


RESEARCH ARTICLE

Initiation of psychotropic medication in hospitalized patients with COVID-19: Association with clinical and biological characteristics

Enrico Capuzzi¹  | Alice Caldiroli¹ | Silvia Leo² | Massimiliano Buoli^{3,4} | Massimo Clerici^{1,2}

¹Psychiatric Department, Azienda Socio Sanitaria Territoriale Monza, Monza, Italy

²Department of Medicine and Surgery, University of Milano Bicocca, Monza, Italy

³Department of Neurosciences and Mental Health, Fondazione IRCCS Ca'Granda Ospedale Maggiore Policlinico, Milan, Italy

⁴Department of Pathophysiology and Transplantation, University of Milan, Milan, Italy

Correspondence

Enrico Capuzzi, Psychiatric Department, Azienda Socio Sanitaria Territoriale Monza, Via Pergolesi 33, 20900 Monza, Italy.
Email: e.capuzzi1@campus.unimib.it

Abstract

Introduction: Inpatients with coronavirus disease 2019 (COVID-19) show a high rate of neuropsychiatric manifestations, possibly related to a higher risk of serious illness or death. Use of psychotropic medications (PMs) indicates the presence of neuropsychiatric symptoms in COVID-19 patients. So far, potential clinical predictors of use of PMs have not been much investigated. In order to extend research in this area, we aimed to investigate the prevalence of PM prescription among a sample of inpatients with COVID-19 and to find potential predictors of initiation of PMs in these individuals.

Methods: This is a cross-sectional single-center study, conducted during the first outbreak peak in a hospital of northern Italy. Information on socio-demographic characteristics, comorbidities, routine blood test, use of potential COVID-19 treatments, and length of stay were retrieved from medical records.

Results: Data were available for 151 inpatients. Forty-seven of them (31.1%) started at least one prescription of a PM. PM prescription was significantly inversely associated with lymphocyte and platelet counts. A significant association was also found for lactate dehydrogenase (LDH).

Conclusion: Our findings suggest that the initiation of PMs could be common among COVID-19 inpatients. Lymphocyte and platelet counts as well as LDH levels may reflect neuropsychiatric complications of COVID-19.

KEYWORDS

COVID-19, inpatient, psychotropic medication, prescription, neuropsychiatric symptoms

1 | INTRODUCTION

As the pandemic of coronavirus disease 2019 (COVID-19) spread, there was a growing interest about the possible neuropsychiatric consequences of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and the host immunologic response to the infection in the central nervous system (CNS). A diagnosis of COVID-19 may be related to higher incidence of neuropsychiatric sequelae if

compared to other acute health events (Taquet et al., 2020). A wide spectrum of neuropsychiatric manifestations including cerebrovascular events, encephalopathies, encephalitis, psychotic symptoms, dementia-like syndrome, and affective disorders was observed in patients with SARS-CoV-2 infection (Varatharaj et al., 2020). A recent systematic review by Rogers et al. (2020) showed a high rate of delirium, agitation, and altered consciousness among inpatients with COVID-19, in agreement with previous research studies carried

out in patients who had been hospitalized for severe acute respiratory syndrome (SARS) or Middle East Respiratory Syndrome (MERS) (Dinakaran et al., 2020). Even though psychiatric adverse drug reactions were reported in some patients, especially in those treated with corticosteroids, up to 20%–30% of COVID-19 patients may develop delirium or other behavioral disturbances during their hospitalizations (Garcia et al., 2020). These rates could be as high as 60%–70% in severely ill individuals (Helms et al., 2020).

