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ORIGINAL PAPER

Psychiatric Clinical Profiles and Pharmacological Interactions in COVID-19 Inpatients Referred to a Consultation Liaison Psychiatry Unit: a Cross-Sectional Study

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Abstract
The Coronavirus Disease 2019 (COVID-19) can affect mental health in different ways. There is little research about psychiatric complications in hospitalized patients with COVID-19. The aim of the study was to describe the psychiatric clinical profile and pharmacological interactions in COVID-19 inpatients referred to a Consultation-Liaison Psychiatry (CLP) unit. This is a cross-sectional study, carried out at a tertiary hospital in Spain, in inpatients admitted because of COVID-19 and referred to our CLP Unit from March 17,2020 to April 28,2020. Clinical data were extracted from electronic medical records. The patients were divided in three groups depending on psychiatric diagnosis: delirium, severe mental illness (SMI) and non-severe mental illness (NSMI). Of 71 patients included (median [ICR] age 64 [54–73] years; 70.4% male), 35.2% had a delirium, 18.3% had a SMI, and 46.5% had a NSMI. Compared to patients with delirium and NSMI, patients with SMI were younger, more likely to be institutionalized and were administered less anti-COVID19 drugs. Mortality was higher among patients with delirium (21.7%) than those with SMI (0%) or NSMI (9.45%). The rate of side effects due to interactions between anti-COVID19 and psychiatric drugs was low, mainly drowsiness (4.3%) and borderline QTc prolongation (1.5%). Patients affected by SMI were more often undertreated for COVID-19. However, the rate of interactions was very low, and avoidable with a proper evaluation and drug-dose adjustment. Half of the patients with SMI were institutionalized, suggesting that living conditions in residential facilities could make them more vulnerable to infection.

Keywords COVID-19 · Consultation-liaison psychiatry · Psychopharmacology · Pharmacological interactions · Delirium · Mental health residential facilities

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Introduction

The Coronavirus Disease 2019 (COVID-19) pandemic has been leading to an increase in the burden of mental health issues worldwide [1]. Most of the current published research in the field of Psychiatry is focused on the psychological impact of COVID-19 in the general population and healthcare workers [2–4]. However, little is known about the clinical characteristics and treatment of potential psychiatric manifestations in hospitalized patients with COVID-19 [5].

A high prevalence of psychological reactions to stress, such as anxiety, depression or insomnia, would be expected, since they are common in critically ill patients, and some of them may be expected to require psychiatric intervention [6]. Nevertheless, psychological stress is not the only mechanism for psychiatric complications in COVID-19, as neurotoxicity and side effects of common therapies also contribute [7–9].

SARS-CoV-2, which causes COVID-19, may lead to acute neuropsychiatric symptoms secondary to central nervous system (CNS) damage via cytokine dysregulation or viral infiltration to the central nervous system [10, 11]. In critically ill patients, other factors may contribute to delirium, such as secondary effects of organ failure or sedation strategies, as well as prolonged time of mechanical ventilation and immobilization [12].

In addition, some COVID-19 therapies are known to produce psychiatric complications, such as delirium, psychosis, and affective symptoms. While corticosteroid therapy can lead to neuropsychiatric effects in about one third of treated patients [8], generally of acute onset and rapid remission after treatment termination, the risk for these effects with hydroxychloroquine (HCQ) is lower and may continue several weeks after drug discontinuation due to its longer half-life [8, 9]. Protease inhibitors, such as lopinavir/ritonavir (LPV/r), are unlikely to produce psychiatric complications, but they have been shown to interact with many psychotropic medications [13, 14]. Azithromycin (AZT) is not associated with psychiatric complications, but similarly to HCQ, LPV/r and some antipsychotics and antidepressants, it can produce QTc interval prolongation [14]. Close monitoring and dose adjusting may be required when COVID-19 therapies and psychotropic medications are co-administered [14–16].

Limited information is available about the impact of the epidemic on people with mental health disorders. This group may be more susceptible to infections for several reasons: cognitive impairment, little awareness of risk, confined conditions in psychiatric wards and more barriers in accessing timely health services [17]. Furthermore, the emotional response to the epidemic itself may result in relapses or worsening of pre-existing mental disorders [17].

