release, and reuptake of neurotransmitters, including dopamine, norepinephrine, and serotonin (10). These changes in neurotransmitter metabolism are involved in the pathophysiology of various psychiatric disorders, such as depression, anxiety, PTSD, and obsessive-compulsive disorder (11, 12).

The majority of studies about the impact on the mental health of patients with COVID-19 were conducted in hospital settings using convenience samples, with just a few evaluating surviving patients during their post-discharge follow-up in outpatient settings (13). Moreover, the majority of studies were conducted in Chinese populations, probably because China was the first country affected by the pandemic (13). Despite the usefulness of these data, demographic and inter-individual characteristics are determining factors in the psychological responses of different populations to a large-scale stressful event such as the current pandemic (14). Hence, it is crucial to carry out studies that assess the impact of this disease in each of the affected countries, especially in countries like Peru, which has been worldwide one of the most affected by this pandemic (3).

Due to the scarce information regarding the impact of this novel pandemic on mental health in patients surviving COVID-19, we decided to carry out this study, which aims to describe the characteristics of mental health and the main sociodemographic, clinical, and immune factors related to the disease.

2. Material And Methods

2.1. Study design

This study is observational, analytical, and cross-sectional. It evaluates the influence of sociodemographic, clinical, and immune characteristics on the levels of depression, anxiety, somatic symptoms, and distress in outpatients who survived COVID-19.

2.2. Clinical context

This study was carried out at Hospital Nacional Guillermo Almenara Irigoyen (HNGAI), which is the second-largest hospital of the "Seguridad Social de Salud del Perú" (EsSalud), with a total of 815 hospital beds. Furthermore, it is a reference center of the third level of attention and has all the medical specialties. By 2019, the Almenara network met the health needs of 1,634,990 insured (15).

During the COVID-19 pandemic, HNGAI was a national referral center for the care of COVID-19 patients. Due to the high demand for care, hospital beds of different specialties had to be redistributed to care for these COVID-19 patients. Moreover, new hospital environments had to be created. The diagnoses of COVID-19 were made with serological tests, which were later confirmed with molecular tests.

According to EsSalud's records, from the beginning of the pandemic until September 2020, in HNGAI, there were a total of 3,238 hospital discharges of patients diagnosed with COVID-19. For this study, minors (n=369), deceased (n=843), escaped (n=1), referred to another center (n=88), voluntarily withdrawn (n=13), as well as those patients who had two or more hospitalizations during March to September 2020 (n=14), were excluded. Hence, we only considered patients who were discharged from the hospital (n=1,910).

2.3. Participants

The sample was obtained from a population of 1,910 patients with COVID-19 who were discharged from HNGAI hospitalization services between March and September 2020. We used the Paz et al. study (16) to calculate the sample size. In this research, an expected frequency of 55% of mental health problems in patients with COVID-19 was estimated. With this data, and considering a margin of error of 5%, with a design effect of 1 and a single group, we obtained a total of 318 individuals with a 95% confidence interval.

The sample was selected through a simple random sampling using the Epidat v4.2 program (Dirección Xeral de Saúde Pública da Consellería de Sanidade, Galicia, España). Each of the 1,910 patients had a coding.

The variables were collected on a virtual file through telephone calls to the patients between October 22 and November 28, 2020. The cell phone number that was registered in the electronic medical record of each patient was used. The calls were made by the co-investigators, who are psychiatrists with clinical and research experience. If after two calls the selected participant did not answer, they were excluded from the study, and we then made a new random selection of another participant. In addition, a group of selected participants did not wish to continue with the interview (n=8). Therefore, they were removed from the database, and new participants were randomly selected.

2.4. Measures

2.4.1. Depression

For the evaluation of depressive symptoms, Patient Health Questionnaire-9 (PHQ-9) was used. This scale consists of 9 items that evaluated the frequency of depressive symptoms in the previous two weeks, which are rated on a Likert scale ranging from 0 ("not at all") to 3 ("nearly every day"). The PHQ-9 scores reflect 5 categories of severity of depressive disorders: None (0-4), mild (5-9), moderate (10-14), moderately severe (15-19), and severe (20-27). In studies carried out in Latin America, PHQ-9 has been proven to be a valid and reliable tool for detecting depressive symptoms in various types of populations (17, 18). Furthermore, PHQ-9 has been validated in Peru. Validity indicators include internal structure, measurement invariance, and acceptable internal consistency values (19).

2.4.2. Anxiety

Generalized Anxiety Disorder-7 (GAD-7) was used, which is a valid and efficient scale to assess the severity of anxiety disorders in clinical practice and investigation (20). The scale consists of 7 items that evaluate the anxiety symptomatology during the two weeks prior to the application of the scale. Each item is rated according to a Likert scale ranging from 0 ("not at all") to 3 ("nearly every day"). GAD-7 reflects 4 categories of severity of the anxiety disorder: normal (0-4), mild (5-9), moderate (10-14), and severe anxiety (15-21). This scale has been translated into Spanish and validated (21).

2.4.3. Somatic symptoms

For the evaluation of somatic symptoms, Patient Health Questionnaire-15 (PHQ-15) was used. It consists of 15 items related to 15 possible somatic symptoms that could have bothered the patients during the previous 4 weeks (22). Each item is rated as: "nothing" or absence of the problem (0 points), "a little" or presence of the problem (1 point), or "a lot" or high presence of the problem (2 points). The PHQ-15 scores reflect 4 categories of severity of somatic symptoms: normal (0-4), mild (5-9), moderate (10-14), and severe (15-30). This scale has been translated into Spanish and validated (23).

2.4.4. Distress

In order to validate distress, the Impact of Event Scale-Revised (IES-R) was used (24). This scale measures the degree of suffering caused by a life event (for this study, the hospitalization for COVID-19 was considered as the stressful event), which is conceptualized as a form of subjective stress. IES-R consists of 22 items: 7 assess intrusion symptoms, 8 avoidance, and 7 hyperarousal (25). It is rated according to the Likert scale that ranges from 0 ("not at all") to 4 ("extremely"). The IES-R scores reflect 5 categories of distress severity: normal (0-8), mild (9-25), moderate (26-43), and severe (44-88). This scale has been translated into Spanish and validated (25).