In the light of the wide spectrum of neuropsychiatric complications in COVID-19 and the risks of drug–drug pharmacokinetic and pharmacodynamic interactions, most studies provided some practical recommendations on the use of psychotropic medications (PMs) in acute inpatients. First of all, before prescribing PMs clinicians should take into account the risk/benefit ratio in the light of the frequent medical comorbidities of subjects with severe forms of COVID-19 (Yahya et al., 2020). In particular, the administration of antipsychotic medications at high doses, especially those with a highly sedative profile and in combination with other PMs, should be avoided for the risk of severe dyspnea, arrhythmias and thromboembolism (Ostuzzi, Gastaldon et al., 2020). In line with these considerations, risperidone, quetiapine and aripiprazole seem to be more effective than first generation antipsychotics (e.g., haloperidol) for the short-term treatment of COVID-19 associated delirium (Ostuzzi, Papola et al., 2020). On the other hand, precautionary further measures, including routine complete blood count and plasmatic dosage, were recommended in case of clozapine prescription for patients with SARS-CoV-2 infection (Sabe et al., 2021). Furthermore, patients who started an antidepressant medication should be closely monitored to assess the risk of bleeding disorders associated with serotonergic agents. Nevertheless, antidepressants with anticholinergic properties (tricyclic antidepressants and paroxetine) may increase the vulnerability to delirium and should be avoided. In the light of the associated respiratory inhibition and delirium, the use of benzodiazepines should be limited only for very short periods (Ostuzzi, Gastaldon et al., 2020). Finally, plasma levels of lithium, valproic acid and carbamazepine should be carefully monitored for the increased risk of life-threatening side-effects associated with the administration of these compounds (Buoli et al., 2018; Sabe et al., 2021). Clinicians need to identify those patients at increased risk of neuropsychiatric complications of COVID-19. Thus, the use of PMs can be seen as an early indicator of worsening of neuropsychological functioning among COVID-19 patients in addition to markers of immune response and inflammation (Helms et al., 2020; Jansen van Vuren, et al., 2021). As reported by a recent UK-wide surveillance study (CORONERVE), a large proportion of psychiatric symptoms was reported by inpatients who had severe COVID-19 and presented a concomitant lymphocytopenia (Poloni et al., 2020; Varatharaj et al., 2020). Nevertheless, abnormal values of C-reactive protein, D-dimer, platelet count, interleukin-6, lactate dehydrogenase (LDH), neutrophil-to-lymphocyte ratio (NLR), cardiac troponin, and kidney function were detected in patients with serious complications of COVID-19 infection compared to their nonsevere counterparts (Kermali et al., 2020). To the best of our knowledge, there are no

currently comprehensive descriptive data regarding the characteristics of hospitalized patients with COVID-19 pneumonia beginning a treatment with PMs. Therefore, the current study was designed to investigate the prevalence of initiation of PMs among inpatients with COVID-19 and whether some sociodemographic, biochemical variables or pharmacological treatments for COVID-19 may increase the likelihood of PM prescription.

Our main research questions were:

1. What is the prevalence of PM use in hospitalized patients with COVID-19?
2. Are there some potential clinical predictors of initiation of PMs during hospitalization in COVID-19 patients?

The results of this study could be important to implement prevention strategies aimed to avoid short and long-term complications (Alonso-Lana et al., 2020). Particularly, preliminary studies reported an association between the duration of delirium and a longer hospitalization as well as a higher mortality among severely ill patients (Kennedy et al., 2020). On the other hand, similarly to SARS and MERS, COVID-19 seems to have long-term neuropsychiatric sequelae that include cognitive impairment, fatigue and psychotic symptoms (Banerjee & Viswanath, 2020).

2 | METHODS

We conducted a cross-sectional study, including inpatients consecutively admitted to the isolated COVID-19 wards at Desio Hospital (Monza, Lombardy region) during the peak of COVID-19 outbreak, between March 4 and May 6, 2020. We defined COVID-19 cases as subjects who tested positive to the reverse transcriptase-polymerase chain reaction (PCR) carried out by our laboratory. We excluded patients from other hospitals or referred to another clinic, with pre-existing mental, substance use or neurological disorder or taking any PM before hospitalization. Finally, participants with any missing data were ruled out. Information on sociodemographic characteristics, pre-existing comorbidities, routine blood tests, prescription of pharmacological treatments and length of hospitalization were retrieved from medical records. Pre-existing comorbidities were defined as follows: hypertension, diabetes, cardiovascular diseases (CVD) (coronary artery disease, congestive heart failure, heart muscle disease, cardiac arrhythmia), cancer, liver and lung diseases or other disorders. We considered only serum blood tests carried out within 24 h after hospitalization. Prescription of PMs was defined by the use of at least one of the following drugs: anti-anxiety agents, antidepressants, mood stabilizers (lithium and anticonvulsant agents) and antipsychotics. PMs were prescribed by both psychiatrists and other specialists. Mental health specialists were not directly engaged in diagnosing and treating COVID-19 patients, unless for psychiatric assessments. Moreover, in accordance with our hospital policies, psychiatrist on duty is allowed to stay in hospital for a maximum of 12 h, although available for urgent consultations in the remaining hours.