In many hospitals, staff assigned to Consultation-Liaison Psychiatry (CLP) is taking over the management of psychiatric complications in inpatients with COVID-19 [18]. Moreover, because many patients are already on psychotropic drugs, which may potentially interact with COVID-19 therapies, consultations to CLP are made for dose adjustment.

Taking the foregoing statements into account we hypothesised that three general clinical profiles were expected to be found among patients referred to a CLP unit: Delirium patients, Severe Mental Illness (SMI) patients and Non-Severe Mental Illness (NSMI) patients.

The objectives of the study were to:

1. Describe and assess clinical and socio-demographic differences among these three groups of psychiatric patients with COVID-19 referred to a CLP unit.
2. Evaluate pharmacological interactions between medication for mental illness and for COVID-19, in particular as to QTc changes.

Methods

Study Design and Participants

This cross-sectional study was carried out at a tertiary general university hospital in Barcelona, Spain, on inpatients admitted because of COVID-19 to medical wards, and referred to our CLP Unit from March 17, 2020 to April 28, 2020.

Selection criteria was: patients confirmed as a case of COVID-19 on polymerase chain reaction (PCR) analysis of nasopharyngeal or throat swab specimens, as per the hospital protocol. There was no exclusion criteria.

The study was performed in accordance with the principles of the Declaration of Helsinki. This study was approved by the Ethics Committee of Hospital Clinic, Barcelona, Spain, under resolution number HCB/2020/0496.

Data Collection

We reviewed electronic medical records and laboratory findings from all patients and collected data on the following variables:

- Sociodemographic variables: age, sex, institutionalization, social support.
- Medical and psychiatric history: presence of severe comorbidities (defined as severe chronic lung, kidney, liver or heart disease, neoplasm or ischemic brain disease), psychiatric history (diagnosis according to DSM-5), previous psychiatric medication.
- Hospitalization variables: Date of admission, Intensive Care Unit (ICU) admission, incidental SARS-CoV-2 diagnosis (asymptomatic inpatients with a positive test for SARS-CoV-2 and admitted for other reasons), reason for referral, prolonged weaning, current DSM-5 diagnosis, clinical features of delirium (hyperactive, hypoactive, mixed, presence of hallucinations, delusions or mood disturbances such as depression or mania), COVID-19 therapies (HCQ, LPV/r, AZT, tocilizumab, corticosteroids or others), side effects due to interaction between COVID-19 and psychiatric medication (drowsiness, confusion, extrapyramidal effects or others), requirements of psychiatric drug dose adjustment, QTc interval before and after consultation, date of discharge, total days of stay, outcome at discharge (death, home, nursing homes and others).

Procedure

The patients were divided in three groups depending on psychiatric diagnosis after assessment by the CLP unit: (1) patients affected by delirium, (2) patients affected by severe mental illness (defined as psychotic disorder [including schizophrenia, schizoaffective disorder and other types of psychosis], bipolar disorder, severe major depressive disorder, severe autism spectrum disorder or intellectual disability and severe chronic organic mental disease), and (3) patients affected by non-severe mental illness (defined as mild-moderate major depressive disorder, dysthymic disorder, anxiety disorder, adjustment disorder, substance use disorder, personality disorder or others) or without any DSM-5 diagnosis. If a patient met criteria for more than one group, delirium prevailed over the other two groups and severe over non-severe mental illness.

The electrocardiogram (ECG) QTc interval was evaluated at two timepoints: Baseline ECG and control ECG after psychiatric drug dose adjustment. It was interpreted as "pathological" when there was a prolongation greater than 450 milliseconds (ms) in men and 470 ms in women [19]. QTc intervals of 431-450 ms in men or 451-470 ms in women were interpreted as "borderline" [19].