2.4.5. Further variables

In addition, information regarding the following variables was collected: a) Sociodemographic data, including sex, age, educational degree, job status, place of origin before hospitalization, current place of residence, with whom they live, history of a relative infected and/or death by

COVID-19; b) Clinical and hospitalization data, including history of diagnosis and/or treatment for psychiatric diagnosis, self-perception of the severity of COVID-19, hospitalization area, days of hospitalization, days from discharge to the interview, presence of COVID-19 symptoms at the time of the interview; and c) Immune data, including neutrophil-to-lymphocyte ratio (NLR) and monocyte-to-lymphocyte ratio (MLR) at the beginning of hospitalization. Immune variables were obtained by reviewing electronic medical records.

2.5. Statistical analyses

The relative and absolute frequency of the categorical variables were described. For quantitative variables with normal distribution, the mean and standard deviation (SD) are described, and for those without normal distribution, the median and interquartile range (IQR) are described. Then, the outcome variables of mental health, depression, anxiety, somatic symptoms, and distress were dichotomized into clinically irrelevant (normal-mild) and clinically relevant (moderate-severe). At the same time, hospitalization time was categorized into 1-7 days, 8-14 days, and more than 14 days.

In the dichotomous analysis, the association between each covariate with each dichotomized mental health outcome variable was evaluated. Chi-2 and Fisher's exact tests were used for categorical covariates, depending on the fulfillment of assumptions. For numerical covariates, Student's T-test was used when they had a normal distribution, and the Mann Whitney's U test was used when they had a non-normal distribution.

Prior to the regression analysis, the age variable was categorized into quartiles. Additionally, the NLR was categorized as <6.5 and ≥ 6.5 (26), and the MLR was categorized as <0.364 and ≥ 0.364 (27). The cut-off points were chosen considering their ability to predict in-hospital mortality in patients with COVID-19. The COVID-19 symptoms variable during the interview was categorized into asymptomatic (without any symptoms at the time of follow-up) and with symptoms (at least one symptom at the time of follow-up).

In order to calculate the Prevalence Ratio (PR) with their 95% confidence interval (95% CI), Poisson regression analyses were performed with their adjusted variances, using the service variable as a cluster. All regression models were adjusted (PRa) for follow-up time. Furthermore, the regression models of the covariates "Severity of COVID-19" and "COVID-19 symptoms during the interview" were also adjusted for the presence of COVID-19 symptoms at the moment of admission to hospitalization. A p-value <0.05 was considered as a statistically significant result. Stata MP v.16.0 statistical software was used for all analyses.

2.6. Ethical aspects

Informed consent was requested from each participant verbally. This included an explanation of the objectives of the investigation as well as an explanation of the rights of the participants (anonymity and the right to refrain from participating in case they considered appropriate). Furthermore, psychiatric help was offered when the interviewer considered it necessary at some point, either during or after the phone interview. This investigation was carried out with the authorization of the EsSalud's Research Ethics Committee Specific to COVID-19.

3. Results

In a representative sample of outpatient survivors of COVID-19, the majority were women (61.6%), professed a religion (92.8%), were from Lima (94.3%), with an average age of 54.4 years, lived with a partner, and/or children (80.5%), had at least one family member infected (83.0%), and at least one relative died (30.5%) from COVID-19. 31.1% of survey respondents perceived that their COVID-19 disease had been severe, and 33.7% perceived that it had been moderate. The median NLR was 6 (IQR: 3.8-11.1), and the MLR was 0.3 (IQR: 0.2-0.5). Regarding COVID-19 symptoms, 7.9% of survey respondents were asymptomatic at the time of admission to the hospital, while 39% were asymptomatic at the time of the interview. The median time of hospitalization was 8 days (IQR: 4-15), and the mean follow-up time was 100.8 days \pm SD: 37.7.

This study found that 96 (30.3%) patients had some type of depressive symptoms, 95 (29.9%) anxious symptoms, 108 (33.7%) somatic symptoms, and 91 (28.7%) distress symptoms. Regarding the clinically relevant symptoms (moderate-severe), 34 (10.8%) were depressive, 24 (7.6%) anxious, 43 (13.5%) somatic, and 25 (7.9%) distressed. The rest of the characteristics are described in Table 1.

In the bivariate analysis, women had a higher frequency of clinically relevant symptoms (moderate-severe) of the depressive type ($p=0.009$), anxious type ($p=0.011$), somatic type ($p=0.011$), and distress type ($p=0.059$). Patients with history or treatment of psychiatric illness presented a higher frequency of clinically relevant mental symptoms ($p < 0.05$). Those patients who self-reported having had severe or critical COVID-19 had a higher frequency of clinically relevant depressive symptoms ($p=0.004$) and distress ($p=0.009$). NLR, in its numerical nature, was associated with clinically relevant depressive symptoms ($p=0.037$). Further associations can be found in Table 2.

In the regression analysis, it was found that women have a higher frequency of clinically relevant symptoms of depression (PRa=2.29; CI 95%: 1.06-4.92), anxiety (PRa=2.71; CI 95%: 1.62-4.53), somatic (PRa=2.04; CI 95%: 1.06-3.89), and distress (PRa=2.11; CI 95%: 1.05-4.24). On the other hand, those patients with a higher level of education had a lower frequency of having mental symptoms than those with no education or only a primary level. Likewise, those patients with a job or who are retired also have less frequency of having an adverse mental health outcome, compared to those who do not work. Those patients who had had a family member infected or who died by COVID-19, or those who have a history of psychiatric diagnosis, have a higher frequency of developing adverse mental health outcomes. Patients who self-reported having severe or critical COVID-19 are more likely to have clinically relevant depression, anxiety, somatic symptoms, and distress, compared to those who self-reported a mild infection. Having a high NLR (≥ 6.5) was associated with a higher frequency of depressive symptoms (PRa=1.67; CI 95%: 1.13-2.47) and anxious symptoms (PRa=1.82; CI 95%: 1.18-2.81) that were clinically relevant compared to those who had a low NLR (< 6.5). Lastly, those patients who had persistent COVID-19 symptoms during the interview were more likely to have a higher frequency of clinically relevant symptoms of depression (PRa=8.55; CI 95%: 4.70-15.56), somatic (PRa=5.46; CI 95%: 1.60-18.64), anxiety (PRa=11.38; CI 95%: 7.34-17.62), and distress (PRa=20.55; CI 95%: 2.53-167.21) (Table 3).

4. Discussion

4.1. Main findings and meaning of the results

This study sought to describe the characteristics of mental health in Peruvian patients surviving COVID-19, as well as the main sociodemographic, clinical, and immune factors related to this. We found that mental symptoms were present after an average of 100 days after discharge of the patients. In a previous respiratory infection epidemic in South Korea, it was reported that mental symptoms might be present for up to a year after the epidemic outbreak (28).