Descriptive analyses were originally performed for the whole sample. Then, we carried out univariate analysis to detect statistically significant differences between subjects starting or not starting any treatment with PMs. The normal distribution of quantitative variables was verified by using Shapiro–Wilk's test. The groups were compared for qualitative variables by χ^2 tests. Laboratory indicators were included as both continuous and categorical variables in order to define possible thresholds of PMs prescription. Apart from NLR (Fest et al., 2018), for blood exams we referred to the normal ranges defined by Desio Hospital and based on Italian population. Finally, all the variables from the univariate analysis with $p < 0.05$, together with age, gender, and length of hospitalization, were inserted as independent variables into a logistic regression model with the initiation of PMs as dependent variable. Statistical significance was set at $p < 0.05$. Analysis were conducted using Stata Version 13.1 SE.

3 | RESULTS

The original sample consisted of 370 inpatients. Among these, 219 were excluded because they did not meet the inclusion criteria: 24 showed a negative COVID-19 test result; 99 were transferred to another hospital; 15 had pre-existing psychiatric disorders (14 were previously diagnosed with major depressive disorder and 1 with schizophrenia); 24 patients suffered from neurological disorders (22 Alzheimer's disease and 2 Parkinson's disease); 8 were taking PMs before the hospitalization; 49 patients were excluded because of missing data. Data were therefore available for 151 individuals. Fifty-four of them (35.8%) exhibited at least one neuropsychiatric symptom whilst 32 died during hospitalization. Forty-seven patients (31.1%) initiated at least one PM during hospitalization (Table 1).

Anti-anxiety agents (19.9%) and antipsychotics (19.2%) were the most commonly prescribed PMs in the whole sample. Antidepressants were prescribed in 2% of individuals. No patients were treated with mood stabilizers. Among those presenting at least one specific neuropsychiatric symptom (rather than generic agitation or tension), 43 started a PM whilst 11 patients did not receive any psychotropic drugs ($p = 0.000$). Age was statistically higher in the group of subjects starting PMs. CVD were significantly more frequent in patients who received PMs. Significant correlations were found for red cell count, platelet count, lymphocyte count, and LDH. After discretizing biochemical variables, we found that patients starting any PMs had a higher frequency of lower levels of lymphocyte than patients not taking PMs. In particular, a comparative analysis, including different degree of lymphocytopenia, showed that mild-moderate lymphocytopenia ($0.4\text{--}0.85 \times 10^9/\text{L}$) was related to the initiation of PMs ($p = 0.002$). No statistical differences were observed between the two groups with regard to COVID-19 treatments and duration of hospitalization. Finally, after controlling for age, gender and duration of hospitalization, we found an inverse association between use of PMs and platelet (adjusted odds ratio [aOR] = 0.99, $p = 0.035$) and lymphocyte (aOR = 0.35, $p = 0.045$) counts. Furthermore, baseline levels of LDH (aOR = 1.01, $p = 0.013$) were associated with start of

taking PMs. The presence of CVD was related with a borderline statistical significance to the prescription of PMs (aOR = 2.56, $p = 0.054$) (Table 2).

4 | DISCUSSION

4.1 | Interpretation of findings

To our knowledge, no study previously explored potential clinical predictors associated with the risk to begin treatment with PMs during acute COVID-19. According to our findings, almost one-third of COVID-19 inpatients without any apparent neuropsychiatric history initiated at least one PM. Neuropsychiatric symptoms as initial presentation or complications of COVID-19 may be therefore a frequent manifestation of the infection, in line with recent reports (Dinakaran et al., 2020). In particular, patients with COVID-19 who require hospitalization may be at higher risk of neuropsychiatric sequelae than individuals not requiring inpatient admission (Taquet et al., 2020). Neuropsychiatric symptoms, in turn, could be related to a higher risk of serious illness or death (Poloni et al., 2020; Rogers et al., 2020). In line with these considerations, an early identification and an effective treatment of coexisting neuropsychiatric symptoms may improve the prognosis of patients with severe forms of COVID-19. In particular, changes in the blood values of some parameters were hypothesized to increase the vulnerability to neuropsychiatric manifestations of COVID-19 (Jansen van Vuren, et al., 2021). Based on our study, an inverse association between the initiation of PMs and lymphocyte count was detected. Particularly, mild-moderate lymphocytopenia was found to be associated with start of treatment with PMs. Some studies reported a possible association between neuropsychiatric manifestations and lymphopenia (Mao et al., 2020; Poloni et al., 2020), which in turn predicts poor outcomes of COVID-19 (Tan et al., 2020). Even though the etiology of the neuropsychiatric symptoms is likely to be multifactorial (Banerjee & Viswanath, 2020), dysregulated immune responses to infection, that is, 'cytokine storm', might play a major role (Jung & Rujescu, 2020). Multiple mechanisms leading to lymphocyte deficiency and neuroinflammation were hypothesized (Troyer et al., 2020). With regard to the association of initiation of PMs with the platelet count and LDH serum levels, some authors argued that higher levels of LDH and low platelet count may reflect more severe forms of COVID-19 (Lippi et al., 2020). In particular, Mao et al. (2020) found that patients with CNS symptoms had lower lymphocyte levels and platelet counts, compared with those without CNS symptoms suggesting the probable onset of acute cerebrovascular events in patients with COVID-19 (Banerjee & Vishwanath, 2020). Nevertheless, thrombocytopenia and elevated LDH levels reflect an hypercoagulable state, in turn related to increased severity of illness and mortality. Moreover, higher levels of LDH may be the consequence of the multiple organ injury and failure related to fatal forms of COVID-19 (Henry et al., 2020). Overall, reduced lymphocyte and platelet counts as well as higher levels of LDH may be common in COVID-19 patients with