Statistical Analysis

Descriptive statistics were calculated to summarize the sociodemographic and clinical characteristics of the sample. The distribution was non-parametric. Categorical variables were expressed by using frequencies and percentages, while medians and interquartile ranges were used for continuous variables. The chi-square-test (χ^2) or Fisher's exact test where appropriate were used to analyse categorical data. Mann-Whitney U-test was used to compare quantitative data between two groups, and for more than two groups, the Kruskal-Wallis test by ranks was used instead. Significance was pre-assigned at $p < 0.05$. Missing cases were excluded from analysis using pairwise deletion. Statistical evaluation was performed using IBM SPSS Statistics software package ver. 25. [20]

Results

Sociodemographic and Clinical Characteristics

A total of 71 patients were included in the final analysis. There were 25 patients (35.2%) in the Delirium group, 13 patients (18.3%) in the SMI group and 33 patients (46.5%) in the NSMI group.

The median age of the sample was 64 years (IQR: 54–73). The SMI group (median age: 48 years) was younger than the Delirium (median age: 69 years; $p = 0.002$) and NSMI group (median age: 67 years; $p = 0.001$).

The sociodemographic and clinical characteristics of all the sample and each clinical group of patients, just as the main differences among the three groups, are summarized in Table 1.

About three-quarters ($n = 53$; 74.6%) of the sample had at least one previous psychiatric diagnosis, and 63.4% ($n = 45$) were taking at least one psychiatric drug; the most common were antidepressants ($n = 30$; 42.3%) (Table 2).

Referral to Consultation-Liaison Psychiatry

The most common reason for referral was psychiatric drug dose adjustment (38.8% of all consultations), whereas suspected substance abuse was the least (1.4%). Difficult weaning was present in 14.1% of the sample (mainly those with delirium) and was related mostly to confusion (50%) or agitation (20%). (Table 3).

The most common type of delirium was mixed (48%), followed by hyperactive (32%) and hypoactive (20%). The symptomatology also included persecutory delusion in 12% ($n = 3$), mood disturbances in 12% ($n = 3$) and visual hallucinations in 4% ($n = 1$).

Table 1 Sociodemographic and clinical variables

Socio-demogra phic and clinical variables	Total ($n = 71$)	DEL ($n = 25$)	SMI ($n = 13$)	SMI ($n = 33$)	Group comparisons							
					DEL-SMI-NSMI		DEL-SMI		DEL-NSMI		SMI-NSMI	
	N (%)	N (%)	N (%)	N (%)	χ^2	*P*	χ^2	*p*	χ^2	*p*	χ^2	*p*
Male	50 (70.4)	19 (76)	9 (69.2)	22 (66.7)	*0.606*	*0.739*	–	–	–	–	–	–
Institutionalization	16 (22.5)	6 (24)	7 (53.8)	3 (9.1)	*10.478*	***0.050***	*F's**	*0.071*	*F's **	*0.118*	*F's **	***0.002***
Social support	62 (87.3)	22 (88)	11 (84.6)	29 (87.9)	*0.106*	*0.949*	–	–	–	–	–	–
ICU setting	18 (25.4)	13 (52)	0 (0)	5 (15.2)	*15.61*	***0.000***	*F's**	***0.001***	*F's **	***0.003***	*F's **	*0.173*
COVID-19 Incidental Diagnosis	5 (7.0)	1 (4)	4 (30.8)	0 (0)	*14.033*	***0.001***	*F's**	***0.038***	*F's **	*0.431*	*F's **	***0.004***
Severe somatic comorbidity	35 (49.3)	11 (44)	3 (23.1)	21 (49.3)	*6.571*	***0.037***	*F's**	*0.181*	*2.218*	*0.136*	*6.148*	***0.013***

* χ^2 : Chi-squared statistic; *p: *P* value; *F's: Fisher's test; *DEL: Patients with delirium; *SMI: Patients with severe mental illness; *NSMI: Patients with non-severe mental illness
Result of the study were presented in bold ($p <= 0.05$)