The reported prevalence of depressive (30.3%) and anxious (29.9%) symptoms in COVID-19 survivors is similar to what was reported in other studies that include patients with mild COVID-19 (29, 30). Notwithstanding, a recent meta-analysis has documented a prevalence of depression of 52% and anxiety of 47% (13), which is higher than that reported in our study. This difference may be because most of the included studies were conducted in hospitalized patients. The mentioned meta-analysis also reported that the prevalence of depression and anxiety was lower in outpatients (35% and 33%, respectively) compared to hospitalized patients (48% and 42%, respectively) (13). The prevalence of clinically relevant depressive symptoms (moderate-severe) (10.8%) reported in this study is higher than what was documented in the Peruvian population prior to the pandemic, in which a prevalence of 6.4% was reported using the PHQ- 9

(31). This would suggest that the COVID-19 infection has some impact on mental health in the Peruvian population by increasing the prevalence of clinically relevant depressive symptoms.

We found a high prevalence of distress symptoms (28.7%) and somatic symptoms (33.7%). In a study of 34 patients with COVID-19 conducted in Italy, distress was found in 82% of the participants. However, after 4 months, there was a decrease in these symptoms up to 46.6% (32). Regarding the somatic symptoms, we did not find any research in which this variable was evaluated in survivors of COVID-19. Nonetheless, in

a study carried out in the general population in China, during the peak of the pandemic, researchers found a prevalence of 45.9% of somatic symptoms (33), higher than what was reported by our study.

4.2. Variables associated with mental symptoms

Some sociodemographic variables had a relation to a higher prevalence of clinically relevant mental symptoms. Being a woman is one of the main variables, which is similar to what was reported in other studies (16, 29, 34-36). These could probably be because women tend to have greater symptoms of hyperactivity, recurrent distressing memories, and negative cognitive and mood disturbances (37). Moreover, proceeding out of the capital before hospitalization was associated with a higher frequency of clinically relevant depressive and anxiety symptoms. This result was expected since leaving home, family, and community could have an impact on mental health (38). Furthermore, it is likely that those patients who were required to travel to Lima are also those with a more serious illness.

Patients who had family members who were diagnosed and died of COVID-19 had a higher prevalence of somatic and anxious symptoms. This finding was also reported in other studies in China (30, 39). Specifically, in a study carried out in Wuhan in patients with COVID-19, having family members diagnosed and/or deceased by the same disease were independent predictors of both the depression severity index, as well as presenting higher anxiety scores (39). Likewise, a history of psychiatric diagnosis and treatment has been associated with a higher frequency of clinically relevant mental symptoms in COVID-19 survivors. This could be because the current pandemic causes reactive symptoms such as stress, depression, and anxiety, which in combination with hospitalization, can aggravate the mental health of people with a previous psychiatric diagnosis (40).

Self-perception regarding a greater severity of COVID-19 was a variable associated with a higher prevalence of mental symptoms in survivors of the disease. A study carried out in patients hospitalized for COVID-19 in Wuhan reported a similar result (35). This could be because the patients' concerns about their disease would be added to their psychological burden, which would be associated with anguish and a poor result in their mental health. Similarly, another study from Turkey reported that perception of the severity of COVID-19 infection was associated with the risk of having PTSD symptoms, although this association became non-significant after controlling the effects of other variables (41).

We found a high frequency of persistent COVID-19 symptoms (61%). This finding is similar to what was reported in a study conducted in Chinese patients who survived COVID-19, where it was found that up to 76% of patients reported at least one COVID-19 symptom after 6 months of follow-up (42). The persistence of these symptoms was associated with a higher prevalence of mental symptoms.

4.3. The immune system's role in mental symptoms

The presence of an NLR greater than 6.5 at hospital admission was a variable associated with a higher prevalence of clinically relevant depressive and anxiety symptoms. In a study conducted in patients who survived COVID-19, in their convalescent phase, researchers found that those who reported depressive symptoms showed a greater immune response evidenced by a higher mean of NLR (2.4 vs 1.8; $p < 0.001$) (43). In another study from China, conducted with hospitalized patients, it has been documented that those with mental symptoms have higher levels of interleukins (IL) 1 β , NLR, and lower levels of IL-10 and lymphocyte count (35).

When SARS-CoV-2 infects the respiratory tract, it can cause an acute respiratory syndrome with the consequent release of pro-inflammatory cytokines, such as IL-1 β and IL-6, producing a "cytokine storm" (44). These cytokines may be increased in psychiatric disorders such as depression, schizophrenia, and PTSD (9). However, in some circumstances, it is not possible to make a study of these cytokines. Therefore, we can indirectly value their increase through an elevation of various inflammatory parameters with the NLR. This provides a quick and easy way to value the state of systemic inflammation, which can be calculated from a complete blood count. NLR elevations have been associated with an increase in cytokines, such as IL-6 and IL-8 (45).

Given the relationship between elevated levels of cytokines in COVID-19 as well as in psychiatric disorders, the immune/inflammatory pathways can be considered as one of the mechanisms involved in the mental health problems of this infection (9). Considering the impact of COVID-19 infection on mental health and the involvement of the immune system, it is necessary to evaluate the psychopathology of survivors of COVID-19. Consequently, the investigation of inflammatory biomarkers should be deepened in order to adequately diagnose, treat, and monitor emerging psychiatric conditions (36). Nonetheless, it is important to consider that related biological factors (such as advanced age, female sex, and excess fat), along with other factors inherent to COVID-19 (such as social isolation, financial stress, and adverse effects of treatments), can influence psychiatric outcomes. As a consequence, it is probable that the psychiatric symptoms in COVID-19 patients that were observed are due to a combination of the processes involved in the virus-host relationship and the psychosocial and therapeutic problems associated with the pandemic and the disease (9).

4.4. Implications for public health and decision making

This study evidences a high impact on the mental health of survivors of COVID-19. Hence, Peruvian Public Health must focus on the early diagnosis and treatment of the mental health problems of these patients. It is indispensable to evaluate all factors that influence these problems, including sociodemographic factors, proper clinical factors, and immune factors. This allows health care professionals to establish individual management to improve the psychological well-being of the survivors.

On the other hand, it is suggested to implement health policies that aim to implement diverse mental health services. These policies include screenings with standardized online evaluations, educational intervention in mental health, provision of psychological support after the detection of vulnerable patients, assessment of the state of systemic inflammation using a complete blood count, adequate psychiatric care for mental health management, and timely management of emergency situation in public health. All of these measures will empower Peru in the containment and future eradication of the COVID-19 pandemic (46).