TABLE 1 Baseline characteristics of the total sample and of groups divided according to initiation of psychotropic medications

Variables	Total sample N = 151	No psychotropic medication N = 104 (68.9%)	Psychotropic medication N = 47 (31.1%)	p Value
Sociodemographic				
Age (years) mean (SD)	66.4 (13.6)	64.3 (13.7)	71.0 (12.5)	0.005^a
Female gender	42 (27.8%)	30 (28.8%)	12 (25.5%)	0.674 ^b
Existing comorbidities				
High blood pressure	77 (51.0%)	51 (49.0)	26 (55.3)	0.475 ^b
Diabetes	32 (21.2%)	21 (20.2)	11 (23.4)	0.655 ^b
Cardiovascular disease	69 (45.7%)	38 (36.5)	31 (66.0)	0.001^b
Cancer	23 (15.2%)	12 (11.5)	11 (23.4)	0.060 ^b
Liver disease	6 (4.0%)	5 (4.8)	1 (2.1)	0.666 ^c
Lung disease	33 (21.8%)	21 (20.2)	12 (25.5)	0.462 ^b
Other disease	57 (37.7%)	33 (31.7)	24 (51.1)	0.023^b
Biochemical factors				
Red blood cells (10 ⁶ /μl) mean (SD)	4.7 (0.7)	4.8 (0.8)	4.5 (0.7)	0.012^a
<4.5	54 (35.8%)	34 (32.7)	20 (42.6)	
4.5-6.5	95 (62.9%)	68 (65.4)	27 (57.4)	
>6.5	2 (1.3%)	2 (1.9)	0 (0.0)	0.381 ^c
White blood cells (10 ⁹ /L) mean (SD)	7.7 (4.0)	7.8 (3.7)	7.5 (4.6)	0.272 ^d
<4	18 (11.9%)	8 (7.7)	10 (21.3)	
4-11	106 (70.2%)	77 (74.0)	29 (61.7)	
>11	27 (17.9%)	19 (18.3)	8 (17.0)	0.057 ^b
Platelets (10 ⁹ /L) mean (SD)	216.3 (86.9)	228.9 (94.1)	188.5 (60.4)	0.031^d
<140	24 (15.9%)	15 (14.4)	9 (19.2)	
140-450	125 (82.8%)	87 (83.7)	38 (80.8)	
>450	2 (1.3%)	2 (1.9)	0 (0.0)	0.596 ^c
Neutrophils (10 ⁹ /L) mean (SD)	6.0 (3.6%)	5.9 (3.2)	6.0 (4.5)	0.638 ^d
<1.2	0 (0.0%)	0 (0.0)	0 (0.0)	
1.2-6.9	107 (70.9%)	73 (70.2)	34 (72.3)	
>6.9	44 (29.1%)	31 (29.8)	13 (27.7)	0.788 ^b
Lymphocytes (10 ⁹ /L) mean (SD)	1.1 (1.2)	1.3 (1.5)	0.8 (0.4)	0.000^d
<0.85	64 (42.4%)	35 (33.7)	29 (61.7)	
0.85-3.2	85 (56.3%)	67 (64.4)	18 (31.3)	
>3.2	2 (1.3%)	2 (1.9)	0 (0.0)	0.003^c
Lymphocytopenia				
0.4-0.85 (mild-moderate)	57 (37.8%)	30 (28.8)	27 (54.4)	
<0.4 (severe)	7 (4.6%)	5 (4.8)	2 (4.3)	0.002^c
Monocytes (10 ⁹ /L) mean (SD)	0.5 (0.3)	0.5 (0.3)	0.4 (0.2)	0.262 ^a
<0	0 (0.0%)	0 (0.0)	0 (0.0)	
0-0.67	129 (85.4%)	86 (82.7)	43 (91.5)	
>0.67	22 (14.6%)	18 (17.3)	4 (8.5)	0.214 ^c