Table 2 Previous psychiatric history and treatment

	Total N (%)	DEL N (%)	SMI N (%)	NSMI N (%)
Previous psychiatric history				
Any diagnosis	53 (74.6)	16 (64)	12 (92.3)	25 (75.8)
Depressive disorder	18 (25.3)	4 (16)	0 (0)	14 (22.4)
Psychotic disorder	13 (18.3)	3 (12)	9 (69.2)	1 (3)
Substance use disorder	11 (13.5)	3 (12)	4 (30.8)	4 (12.1)
Chronic organic mental disorder	9 (12.7)	5 (20)	2 (15.2)	2(6)
Anxiety disorder	8 (11.2)	0 (0)	0 (0)	8 (24.3)
Personality disorder	6 (8.5)	2 (8)	0 (0)	4 (12.1)
Bipolar disorder	3 (4.2)	3 (12)	0 (0)	0 (0)
Neurodevelopmental disorder	3 (4.2)	0 (0)	3 (23.1)	0 (0)
Adaptation disorder	1 (1.4)	0 (0)	0 (0)	1 (3)
Other	1 (1.4)	1 (4)	0 (0)	0 (0)
None	18 (25.4)	9 (36)	1 (7.7)	8 (24.2)
Psychotropic treatment				
Any drug	45 (63.4)	14 (56)	10 (76.9)	21 (63.6)
Antidepressant	30 (42.3)	8 (32)	6 (46.2)	16 (48.5)
Benzodiazepine	25 (35.2)	7 (28)	4 (30.8)	14 (42.4)
Antipsychotic	17 (23.9)	8 (32)	8 (61.5)	1 (3)
Anticonvulsant	13 (18.3)	5 (20)	5 (38.5)	3 (9.1)
Other psychiatric treatment	1 (1.4)	0 (0)	0 (0)	1 (3)

*DEL: Patients with delirium; *SMI: Patients with severe mental illness; *NSMI: Patients with non-severe mental illness

COVID-19 Therapies and Dose Adjustment

The most common therapies were HCQ, AZT and LPV/r, usually in combination. The rate of patients receiving any drug was statistically significantly lower in the SMI-group than the others, especially in the case of LPV/r and HCQ (Table 4).

Some patients with prior psychiatric treatment required dose adjustment: antipsychotics were reduced in 37.5% and stopped in 18.8%, antidepressants were reduced in 17.2% and stopped in 10.3%, benzodiazepines were stopped in 41.7% and reduced in 4.2%, while anticonvulsants were reduced or stopped only in 7.7%.

Moreover, almost two-thirds of the sample ($n = 44$; 62%) were started on new medication, mostly olanzapine ($n = 12$; 17.1%) and intravenous haloperidol ($n = 6$; 8.6%).

Table 3 Reason for referral and difficult weaning

Reason for referral	Total N (%)	DEL N (%)	SMI N (%)	NSMI N (%)
Drug dose adjustment	27 (38.8)	8 (32)	6 (46.2)	13 (39.4)
Confusion	15 (21.1)	14 (56)	1(7.7)	0(0,0)
Anxiety	10 (14.1)	0 (0)	0 (0)	10 (30.3)
Psychomotor agitation	7 (9.9)	2 (8)	3 (23.1)	2 (6.1)
Depression	6 (8.5)	0 (0)	0 (0)	6 (18.2)
Psychosis	3 (4.2)	0 (0)	3 (23.1)	0 (0)
Suicidal behaviour	2 (2.8)	1 (4)	0 (0)	1 (3)
Substance use	1(1.4)	0 (0)	0 (0)	1 (3)
Difficult weaning	10 (14.1)	9 (36)	0 (0)	1 (3)

*DEL: Patients with delirium; *SMI: Patients with severe mental illness; *NSMI: Patients with non-severe mental illness