4.5. Strengths and limitations of the study

This study has strengths that include the size of the sample and the fact that a random sample was made, which ensures the results' representativeness of the prevalence of mental disorders in the target population at a hospital level. Furthermore, to our knowledge, the study provides first-time exploratory data on different factors associated with mental health problems in patients that survived COVID-19 in Peru, during a follow-up.

Notwithstanding, this study must be understood in the context of its methodological limitations. Since the study is cross-sectional, we were neither able to evaluate a causal relationship nor how the different mental health outcomes evolve from hospital discharge to the moment of the evaluation. Future studies should evaluate how anxiety, depression, and distress levels are modified as the pandemic evolves in Peru. Since we only evaluate patients from one single hospital, we cannot generalize the results to all patients from other hospitals. Nonetheless, our findings are in line with what was reported in other countries.

5. Conclusions

The results of this study indicate a high prevalence of mental symptoms in COVID-19 survivors from a third-level hospital in Peru. Female sex, being from outside the capital, self-perception of greater severity of the infection, the presence of persistent COVID-19 symptoms, prior psychiatric diagnosis or treatment, and peripheral inflammatory markers have been associated with a higher prevalence of clinically relevant mental symptoms. All these variables could be useful when identifying vulnerable patients who require timely psychiatric care.

Declarations

Compliance with ethical standards

This study has been approved by the Research Ethics Committee Specific for COVID-19 of the "Seguro Social del Perú" (EsSalud). Each and every participant gave their informed consent to participate in this study.

Conflict of interests

The authors declare that they have no conflict of interest.

Financing sources

Self-financing.

Contribution of the authors

Jeff Huarcaya-Victoria: **Conceptualization**, Investigation, Project administration, Supervision, Drafting of the manuscript, Review, and editing of the manuscript.

Jessica Barreto: Conceptualization, Investigation, Data collection, Supervision, Draft of the manuscript, Review, and edition of the manuscript.

Lucia Aire: Data collection, Review, and edition of the manuscript.

Angela Podestá: Data collection, Review, and edition of the manuscript.

Mónica Caqui: Data collection, Review, and edition of the manuscript.

Rosa Guija-Igreda: Data collection, Review, and edition of the manuscript.

Claudia Castillo: Data collection, Review, and edition of the manuscript.

Christopher A. Alarcon-Ruiz: Data cleaning, Methodology, Statistic analysis, Review and edition of the manuscript.

References

1. Velavan TP, Meyer CG. The COVID-19 epidemic. *Trop Med Int Health*. 2020;25(3):278-80. doi:10.1111/tmi.13383
2. World Health Organization. Coronavirus Disease (COVID-19) Dashboard | WHO Coronavirus Disease (COVID-19) Dashboard 2020 [cited 2020 27 Dec]. Available from: https://covid19.who.int/?gclid=CjwKCAiAqJn9BRB0EiwAJ1Sstem0Dula_N2Ks2YpcEOGgyyvJlluRLQTimQ0xkrfjR-OY0sfiF9l1BoC1sQQAvD_BwE.
3. Gobierno del Perú. Sala Situacional COVID-19 Perú Lima: Gobierno del Perú; 2020 [cited 2021 12 ene]. Available from: https://covid19.minsa.gob.pe/sala_situacional.asp.
4. Zhou X. Psychological crisis interventions in Sichuan Province during the 2019 novel coronavirus outbreak. *Psychiatry Res*. 2020;286:112895. doi:10.1016/j.psychres.2020.112895
5. Rogers JP, Chesney E, Oliver D, Pollak TA, McGuire P, Fusar-Poli P, et al. Psychiatric and neuropsychiatric presentations associated with severe coronavirus infections: a systematic review and meta-analysis with comparison to the COVID-19 pandemic. *Lancet Psychiatry*. 2020;7(7):611-27. doi:10.1016/s2215-0366(20)30203-0
6. Huarcaya-Victoria J, Meneses-Saco A, Luna-Cuadros MA. Psychotic symptoms in COVID-19 infection: A case series from Lima, Peru. *Psychiatry Res*. 2020;293:113378-. doi:10.1016/j.psychres.2020.113378
7. Bo HX, Li W, Yang Y, Wang Y, Zhang Q, Cheung T, et al. Posttraumatic stress symptoms and attitude toward crisis mental health services among clinically stable patients with COVID-19 in China. *Psychol Med*. 2020:1-2. doi:10.1017/s0033291720000999
8. Kontoangelos K, Economou M, Papageorgiou C. Mental Health Effects of COVID-19 Pandemia: A Review of Clinical and Psychological Traits. *Psychiatry Investig*. 2020;17(6):491-505. doi:10.30773/pi.2020.0161