TABLE 1 (Continued)

Variables	Total sample N = 151	No psychotropic medication N = 104 (68.9%)	Psychotropic medication N = 47 (31.1%)	p Value
Eosinophils (10 ⁹ /L) mean (SD)	0.02 (0.05)	0.02 (0.06)	0.02 (0.05)	0.541 ^a
<0	0 (0.0%)	0 (0.0)	0 (0.0)	
0–0.37	151 (100%)	104 (100)	47 (100)	
>0.37	0 (0.0%)	0 (0.0)	0 (0.0)	
Basophils (10 ⁹ /L) mean (SD)	0.00 (0.02)	0.00 (0.02)	0.00 (0.02)	0.983 ^a
<0	0 (0.0%)	0 (0.0)	0 (0.0)	
0–0.1	148 (98.0)	102 (98.1)	46 (97.9)	
>0.1	3 (2%)	2 (1.9)	1 (2.1)	1.000 ^c
Neutrophil-to-lymphocyte ratio (%) ^e	7.8 (10.4)	7.1 (7.5)	9.3 (15.0)	0.081 ^d
<0.83	1 (0.7%)	1 (1.0)	0 (0.0)	
0.83–3.92	51 (33.8%)	40 (38.5)	11 (23.4)	
>3.92	99 (65.5%)	63 (60.5)	36 (76.6)	0.106 ^c
Prothrombin time (s) mean (SD)	13.7 (4.6)	13.5 (4.2)	14.1 (5.4)	0.500 ^a
<10	1 (0.7%)	0 (0.0)	1 (2.1)	
10–15	136 (90.1%)	96 (92.3)	40 (85.1)	
>15	14 (9.3%)	8 (7.7)	6 (12.8)	0.158 ^c
Partial thromboplastin time (s) mean (SD)	80.1 (21.7)	82.2 (19.2)	75.2 (25.9)	0.170 ^d
<70	26 (17.2%)	15 (14.4)	11 (23.4)	
70–120	125 (82.8%)	89 (85.6)	36 (76.6)	
>120	0 (0.0%)	0 (0.0)	0 (0.0)	0.176 ^b
International normalized ratio (%) mean (SD)	1.2 (0.5)	1.2 (0.4)	1.2 (0.5)	0.551 ^d
<0.8	1 (0.7%)	0 (0.0)	1 (2.1)	
0.8–1.2	127 (84.1%)	90 (86.5)	37 (78.7)	
>1.2	23 (15.2%)	14 (13.5)	9 (19.2)	0.164 ^c
Procalcitonin (ng/ml) mean (SD)	1.7 (9.0%)	2.0 (10.6)	0.9 (3.6)	0.236 ^d
<0.5	28 (18.5%)	18 (17.3)	10 (21.3)	
≥0.5	123 (81.5%)	86 (82.7)	37 (78.7)	0.561 ^b
Lactate dehydrogenase (U/L) mean (SD)	390.4 (211.5)	354.1 (126.2)	470.6 (317.3)	0.002 ^d
<125	0 (0.0%)	0 (0.0)	0 (0.0)	
125–220	15 (9.9%)	11 (10.6)	4 (8.5)	
>220	136 (90.1%)	93 (89.4)	43 (91.5)	0.778 ^c
C-reactive protein (mg/dl) mean (SD)	100.3 (76.1)	99.1 (73.7)	103.2 (82.0)	0.761 ^a
<50	47 (31.1%)	31 (29.8)	16 (34.0)	
≥50	104 (68.9%)	72 (70.2)	31 (66.0)	0.705 ^b
Treatments				
Hydroxychloroquine	28 (18.5%)	22 (21.5%)	6 (12.8%)	0.264 ^b
Antibiotics	24 (15.9%)	18 (17.3%)	6 (12.8%)	0.632 ^b
Corticosteroids	29 (19.2%)	21 (20.2%)	8 (17.0%)	0.824 ^b

(Continues)

TABLE 1 (Continued)

Variables	Total sample N = 151	No psychotropic medication N = 104 (68.9%)	Psychotropic medication N = 47 (31.1%)	p Value
Antiviral agents	14 (9.3%)	11 (10.6%)	3 (6.4%)	0.551 ^b
Hospital stay (days) mean (SD)	16.1 (10.4)	15.7 (9.4)	16.6 (12.3)	0.686 ^d

Note: Values are numbers (%), unless otherwise specified. Statistically significant *p* values are reported in bold. In case of two values first are reported *p* for the variables considered as continuous and then for categories.