Table 4 COVID-19 therapies

COVID-19 therapies	Total ($n = 71$)	DEL ($n = 25$)	SMI ($n = 13$)	NSMI ($n = 33$)	Group comparisons							
					DEL-SMI-NSMI		DEL-SMI		DEL-NSMI		SMI-NSMI	
	N (%)	N (%)	N (%)	N (%)	$\chi 2$	p	$\chi 2$	p	$\chi 2$	p	$\chi 2$	p
Any drug	62 (87.3)	24 (96)	8 (61.5)	30 (90.9)	9.892	0.007	F's*	0.012	F's*	0.418	F's*	0.031
Hydroxy chloroquine	58 (81.7)	24 (96)	7 (53.8)	27 (81.8)	10.161	0.006	F's*	0.004	F's*	0.106	F's*	0.061
Azithro mycin	53 (74.6)	20 (80)	8 (61.5)	25 (75.8)	1.58	0.454	–	–	–	–	–	–
Lopinavir-ritonavir	50 (70.4)	20 (80)	5 (38.5)	25 (75.8)	7.927	0.019	F's*	0.019	0.147	0.701	F's*	0.021
Corticoste roids	17 (23.9)	8 (32)	1 (7.7)	8 (24.2)	2.778	0.249	–	–	–	–	–	–
Tocilizumab	17 (23.9)	7 (28)	1 (7.7)	9 (27.3)	2.312	0.315	–	–	–	–	–	–
Other	20 (28.2)	10 (40)	2 (15.4)	8 (24.2)	3.031	0.220	–	–	–	–	–	–

* χ^2 : Chi-squared statistic; *p: P value; *F's: Fisher's test; *DEL: Patients with delirium; *SMI: Patients with severe mental illness; *NSMI: Patients with non-severe mental illness

Side Effects and Pharmacological Interactions

A 5.9% (n = 4) of the sample had a pathological QTc interval at admission, before starting any medication for COVID-19, and none in the SMI-group. Only one patient, with asymptomatic COVID-19, was admitted for Torsades de Pointes due to intoxication with methadone 400 mg.

After adjusting the dose or starting a new psychiatric drug, the QTc interval remained without any significant change in most of the sample ($n = 62$; 95.4%), and 100% of the SMI-group. Normalization of QTc interval was present in 3,1% ($n = 2$) of the sample. Only one patient (1.5%) had a borderline prolongation of the QTc interval, probably due to the interaction between three antidepressants (vortioxetine 10 mg/day, trazodone 50 mg/day and venlafaxine 225 mg/day) and LPV/r/HCQ/AZT.

Other probable adverse effects secondary to interaction between psychiatric and COVID-19 medications were drowsiness ($n = 3$; 4.3%) and confusion ($n = 1$; 1.4%). They were secondary to the combination of LPV/r (dose 200/50 mg 2 U/12 h) and one of the following sedative drugs: quetiapine 300 mg/day (the patient was in antipsychotic therapy before starting LPV/r, and because he presented both drowsiness and confusion, LPV/r was immediately stopped), haloperidol 3 mg/day, and trazodone 50 mg/day.

Clinical Course during Hospitalization

The median length of stay for all patients was 12 days (IQR: 7–16.5); it was statistically significantly larger ($p = 0.027$) in the delirium-group (19 days) in comparation with the SMI-group (9 days). There were not statistically significant differences when comparing any of the mentioned groups with the NSMI-group (13.5 days).

Hospital-to-home discharge was the intended destination in the majority of the patients ($n = 32$; 48.5%), while 39.4% ($n = 26$) were admitted to a low complexity center and 12.1% ($n = 8$) died. The mortality was higher among patients with delirium (21.7%) than those with SMI (0%) or NSMI (9.45%), although there were not statistically significant differences. The median number of days between onset of delirium and death was 7 (2.5–7.75). No patient with severe mental illness (including the SMI-group and patients with SMI in the delirium group) died.

Discussion

To our knowledge, this is the first report analyzing the clinical features and outcomes of hospitalized patients with COVID-19 referred to a CLP unit.

The patients with delirium were older and had a more severe infection, as they were five more times admitted to ICU than the other groups, and almost a third had difficult weaning. The most common presentation of delirium was mixed, which is the usual presentation in elderly hospitalized patients [21]. Moreover, the rate of agitation seems to be higher in delirium associated with COVID-19, as suggested by other studies [22]. One-quarter of patients with delirium died at the hospital, approximately one week after the onset of delirium, which may indicate that acute confusional states implies a worse prognosis in COVID-19, as described in critically-ill patients [23].