9. Raony Í, de Figueiredo CS, Pandolfo P, Giestal-de-Araujo E, Oliveira-Silva Bomfim P, Savino W. Psycho-Neuroendocrine-Immune Interactions in COVID-19: Potential Impacts on Mental Health. *Front Immunol.* 2020;11:1170. doi:10.3389/fimmu.2020.01170
10. Miller AH, Haroon E, Raison CL, Felger JC. Cytokine targets in the brain: impact on neurotransmitters and neurocircuits. *Depress Anxiety.* 2013;30(4):297-306. doi:10.1002/da.22084
11. Grace AA. Dysregulation of the dopamine system in the pathophysiology of schizophrenia and depression. *Nat Rev Neurosci.* 2016;17(8):524-32. doi:10.1038/nrn.2016.57
12. Bandelow B, Baldwin D, Abelli M, Bolea-Alamanac B, Bourin M, Chamberlain SR, et al. Biological markers for anxiety disorders, OCD and PTSD: A consensus statement. Part II: Neurochemistry, neurophysiology and neurocognition. *World J Biol Psychiatry.* 2017;18(3):162-214. doi:10.1080/15622975.2016.1190867
13. Deng J, Zhou F, Hou W, Silver Z, Wong CY, Chang O, et al. The prevalence of depression, anxiety, and sleep disturbances in COVID-19 patients: a meta-analysis. *Ann N Y Acad Sci.* 2020. doi:10.1111/nyas.14506
14. Moccia L, Janiri D, Pepe M, Dattoli L, Molinaro M, De Martin V, et al. Affective temperament, attachment style, and the psychological impact of the COVID-19 outbreak: an early report on the Italian general population. *Brain Behav Immun.* 2020;87:75-9. doi:10.1016/j.bbi.2020.04.048
15. Seguro Social de Salud. Estadística institucional Lima: Seguro Social de Salud; 2020 [cited 2021 10 Jan]. Available from: <http://www.essalud.gob.pe/estadistica-institucional/>.
16. Paz C, Mascialino G, Adana-Díaz L, Rodríguez-Lorenzana A, Simbaña-Rivera K, Gómez-Barreno L, et al. Behavioral and sociodemographic predictors of anxiety and depression in patients under epidemiological surveillance for COVID-19 in Ecuador. *PLoS One.* 2020;15(9):e0240008-e. doi:10.1371/journal.pone.0240008
17. Cassiani-Miranda CA, Vargas-Hernández MC, Pérez-Aníbal E, Herazo-Bustos MI, Hernández-Carrillo M. Confiabilidad y dimensión del cuestionario de salud del paciente (PHQ-9) para la detección de síntomas de depresión en estudiantes de ciencias de la salud en Cartagena, 2014. *Biomédica.* 2017;37(Supl. 1):112-20.
18. Saldivia S, Aslan J, Cova F, Vicente B, Inostroza C, Rincón P. Propiedades psicométricas del PHQ-9 (Patient Health Questionnaire) en centros de atención primaria de Chile. *Rev méd Chile.* 2019;147:53-60.
19. Villarreal-Zegarra D, Copez-Lonzoy A, Bernabe-Ortiz A, Melendez-Torres GJ, Bazo-Alvarez JC. Valid group comparisons can be made with the Patient Health Questionnaire (PHQ-9): A measurement invariance study across groups by demographic characteristics. *PloS one.* 2019;14(9):e0221717. doi:10.1371/journal.pone.0221717
20. Spitzer RL, Kroenke K, Williams JB, Lowe B. A brief measure for assessing generalized anxiety disorder: the GAD-7. *Arch Intern Med.* 2006;166(10):1092-7. doi:10.1001/archinte.166.10.1092
21. Garcia-Campayo J, Zamorano E, Ruiz MA, Pardo A, Perez-Paramo M, Lopez-Gomez V, et al. Cultural adaptation into Spanish of the generalized anxiety disorder-7 (GAD-7) scale as a screening tool. *Health Qual Life Outcomes.* 2010;8:8. doi:10.1186/1477-7525-8-8
22. Kroenke K, Spitzer RL, Williams JB. The PHQ-15: validity of a new measure for evaluating the severity of somatic symptoms. *Psychosom Med.* 2002;64(2):258-66. doi:10.1097/00006842-200203000-00008
23. Ros Montalbán S, Comas Vives A, Garcia-Garcia M. Validation of the Spanish version of the PHQ-15 questionnaire for the evaluation of physical symptoms in patients with depression and/or anxiety disorders: DEPRE-SOMA study. *Actas Esp Psiquiatr.* 2010;38(6):345-57.
24. Weiss DS, Marmar CR. The Impact of Event Scale—Revised. In: Wilson JP, Keane TM, editors. *Assessing psychological trauma and PTSD.* New York: Guilford Press; 1997. p. 399-411.
25. Caamaño W L, Fuentes M D, González B L, Melipillán A R, Sepúlveda C M, Valenzuela G E. Adaptación y validación de la versión chilena de la escala de impacto de evento-revisada (EIE-R). *Rev méd Chile.* 2011;139(9):1163-8.
26. Li X, Liu C, Mao Z, Xiao M, Wang L, Qi S, et al. Predictive values of neutrophil-to-lymphocyte ratio on disease severity and mortality in COVID-19 patients: a systematic review and meta-analysis. *Crit Care.* 2020;24(1):647. doi:10.1186/s13054-020-03374-8
27. Fois AG, Paliogiannis P, Scano V, Cau S, Babudieri S, Perra R, et al. The Systemic Inflammation Index on Admission Predicts In-Hospital Mortality in COVID-19 Patients. *Molecules.* 2020;25(23). doi:10.3390/molecules25235725
28. Park HY, Park WB, Lee SH, Kim JL, Lee JJ, Lee H, et al. Posttraumatic stress disorder and depression of survivors 12 months after the outbreak of Middle East respiratory syndrome in South Korea. *BMC Public Health.* 2020;20(1):605. doi:10.1186/s12889-020-08726-1
29. Ma YF, Li W, Deng HB, Wang L, Wang Y, Wang PH, et al. Prevalence of depression and its association with quality of life in clinically stable patients with COVID-19. *J Affect Disord.* 2020;275:145-8. doi:10.1016/j.jad.2020.06.033
30. Zhang J, Yang Z, Wang X, Li J, Dong L, Wang F, et al. The relationship between resilience, anxiety and depression among patients with mild symptoms of COVID-19 in China: A cross-sectional study. *J Clin Nurs.* 2020;29(21-22):4020-9. doi:10.1111/jocn.15425
31. Hernández-Vásquez A, Vargas-Fernández R, Bendezu-Quispe G, Grendas LN. Depression in the Peruvian population and its associated factors: analysis of a national health survey. *J Affect Disord.* 2020;273:291-7. doi:10.1016/j.jad.2020.03.100