Abbreviations: dl, deciliter; L, liter; μ l, microliter; mg, milligram; ml, milliliter; ng, nanogram; SD, standard deviation.

^at-Test.

^bPearson's χ^2 test.

^cFisher's exact test.

^dWilcoxon–Mann–Whitney test.

^eFrom Fest et al. (2018).

	Variables	aOR	95% CI	p Value
Sociodemographic	Age (years)	1.00	0.96–1.04	0.968
	Female gender	0.55	0.20–1.51	0.243
Existing comorbidities	Cardiovascular diseases	2.56	0.98–6.66	0.054
	Other diseases	1.41	0.60–3.27	0.430
Biochemical factors	Red blood cells ($10^6/\mu$ l)	0.85	0.45–1.64	0.636
	Platelets ($10^9/L$)	0.99	0.99–1.00	0.035
	Lymphocytes ($10^9/L$)	0.35	0.12–0.98	0.045
	Lactate dehydrogenase (U/L)	1.01	1.00–1.01	0.013
Hospital stay	Hospital stay (days)	1.02	0.98–1.05	0.484

Note: Adjusted odds ratios (aOR) and their 95% confidence interval (CI). Statistically significant findings are reported in bold.

TABLE 2 Logistic regression analysis for the odds of initiation of psychotropic medications

neuropsychiatric manifestations (Favas et al., 2020; Malik et al., 2020). In the same way, the presence of concomitant CVD was found to predict a more severe course of the COVID-19 and the onset of neuropsychiatric manifestations (Mehra et al., 2020). Indeed, different studies hypothesized a bidirectional interaction between COVID-19 and the cardiovascular system. The high burden of systemic inflammation related to COVID-19 may accelerate the development of subclinical CVD or cause de novo cardiovascular damage (Inciardi et al., 2020). Nevertheless, biological pathways involving the expression of angiotensin-converting enzyme two in the endothelial, neural, and glial cells may explain the considerable rate of neuropsychiatric complications among patients with CVD (Soltani Zangbar et al., 2021).

In sum, initiation of PM could be common among COVID-19 inpatients. Lymphocyte and platelet counts as well as LDH levels should be closely monitored as possible markers of neuropsychiatric complications. Short and long-term monitoring of mental health status should be therefore recommended for COVID-19 inpatients starting PMs. On the other side, the growing use of PMs in COVID-19 patients calls on the development of evidence-based guidelines

that may help clinicians to manage these subjects in case of neuropsychiatric manifestations (Kermali et al., 2020).

4.2 | Limitations

This study has some limitations. First, as the sample consisted of medical records from inpatients of a single hospital, the results might not be generalizable to all individuals with acute COVID-19. Second, we could not define the different type of neuropsychiatric manifestations because most of medical records lacked of comprehensive information. Similarly, even though we excluded inpatients with a history of neuropsychiatric disorders, our sample may have included some individuals who had previously suffered from mild psychiatric conditions. Third, as this study was a cross-sectional one, we cannot evaluate the changes over the time as regards the biochemical indicators. Indeed, findings from other studies suggested that some PMs decrease plasma levels of inflammatory mediators and therefore reduce the risk of severe complications from COVID-19 (Hoertel et al., 2020). On the other hand, a possible association between the

use of PMs and worsening of COVID-19 was argued (McKeigue et al., 2021).

5 | CONCLUSIONS

In this study, almost one-third of COVID-19 inpatients started at least one PM. Lymphocytopenia, low platelet count and elevated levels of LDH were associated with the beginning of a treatment with PMs. The findings reported in the present manuscript have to be interpreted cautiously in the light of some limitations such as the recruitment of patients in a single center. Therefore, further longitudinal studies with larger samples as well as suitable control groups are needed to confirm the results of the present article and to investigate other potential biochemical indicators associated with the initiation of PM during the SARS-CoV-2 infection.

CONFLICT OF INTEREST

The authors have declared no conflict of interest.

DATA AVAILABILITY STATEMENT

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

ORCID

Enrico Capuzzi  <https://orcid.org/0000-0001-8350-499X>

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