Patients with NSMI had a similar rate of severe somatic comorbidities compared to patients with delirium, and an intermediate age range and prognosis compared to the other groups. The

most common problems were anxiety and depressive disorders, and they were usually referred for anxiety or dose adjustment.

Patients with SMI were younger and had less severe comorbidities than patients with delirium or NSMI. The most common diagnosis was psychotic disorder and almost half resided in long-term care facilities (LTCF). While the institutionalized elderly have been a constant subject of public attention because of their vulnerability to COVID-19 [24, 25], little attention has been focused on institutionalized people with SMI. It has been suggested that people with mental health disorders are more susceptible to infections when epidemics arise [17], and the semi-confined living conditions of LTCFs where some of them live may be one of the reasons. In LTCFs, residents live in close proximity under the care of often under-resourced nurse assistants, and viral infections, with high transmissibility via droplets and contact transmission, are easily brought in by people entering the facilities and widespread [24].

The younger age, lower rate of comorbidities, and higher rate of incidental diagnosis may explain a better prognosis in the patients with severe mental illness, as they had a shorter hospitalization and none died.

The theorical risk of pharmacological interactions between COVID-19 therapies and psychiatric drugs promoted that drug dose adjustment was the most common reason for referral.

Our CLP unit has issued practical recommendations for the psychopharmacological management on the most representative identified case-scenarios on COVID-19 inpatients with psychiatric disorders based on the existing literature, including the Liverpool Interactions Drug Group recommendations [14], and clinical experience [16].

Although sometimes high-risk interaction drug discontinuation was not possible or intravenous haloperidol had to be used for agitated delirium, the incidence of side effects was very low. In fact, the QTc interval was not prolonged after dose adjusting or adding a new drug, in the 98,5% of the sample. Only one patient had a borderline QTc interval without any clinical repercussion, and was due to the interaction between three antidepressants (vortioxetine, trazodone and venlafaxine) and LPV/r/HCQ/AZT. The other probable side effect, with a low rate and reversible after dose adjustment, was drowsiness. It should be highlighted that concomitant administration of LPV/r and quetiapine should be avoided because it may increase considerably quetiapine concentration and its toxicity (coma in the worst-case scenario), and if coadministration is necessary, quetiapine dose should be reduced to 1/6 [14]. Overall, COVID-19 inpatients with psychiatric comorbidities should be managed on a personalized basis considering several clinical criteria and, should not be excluded from receiving COVID-19 treatments [16].

This low rate of interactions contrasts with the fact that patients with SMI were undertreated (specially with LPV/r). The lack of familiarity with psychiatric medications in medical wards may have contributed to this. Furthermore, most of the recommendations for interactions with experimental COVID-19 therapies are based on theory, with a low evidence and do not quantify the changes in serum drug concentrations [14].

Limitations

The small size of the sample may have reduced the statistical power of the study. Because the study population was restricted to inpatients referred to a CLP unit, generalization of results is limited to patients affected by COVID-19 and having a psychiatric diagnosis admitted to the hospital, but gives practical information for the management of pharmacological interactions.

Conclusions

Our study suggests that the incidence of side effects due to interactions between psychiatric and COVID-19 treatments is low. However, patients with SMI were more often undertreated. In order to avoid undertreatment on people with mental illness and COVID-19, the role of consultation-liaison psychiatry is crucial during the pandemic, and further research is needed to determine the real impact of interactions on clinical practice.

Half of the inpatients with SMI were living on LTCF, which usually have semi-confined living conditions that make easier droplets and contact transmission. Therefore, in order to reduce the impact of the pandemic in this part of the population, improvement of COVID-19 prevention and control measures in mental health residential facilities is urgently needed.

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Authors Contributions All authors contributed to the study conception, methodology, investigation and visualization. Formal analysis was performed by N. Arbelo, M. Sagué and H. López. Supervision and project administration were performed by H. López and L. Pintor. Resources were provided by L. Pintor. The first draft of the manuscript was written by N. Arbelo and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.Data AvailabilityAll data and materials as well as software applications support our published claims and comply with field standards.