32. Chieffo DPR, Delle Donne V, Massaroni V, Mastrilli L, Belella D, Monti L, et al. Psychopathological profile in COVID-19 patients including healthcare workers: the implications. *Eur Rev Med Pharmacol Sci.* 2020;24(22):11964-70. doi:10.26355/eurrev_202011_23858
33. Ran L, Wang W, Ai M, Kong Y, Chen J, Kuang L. Psychological resilience, depression, anxiety, and somatization symptoms in response to COVID-19: A this of the general population in China at the peak of its epidemic. *Soc Sci Med.* 2020;262:113261-. doi:10.1016/j.socscimed.2020.113261
34. Guo Q, Zheng Y, Shi J, Wang J, Li G, Li C, et al. Immediate psychological distress in quarantined patients with COVID-19 and its association with peripheral inflammation: A mixed-method study. *Brain Behav Immun.* 2020;88:17-27. doi:10.1016/j.bbi.2020.05.038
35. Hu Y, Chen Y, Zheng Y, You C, Tan J, Hu L, et al. Factors related to mental health of inpatients with COVID-19 in Wuhan, China. *Brain Behav Immun.* 2020;89:587-93. doi:10.1016/j.bbi.2020.07.016
36. Mazza MG, De Lorenzo R, Conte C, Poletti S, Vai B, Bollettini I, et al. Anxiety and depression in COVID-19 survivors: Role of inflammatory and clinical predictors. *Brain Behav Immun* 2020;89:594-600. doi:10.1016/j.bbi.2020.07.037
37. Liu N, Zhang F, Wei C, Jia Y, Shang Z, Sun L, et al. Prevalence and predictors of PTSS during COVID-19 outbreak in China hardest-hit areas: Gender differences matter. *Psychiatry Res.* 2020;287:112921. doi:10.1016/j.psychres.2020.112921
38. Loret de Mola C, Stanojevic S, Ruiz P, Gilman RH, Smeeth L, Miranda JJ. The effect of rural-to-urban migration on social capital and common mental disorders: PERU MIGRANT study. *Soc Psychiatry Psychiatr Epidemiol.* 2012;47(6):967-73. doi:10.1007/s00127-011-0404-6
39. Nie XD, Wang Q, Wang MN, Zhao S, Liu L, Zhu YL, et al. Anxiety and depression and its correlates in patients with coronavirus disease 2019 in Wuhan. *Int J Psychiatry Clin Pract.* 2020:1-6. doi:10.1080/13651501.2020.1791345
40. Yao H, Chen JH, Xu YF. Patients with mental health disorders in the COVID-19 epidemic. *Lancet Psychiatry.* 2020;7(4):e21. doi:10.1016/s2215-0366(20)30090-0
41. Poyraz BÇ, Poyraz CA, Olgun Y, Gürel Ö, Alkan S, Özdemir YE, et al. Psychiatric morbidity and protracted symptoms after COVID-19. *Psychiatry Res.* 2020;295:113604-. doi:10.1016/j.psychres.2020.113604
42. Huang C, Huang L, Wang Y, Li X, Ren L, Gu X, et al. 6-month consequences of COVID-19 in patients discharged from hospital: a cohort study. *The Lancet.* doi:10.1016/S0140-6736(20)32656-8
43. Yuan B, Li W, Liu H, Cai X, Song S, Zhao J, et al. Correlation between immune response and self-reported depression during convalescence from COVID-19. *Brain Behav Immun.* 2020;88:39-43. doi:10.1016/j.bbi.2020.05.062
44. Conti P, Ronconi G, Caraffa A, Gallenga CE, Ross R, Frydas I, et al. Induction of pro-inflammatory cytokines (IL-1 and IL-6) and lung inflammation by Coronavirus-19 (COVI-19 or SARS-CoV-2): anti-inflammatory strategies. *J Biol Regul Homeost Agents.* 2020;34(2). doi:10.23812/conti-e
45. Karageorgiou V, Milas GP, Michopoulos I. Neutrophil-to-lymphocyte ratio in schizophrenia: A systematic review and meta-analysis. *Schizophr Res.* 2019;206:4-12. doi:10.1016/j.schres.2018.12.017
46. Huarcaya-Victoria J. Consideraciones sobre la salud mental en la pandemia de COVID-19. *Rev Peru Med Exp Salud Publica.* 2020;37(2):327-34.

Tables

Table 1. Sample characteristics (n=318)

Characteristics	n (%)
Female	196 (61.6)
Age (years)*	54.4 ± 15.1
Educational degree	
None or incomplete	42 (13.2)
Secondary school	135 (42.5)
Technical degree	34 (10.7)
University	107 (33.7)
Job status	
Unemployed	95 (29.9)
Informal employment	31 (9.8)
Formal employment	143 (45.0)
Retired	49 (15.4)
Live with	
Alone	17 (5.4)
Couple and/or children	256 (80.5)
Parents and/or other family members	45 (14.2)
Family member infected with the COVID-19	264 (83.0)
<i>Loss of a family member due to the COVID-19</i>	97 (30.5)
History of psychiatric diagnosis	32 (10.1)
History of psychiatric treatment	27 (8.5)
Self-perception of the severity of COVID-19	
Mild	89 (28.0)
Moderate	107 (33.7)
Severe	99 (31.1)
Critically ill	23 (7.2)
Hospitalization area	
Internal medicine	240 (75.5)
High-risk obstetrics	35 (11.0)
Neumology	31 (9.8)
Cardiology	12 (3.8)
Time of hospitalization	
1 to 7 days	154 (48.4)
8 to 14 days	84 (26.4)
More than 14 days	80 (25.2)
Depressive symptoms	
Normal	222 (69.8)
Mild	62 (19.5)
Moderate	18 (5.7)
Moderate-Severe	11 (3.5)

Severe	5 (1.6)
Somatic symptoms	
Normal	210 (66.0)
Mild	65 (20.4)
Moderate	36 (11.3)
Severe	7 (2.2)
Anxious symptoms	
Normal	223 (70.1)
Mild	71 (22.3)
Moderate	17 (5.4)
Severe	7 (2.2)
Distress symptoms	
Normal	227 (71.4)
Mild	66 (20.8)
Moderate	18 (5.7)
Severe	7 (2.2)
NLR greater than or equal to 6.5 at income (n=277)	135 (48.7)
MLR greater than or equal to 0.364 upon admission (n=277)	112 (40.4)
*Mean and standard deviation	
NLR: Neutrophil-to-lymphocyte ratio	
MLR: Monocyte-to-lymphocyte ratio	

Table 2. Bivariate association between variables and depressive, somatic, anxious, and distress symptoms (n=318)

