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Letter to the Editor

Anxiety, depression and poor sleep quality as long-term post-COVID sequelae in previously hospitalized patients: A multicenter study

Evidence supports the presence of a plethora of symptoms after suffering severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. The prevalence rate of these post-COVID symptoms ranges from 35 to 60% depending on the symptom and the follow-up period.¹ One letter to the Editor and one full-text in *Journal of Infection* found that fatigue and dyspnea are the most prevalent post-COVID symptoms in both hospitalized² and non-hospitalized³ patients. Post-COVID sequelae include general, respiratory, physical, gastrointestinal, neurological, and mental symptoms. A scoping review observed that anxiety and depression are also prevalent post-COVID symptoms;⁴ however, most of published studies have follow-up periods < 3 months, sample sizes <300 participants, and were conducted at single centers.⁴ We have recently published in a letter to the Editor in *Journal of Infection*, a multicenter study assessing post-COVID symptoms and their associated risk factors seven months after hospital discharge⁵. This study observed that 80% of hospitalized COVID19 survivors exhibited at least one post-COVID symptom seven months after hospital discharge, being fatigue and dyspnea the most prevalent. No data about the prevalence of mood disorders was provided. Here we present secondary data of that multicenter study analyzing the prevalence of depressive and anxiety levels and sleep quality.

Briefly, this multicenter observational study included 1200 hospitalized patients randomly selected from four public hospitals in Madrid, Spain (300 from each hospital) with a diagnosis of SARS-CoV-2 by RT-PCR technique and radiological findings during the first wave of the pandemic (March 10th to May 31st, 2020). Local Ethics Committees of all hospitals approved the study (HCSC20/495E, HUFA 20/126, HUF/EC1517, HUIL /092-20, URJC0907202015920). Informed consent was obtained from all participants.

Patients were scheduled for a telephone interview by trained researchers a mean of 7.0 months (SD 0.6) after hospital discharge. Clinical (i.e., age, gender, height, weight, pre-existing comorbidities) and hospitalization (e.g., symptoms at hospital admission, days at hospital, intensive care unit [ICU] admission) data were collected from hospital medical records. In addition to a predetermined list of post-COVID symptoms previously described⁵, depressive/anxiety level and sleep quality were also collected. The Hospital Anxiety and Depression Scale (HADS) was used to assess anxiety (HADS-A, 7 items, 0–21 points) and depressive (HADS-D, 7 items, 0–21 points) symptoms.⁶ We considered the cut-off scores recommended for Spanish population (HADS-A ≥ 12 points; HADS-D ≥ 10 points) suggestive of clinical anxiety and depressive symptoms, respectively⁷. The Pittsburgh Sleep Quality Index (PSQI) was used to assess the sleep quality the previous month by us-

Table 1

Demographic, clinical and hospitalization data (n = 1142).

Age, mean (SD), years	61 (17)
Gender, male/female (%)	601/541
Weight, mean (SD), kg.	70 (15)
Height, mean (SD), cm.	166 (10)
Medical co-morbidities	
Hypertension	291 (25.5%)
Diabetes	145 (13%)
Chronic Heart Disease - Cardiovascular Disease	144 (13%)
Rheumatological Disease	61 (5.5%)
Asma	55 (5%)
Obesity	54 (5%)
Chronic Obstructive Pulmonary Disease	51 (4.5%)
Stroke	29 (2.5%)
Other (cancer, kidney disease)	105 (9%)
Stay at the hospital, mean (SD), days	14 (12)
Intensive Care Unit (ICU) admission	
Yes/No, n (%)	80 (7%) / 1062 (93%)
Stay at ICU, mean (SD), days	15 (13)
Anxiety/Depressive Symptom, n (%)	
Anxiety Symptoms (HADS-A ≥ 12 points)	185 (16.2%)
Depressive Symptoms (HADS-D ≥ 10 points)	225 (19.7%)
Sleep Quality, n (%)	394 (34.5%)
Poor Sleep Quality (PSQI ≥ 8 points)	

ing 19 self-reported questions assessing the usual bed time, usual wake time, number of hours slept, and number of minutes to fall asleep.⁸ A total score ranging from 0 to 21 points is calculated, higher scores indicate worse sleep quality, and a score > 8.0 points is indicative of poor sleep quality.⁸

Descriptive data are presented as mean (standard deviation, SD) or percentages as appropriate. Multivariate Poisson regression prediction and risk models were constructed to identify clinical/hospitalization variables associated with the presence of post-COVID anxiety/depressive symptoms and poor sleep quality. Adjusted Odd Ratio (OR) with 95% confidence intervals (95%CI) were calculated.