Compliance with Ethical Standards

Conflict of Interest Dr. Arbelo has received CME-related financing and travel grants from Janssen-Cilag and Lundbeck and reports no financial or other relationship relevant to the subject of this article. Dr. López-Pelayo has received travel grants from the laboratories honoraria and travel grants from Janssen and Lundbeck. None of them has relationship with this research. Dr. Sagué has received travel grants and CME-related honoraria from Janssen-Cilag and Lundbeck and reports no financial or other relationship relevant to the subject of this article. Dr. Madero has received travel grants and CME-related honoraria from Janssen-Cilag, Lundbeck, Pfizer and Angelini and reports no financial or other relationship relevant to the subject of this article. Dr. Pinzón has received CME-related honoraria from Lundbeck, all unrelated to the present work. Dr. Gomes-da-Costa has received CME-related honoraria, or consulting fees from Janssen-Cilag, Lundbeck, Italfarmaco and Angelini and reports no financial or other relationship relevant to the subject of this article. Dr. Ilzarbe has received CME-related financing and travel grants from Janssen-Cilag and reports no financial or other relationship relevant to the subject of this article. Dr. Anmella has received CME-related honoraria, or consulting fees from Janssen-Cilag, Lundbeck and Angelini and reports no financial or other relationship relevant to the subject of this article. Dr. Llach has received CME-related financing and travel grants from Janssen-Cilag and reports no financial or other relationship relevant to the subject of this article. All other authors declare no conflicts of interests.

Ethics Approval The study was approved by the Ethics Committee of Hospital Clinic, Barcelona, Spain, under resolution number HCB/2020/0496. The study was performed in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki and its later amendments.

Consent to Participate/ Consent for Publication Not applicable. Because there was no intervention and the participants were isolated, and according to the Ethics Committee policy, no consent to participate or publications were required for this study.

Code Availability Not applicable.