Characteristics	Depression, n (%)	p	Somatic symptoms, n (%)	p	Anxiety, n (%)	p	Distress, n (%)	p
	Moderate-Severe		Moderate-Severe		Moderate-Severe		Moderate-Severe	
Gender†		0.009		0.011		0.011		0.059
Male (n=196)	14 (7.1)		19 (9.7)		9 (4.6)		11 (5.6)	
Female (n=122)	20 (16.4)		24 (19.7)		15 (12.3)		14 (11.5)	
Age (years)*	55.9 ± 14.8	0.300	55.3 ± 15.7	0.369	51.5 ± 13.8	0.529	52.4 ± 14.6	0.718
Marital status†		0.659		0.845		0.886		0.829
Single (n=49)	4 (9.1)		5 (11.4)		3 (6.8)		3 (6.8)	
Married (n=225)	23 (10.2)		32 (14.2)		18 (8.0)		19 (8.4)	
Divorced or widower (n=49)	7 (14.3)		6 (12.2)		3 (6.1)		3 (6.1)	
Educational degree‡		0.424		0.420		0.453		0.121
None or incomplete (n=42)	7 (16.7)		9 (21.4)		4 (9.5)		7 (16.7)	
Secondary school (n=135)	11 (8.2)		17 (12.6)		7 (5.2)		8 (5.9)	
Technical degree (n=34)	4 (11.8)		3 (8.8)		2 (5.9)		1 (2.9)	
University (n=107)	12 (11.2)		14 (13.1)		11 (10.3)		9 (8.4)	
Job status†		0.180		0.136		0.274		0.691
Unemployment (n=95)	14 (14.7)		18 (19.0)		10 (10.5)		8 (8.4)	
Informal employment (n=31)	1 (3.2)		1 (3.2)		0 (0.0)		1 (3.2)	
Formal employment (n=143)	12 (8.4)		17 (11.9)		11 (7.7)		13 (9.1)	
Retired (n=49)	7 (14.3)		7 (14.3)		3 (6.1)		3 (6.1)	
Profess a religion‡		0.288		0.104		0.399		0.408
No (n=23)	4 (17.4)		6 (26.1)		3 (13.0)		3 (13.0)	
Yes (n=295)	30 (10.2)		37 (12.5)		21 (7.1)		22 (7.5)	
Place of origin before hospitalization‡		0.423		0.282		0.635		0.642
Lima (n=300)	31 (10.3)		39 (13.0)		22 (7.3)		23 (7.7)	
Other provinces (n=18)	3 (16.7)		4 (22.2)		2 (11.1)		2 (11.1)	
Current home‡		1.000		0.730		0.379		1.000

Lima (n=299)	32 (10.7)		40 (13.4)		24 (8.0)		24 (8.0)	
Other provinces (n=19)	2 (10.5)		3 (15.8)		0 (0.0)		1 (5.3)	
Live with‡		0.080		0.267		0.190		0.601
Alone (n=17)	1 (5.9)		0 (0.0)		0 (0.0)		0 (0.0)	
Couple and/or children (n=256)	32 (12.5)		37 (14.5)		23 (9.0)		22 (8.6)	
Fathers and/or other family members (n=45)	1 (2.2)		6 (13.3)		1 (2.2)		3 (6.7)	
History of family member infected by COVID-19†		0.180		0.149		0.082		0.213
No (n=54)	3 (5.6)		4 (7.4)		1 (1.9)		2 (3.7)	
Yes (n=264)	31 (11.7)		39 (14.8)		23 (8.7)		23 (8.7)	
Loss of a family member due to the COVID-19†		0.068		0.082		0.754		0.866
No (n=221)	19 (8.6)		25 (11.3)		16 (7.2)		17 (7.7)	
Yes (n=97)	15 (15.5)		18 (18.6)		8 (8.3)		8 (8.3)	
History of psychiatric diagnosis‡		0.062		0.005		0.079		0.028
No (n=286)	27 (9.4)		33 (11.5)		19 (6.6)		19 (6.6)	
Yes (n=32)	7 (21.9)		10 (31.3)		5 (15.6)		6 (18.8)	
History of psychiatric treatment‡		0.053		0.005		0.041		0.012
No (n=291)	28 (9.6)		34 (11.7)		19 (6.5)		19 (6.5)	
Yes (n=27)	6 (22.2)		9 (33.3)		5 (18.5)		6 (22.2)	
Self-perception of the severity of COVID-19†		0.004		0.437		0.505		0.009
Mild (n=89)	3 (3.4)		8 (9.0)		4 (4.5)		2 (2.3)	
Moderate (n=107)	9 (8.4)		15 (14.0)		9 (8.4)		7 (6.5)	
Severe (n=99)	19 (19.2)		17 (17.2)		8 (8.1)		11 (11.1)	
Critically ill (n=23)	3 (13.0)		3 (13.0)		3 (13.0)		5 (21.7)	
Time hospitalized†		0.139		0.959		0.525		0.668
1 a 7 days (n=154)	12 (7.8)		20 (13.0)		14 (9.1)		10 (6.5)	
8 a 14 days (n=84)	9 (10.7)		12 (14.3)		6 (7.1)		8 (9.5)	
More than 14 days (n=80)	13 (16.3)		11 (13.8)		4 (5.0)		7 (8.8)	
NLR upon admission** (n=277)	7.8 (4.5 - 18.8)	0.037	6.2 (3.9 - 15.5)	0.574	8.1 (4.5 - 18.2)	0.146	7.6 (4.2 - 18.4)	0.178
MLR upon	0.3 (0.2 -	0.872	0.3 (0.2 -	0.109	0.3 (0.1 -	0.421	0.3 (0.2 -	0.900

admission** (n=277)	0.5)		0.5)		0.5)		0.6)	
Follow-up time (days)**	101.0 (72.0 - 127.0)	0.872	102.0 (76.0 - 129.0)	0.733	98.0 (75.5 - 151.0)	0.586	118.0 (93.0 - 141.0)	0.070
Persistent COVID- 19 symptoms		<0.001		<0.001		0.001		<0.001
No (n=124)	3 (2.4)		5 (4.0)		2 (1.6)		1 (0.8)	
At least 1 symptom (n=194)	31 (16.0)		38 (19.6)		22 (11.3)		24 (12.4)	
* Mean and standard deviation with Student's t-test								
**Median and interquartile range with Mann Whitney U test; † Chi-2 test; ‡ Fisher's exact test								
NLR: Neutrophil-to-lymphocyte ratio; MLR: monocyte-to-lymphocyte ratio								