As previously reported, a total of 1142 (48% women, mean age: 61, SD: 17 years) were included. Data on symptoms at hospital admission, previous co-morbidities, or other post-COVID symptoms have been previously published.⁵ **Table 1** summarizes clinical and hospitalization data related to the current analysis. Seven months after hospitalisation, 16.2% patients showed anxiety symptoms (≥ 12 points), 19.7% depressive symptoms (≥ 10 points), and 34.5% poor sleep quality (≥ 8 points). Only 50.4% (n = 575) of the included patients did not report depressive/anxiety symptoms or poor sleep quality at seven months after hospital discharge. Significant positive associations between anxiety and depressive symptoms (r: 0.759, $P < 0.001$) and between sleep quality with anxiety (r: 0.239, $P < 0.001$) and depressive (r: 0.340, $P < 0.001$) symptoms observed.

The regression models revealed that female (OR1.88, 95%CI 1.35–2.51, $P < 0.001$), the number of days at the hospital (OR1.02, 95%CI 1.01–1.03, $P = 0.04$), the number of pre-existing medical comorbidities (OR1.23, 95%CI 1.02–1.45, $P = 0.022$) and the number of symptoms at hospital admission (OR1.37, 95%CI 1.13–1.67, $P = 0.001$) were associated with depressive symptoms. Only the number of symptoms at hospital admission (OR1.29, 95%CI 1.04–1.58, $P = 0.015$) was significantly associated with anxiety. Finally, poor sleep quality was associated with female gender (OR2.15, 95%CI 1.65–2.80; $P < 0.001$), number of days at hospital (OR1.02, 95%CI 1.001–1.035, $P < 0.001$), the number of comorbidities (OR1.34, 95%CI 1.15–1.57, $P < 0.001$), and number of symptoms at hospital admission (OR1.31, 95%CI 1.12–1.54, $P < 0.001$).

This multicenter study revealed that almost 50% of hospitalised COVID-19 survivors experienced anxiety or depressive symptoms and/or poor sleep quality seven months after hospital discharge. Specifically, anxiety symptoms were observed in 16.2% of patients, depressive symptoms in 19.7%, and poor sleep quality in 34.5%. Our prevalence rates of post-COVID depressive or anxiety symptoms and poor sleep quality should be considered significant since patients were evaluated seven months after hospital discharge, but were lower than prevalence data previously reported (40–45%) during the acute hospitalisation period.⁹ Previous studies investigating post-COVID mood disorders included follow-up < 3 months, smaller samples and individuals recruited from just one center. The current study increases evidence to the literature with a large, multicenter design evaluating long-term post-COVID anxiety/depressive levels and sleep quality.

Early recognition of long-term post-COVID effects and associated risk factors will facilitate diagnosis and multidisciplinary strategies for these patients.¹⁰ We identified that female gender, longer stay at hospital, higher number of comorbidities, and higher number of symptoms at hospital admission were risk factors associated with depressive symptoms and poor sleep quality, but not with anxiety levels. Similar risk factors were identified for the number of post-COVID symptoms (not including mood disorders) in our previous letter.⁵ Future studies determining the role of these risk factors in the development of long-term post-COVID symptoms are guaranteed.

Finally, these results should be considered attending study weaknesses. First, only hospitalized patients were included. Second, patients with diagnosed psychiatric diseases were excluded. Third, we did not collect objective measures of COVID-19 disease, e.g., inflammatory biomarkers, blood oxygen saturation.

Author contributions

All authors contributed to the study concept and design. CFdIP, DMP, VGM, and VHB conducted literature review and did the statistical analysis. VGM, MVA, CG, CMEM, MLC, JAAN, LJMT, TSV, JTM, MGCD, and SPC recruited participants. JRJ, MPC, AidILR, SFN, LLF, ROS, MGM, and SAQ collected data. DPC supervised the study. All authors contributed to interpretation of data. CFdIP, DPC, VGM, and MLC contributed to drafting the paper. All authors revised the text for intellectual content and have read and approved the final version of the manuscript.

Declaration of Competing Interest

No conflict of interest is declared by any of the authors.

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