References

1. Wang S, Wen X, Dong Y, Liu B, Cui M. Psychological influence of coronovirus disease 2019 (COVID-19) pandemic on the general public, medical workers, and patients with mental disorders and its countermeasures. Psychosomatics. Elsevier Inc.; 2020. https://doi.org/10.1016/j.psym.2020.05.005
2. Wang C, et al. Immediate psychological responses and associated factors during the initial stage of the 2019 Coronavirus disease (COVID-19) epidemic among the general population in China. Int J Environ Res Public Health. 2020;17(5):1729. https://doi.org/10.3390/ijerph17051729.
3. Lai J, Ma S, Wang Y, Cai Z, Hu J, Wei N, et al. Factors associated with mental health outcomes among health care workers exposed to coronavirus disease 2019. JAMA Netw Open. 2020;3(3):e203976–6. https://doi.org/10.1001/jamanetworkopen.2020.3976.
4. Anmella G, et al. Unravelling potential severe psychiatric repercussions on healthcare professionals during the COVID-19 crisis. J Affect Disord. Elsevier B.V.;2020;273:422–424. https://doi.org/10.1016/j.jad.2020.05.061.
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. https://doi.org/10.1016/S2215-0366(20)30203-0.
6. Rattray JE, Johnston M, Wildsmith JAW. Predictors of emotional outcomes of intensive care. Anaesthesia. Nov. 2005;60(11):1085–92. https://doi.org/10.1111/j.1365-2044.2005.04336.x.
7. Mao L, et al. Neurologic manifestations of hospitalized patients with coronavirus disease 2019 in Wuhan, China: JAMA Neurol; 2020. https://doi.org/10.1001/jamaneurol.2020.1127.
8. Warrington TP, Bostwick JM. Psychiatric adverse effects of corticosteroids. Mayo Clin Proc. 2006;81(10):1361–7. https://doi.org/10.4065/81.10.1361.
9. Mascolo A, et al. Neuropsychiatric clinical manifestations in elderly patients treated with hydroxychloroquine: a review article. Inflammopharmacology. Birkhauser Verlag AG; 2018;26(5):1141–1149. https://doi.org/10.1007/s10787-018-0498-5.
10. Wu Y, et al. Nervous system involvement after infection with COVID-19 and other coronaviruses. Brain Behav Immun. Academic Press Inc.; 2020. https://doi.org/10.1016/j.bbi.2020.03.031.
11. Baig AM, Khaleeq A, Ali U, Syeda H. Evidence of the COVID-19 virus targeting the CNS: tissue distribution, host-virus interaction, and proposed neurotropic mechanisms. ACS Chem Neurosci. American Chemical Society; 2020. https://doi.org/10.1021/acschemneuro.0c00122.
12. Kotfis K, Williams Roberson S, Wilson JE, Dabrowski W, Pun BT, Ely EW. COVID-19: ICU delirium management during SARS-CoV-2 pandemic. Crit Care. 2020;24(1):176. https://doi.org/10.1186/s13054-020-02882-x.
13. Abers MS, Shandera WX, Kass JS. Neurological and psychiatric adverse effects of antiretroviral drugs. CNS Drugs. 2014;28(2):131–45. https://doi.org/10.1007/s40263-013-0132-4.
14. Liverpool COVID-19 Interactions. https://www.covid19-druginteractions.org/prescribing-resources. Accessed 25 May 2020.
15. Luykx JJ, van Veen SMP, Risselada A, Naarding P, Tijdink JK, Vinkers CH. Safe and informed prescribing of psychotropic medication during the COVID-19 pandemic. Br J Psychiatry. 2020;217:1–4. https://doi.org/10.1192/bjp.2020.92.
16. Anmella G, et al. COVID-19 inpatients with psychiatric disorders: real-world clinical recommendations from an expert team in consultation-liaison psychiatry. J Affect Disord. 2020;274:1062–7. https://doi.org/10.1016/j.jad.2020.05.149.
17. Yao H, Chen JH, Xu YF. Patients with mental health disorders in the COVID-19 epidemic. Lancet Psychiatry. Elsevier Ltd; 2020; 7(4):e21. https://doi.org/10.1016/S2215-0366(20)30090-0.
18. Funk MC, Beach SR, Shah SB, Boland R. Consultation-liaison psychiatry in the age of COVID-19: reaffirming ourselves and our worth. Psychosomatics. Elsevier Inc.; 2020. https://doi.org/10.1016/j.psym.2020.04.013, .
19. Straus SMJM, Kors JA, de Bruin ML, van der Hooft CS, Hofman A, Heeringa J, et al. Prolonged QTc interval and risk of sudden cardiac death in a population of older adults. J Am Coll Cardiol. 2006;47(2):362–7. https://doi.org/10.1016/j.jacc.2005.08.067.
20. Corp IBM. IBM SPSS statistics for windows. Armonk: IBM Corp; 2017.
21. Liptzin B, Levkoff SE. An empirical study of delirium subtypes. Br J. Psychiatry. 1992;161:843–5. https://doi.org/10.1192/bjp.161.6.843.
22. Baller EB, et al. Neurocovid: pharmacological recommendations for delirium associated with COVID-19. Psychosomatics. 2020. https://doi.org/10.1016/j.psym.2020.05.013.

23. Salluh JIF, Wang H, Schneider EB, Nagaraja N, Yenokyan G, Damluji A, et al. Outcome of delirium in critically ill patients: systematic review and meta-analysis. BMJ. 2015;350:1–10. https://doi.org/10.1136/bmj.h2538.
24. Yen MY, Schwartz J, King CC, Lee CM, Hsueh PR. Recommendations for protecting against and mitigating the COVID-19 pandemic in long-term care facilities. J Microbiol Immunol Infect. Elsevier Ltd; 2020. https://doi.org/10.1016/j.jmii.2020.04.003.
25. Gardner W, States D, Bagley N. The coronavirus and the risks to the elderly in long-term care. J Aging Soc Policy. 2020;32:310–5. https://doi.org/10.1080/08959420.2020.1750543.

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