Table 3. Association between variables and depression, somatic symptoms, anxiety and distress symptoms (n=318)								
Characteristics	Depression moderate-severe		Somatic symptoms moderate-severe		Anxiety moderate-severe		Distress moderate-severe	
	PR* (CI 95%)	p	PR* (CI 95%)	p	PR* (CI 95%)	p	PR* (CI 95%)	p
Gender								
Male	Ref.		Ref.		Ref.		Ref.	
Female	2.29 (1.06 - 4.92)	0.034	2.04 (1.06 - 3.89)	0.032	2.71 (1.62 - 4.53)	<0.001	2.11 (1.05 - 4.24)	0.036
Age								
20 a 41 years	Ref.		Ref.		Ref.		Ref.	
42 a 53 years	0.91 (0.55 - 1.51)	0.722	0.93 (0.40 - 2.17)	0.868	0.51 (0.26 - 1.01)	0.052	1.34 (0.73 - 2.44)	0.341
54 a 65 years	1.33 (0.74 - 2.39)	0.341	1.28 (0.68 - 2.42)	0.450	1.12 (0.54 - 2.33)	0.763	1.19 (0.59 - 2.41)	0.625
66 a 94 years	1.05 (0.44 - 2.49)	0.913	1.19 (0.40 - 3.48)	0.754	0.41 (0.26 - 0.65)	<0.001	0.77 (0.39 - 1.55)	0.464
Marital status								
Single	Ref.		Ref.		Ref.		Ref.	
Married	1.11 (0.73 - 1.70)	0.628	1.26 (0.69 - 2.32)	0.456	1.21 (0.57 - 2.56)	0.617	1.36 (0.82 - 2.24)	0.230
Divorced or widower	1.54 (1.00 - 2.37)	0.053	1.09 (0.56 - 2.12)	0.793	0.95 (0.32 - 2.87)	0.934	1.07 (0.36 - 3.23)	0.903
Educational degree								
None or incomplete	Ref.		Ref.		Ref.		Ref.	
Secondary school	0.49 (0.23 - 1.05)	0.068	0.59 (0.46 - 0.75)	<0.001	0.53 (0.27 - 1.08)	0.079	0.34 (0.22 - 0.51)	<0.001
Technical degree	0.71 (0.24 - 2.10)	0.535	0.41 (0.22 - 0.76)	0.005	0.61 (0.32 - 1.16)	0.134	0.17 (0.01 - 3.26)	0.242
University	0.67 (0.30 - 1.49)	0.331	0.61 (0.27 - 1.36)	0.227	1.07 (0.85 - 1.35)	0.558	0.50 (0.37 - 0.67)	<0.001
Job status								
Unemployment	Ref.		Ref.		Ref.		Ref.	
Informal employment	0.22 (0.01 - 5.25)	0.349	0.17 (0.01 - 2.26)	0.179	.	.	0.38 (0.17 - 0.86)	0.019
Formal employment	0.57 (0.39 - 0.84)	0.004	0.62 (0.46 - 0.85)	0.003	0.72 (0.50 - 1.04)	0.084	1.04 (0.42 - 2.59)	0.937
Retired	0.96 (0.61 - 1.52)	0.869	0.76 (0.57 - 1.02)	0.071	0.60 (0.41 - 0.87)	0.007	0.80 (0.61 - 1.05)	0.105
Profess a religion								
No	Ref.		Ref.		Ref.		Ref.	
Yes	0.59 (0.23 - 1.52)	0.274	0.48 (0.13 - 1.74)	0.262	0.53 (0.22 - 1.28)	0.161	0.54 (0.19 - 1.52)	0.242
Place of origin before hospitalization								
Lima	Ref.		Ref.		Ref.		Ref.	
Other provinces	1.61 (1.10 - 2.35)	0.015	1.71 (0.82 - 3.57)	0.151	1.53 (1.03 - 2.27)	0.036	1.47 (0.73 - 2.96)	0.276

Current home								
Lima	Ref.		Ref.				Ref.	
Other provinces	0.99 (0.35 - 2.78)	0.979	1.18 (0.95 - 1.46)	0.134			0.65 (0.26 - 1.60)	0.346
Live with								
Alone	Ref.							
Couple and/or children	2.12 (1.54 - 2.92)	<0.001	Ref.		Ref.		Ref.	
Fathers and/or other family member	0.38 (0.14 - 1.05)	0.063	0.92 (0.40 - 2.12)	0.840	0.24 (0.06 - 0.96)	0.043	0.72 (0.24 - 2.16)	0.562
History of a family member infected by COVID-19								
No	Ref.		Ref.		Ref.		Ref.	
Yes	2.12 (0.82 - 5.47)	0.122	1.99 (1.07 - 3.71)	0.029	4.71 (1.75 - 12.69)	0.002	2.38 (0.65 - 8.69)	0.191
Loss of a family member due to the COVID-19								
No	Ref.		Ref.		Ref.		Ref.	
Yes	1.81 (0.92 - 3.54)	0.084	1.64 (1.09 - 2.47)	0.018	1.13 (0.86 - 1.48)	0.372	1.05 (0.72 - 1.52)	0.814
History of psychiatric diagnosis								
No	Ref.		Ref.		Ref.		Ref.	
Yes	2.30 (1.49 - 3.56)	<0.001	2.73 (1.85 - 4.03)	<0.001	2.41 (0.69 - 8.37)	0.167	3.01 (1.64 - 5.54)	<0.001
History of psychiatric treatment								
No	Ref.		Ref.		Ref.		Ref.	
Yes	2.29 (1.41 - 3.72)	0.001	2.90 (2.12 - 3.97)	<0.001	2.96 (0.85 - 10.33)	0.088	3.80 (2.15 - 6.74)	<0.001
Self-perception of the severity of COVID-19**								
Mild	Ref.		Ref.		Ref.		Ref.	
Moderate	3.55 (1.95 - 6.48)	0.000	1.49 (0.51 - 4.37)	0.469	2.37 (0.94 - 5.98)	0.069	3.67 (1.23 - 10.91)	<0.001
Severe	8.46 (5.58 - 12.83)	0.000	1.82 (0.80 - 4.11)	0.153	2.29 (1.17 - 4.48)	0.015	6.16 (1.53 - 24.83)	0.011
Critically ill	5.53 (1.88 - 16.32)	0.002	1.39 (0.46 - 4.20)	0.560	3.98 (0.78 - 20.33)	0.097	14.78 (4.26 - 51.31)	<0.001
NLR upon admission (n=277)								
< 6.5	Ref.		Ref.		Ref.		Ref.	
≥ 6.5	1.67 (1.13 - 2.47)	0.010	1.00 (0.79 - 1.27)	0.995	1.82 (1.18 - 2.81)	0.007	1.42 (0.96 - 2.12)	0.081
MLR upon admission (n=277)								
< 0.364	Ref.		Ref.		Ref.		Ref.	
≥ 0.364	1.21 (0.73 - 2.01)	0.462	0.85 (0.51 - 1.41)	0.530	0.85 (0.60 - 1.20)	0.346	1.06 (0.79 - 1.42)	0.697
Persistent COVID-19 symptoms**								
No								

At least 1 symptom	8.55 (4.70 - 15.56)	<0.001	5.46 (1.60 - 18.64)	0.007	11.38 (7.34 - 17.62)	<0.001	20.55 (2.53 - 167.21)	0.005
*Poisson regression model adjusted for follow-up time and cluster according to hospitalization service								
** Regression models, in addition, adjusted for the presence of COVID-19 symptoms at admission								
95% CI: 95% confidence interval; NLR: Neutrophil-to-lymphocyte ratio; MLR: monocyte-to-lymphocyte ratio; PR: prevalence ratio								