



# Emerging Psychiatric Themes in Post-COVID-19 Patients on a Psychiatry Consultation-liaison Service

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## Abstract

The need for consultation-liaison psychiatry on COVID-19 wards has substantially increased since the start of the pandemic. In this cross-sectional study, we aimed to summarize the characteristics of patients admitted to the post-COVID-19 ward of the American University of Beirut Medical Center who received a psychiatric consultation. We collected relevant sociodemographic and medical data, information about past psychiatric history, psychiatry consultation details, hospital course, and disposition outcome. We also conducted chi-square and binary logistic regression analyses to assess the association between the different variables and disposition outcome. A total of 52 patients (mean age 57.33 years; equal gender distribution) were seen by the psychiatry consult-liaison team. Most had medical comorbidities and 21.2% required intubation. The most prevalent psychiatric diagnoses were delirium (30.8%), major depressive episode (15.4%), and other anxiety disorder (15.4%). Pharmacological management was implemented in 90.4% of cases and mainly included second-generation antipsychotics (36.5%). Non-pharmacological interventions consisted of those related to delirium and therapy for anxiety. Only intubation was significantly associated with disposition outcome ( $p=0.004$ ). This study highlights the various psychiatric themes emerging during the acute and post-acute periods of hospitalization for COVID-19. Hospitalized individuals recovering from the infection should be diligently screened and referred to the psychiatry consultation-liaison team to ensure the implementation of appropriate interventions.

**Keywords** COVID-19 · Psychiatry · Consultation-liaison · Inpatient · Delirium · Anxiety

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## Introduction

Growing evidence suggests that the Coronavirus Disease 2019 (COVID-19) has increased the burden of mental disorders in the world [1, 2]. Most of this evidence portrays the psychological impact of the pandemic on the general population and healthcare workers [3, 4]. In patients infected with COVID-19, a negative psychological impact has also taken its toll on their mental health. A study evaluating 40,469 affected outpatients noted that 22.5% had neuropsychiatric manifestations, including anxiety (4.6%), mood (3.8%), and sleep disorders (3.4%) [5]. A recent study of 402 adults who surpassed COVID-19 infection found that 56% scored in the pathological range in at least one psychiatric clinical dimension one month following hospital treatment. This included post-traumatic stress, depression, insomnia, and anxiety. A significant risk factor for these patients was the presence of premorbid psychiatric illness [6]. Along the same lines, a literature review hypothesized that individuals who acquired COVID-19 infection, particularly those who had a severe illness course, may have a heightened risk of suicide [7].

Alternatively, little is known about psychiatric symptoms in patients hospitalized with post-COVID-19 complications and their treatment options [8]. One study postulated that the incidence of psychiatric sequelae would be 22% to 24% for post-traumatic stress, 26% to 33% for depression, and 38% to 44% for generalized anxiety when using data from patients with acute respiratory distress syndrome with intensive care unit admissions as a predictive model [9]. Such elevated incidence rates would also be expected in a prolonged hospital stay in the setting of COVID-19 infection.

Psychiatric symptoms and disorders developing in the acute and post-acute periods in patients hospitalized for COVID-19 may arise due to several factors. These include concerns about the repercussions of the disease [10], social isolation [11], and financial difficulties [12]. Nevertheless, psychological stress is not the only mechanism for emerging psychiatric manifestations following the infection. These symptoms can also occur either secondary to the direct effects of the virus on the central nervous system, the indirect activated immune-inflammatory responses, or the medications commonly provided for treatment [8, 13–16]. Other factors can have a role in critically ill patients, such as sedation, organ failure, mechanical ventilation, and immobilization [17].

As such, the need for consultation-liaison psychiatry (CLP) on COVID-19 wards has substantially increased [18, 19]. Indeed, in many hospitals, staff assigned to the CLP have been taking over the management of psychiatric complications in inpatients infected or recovering from the virus [18].

Taking the preceding statements into account, this cross-sectional study aimed to quantify the characteristics, psychiatric symptomatology, and treatments of patients hospitalized at the post-COVID-19 ward of the American University of Beirut Medical Center (AUBMC) and on whom the CLP team was consulted. A further objective of this study was to identify potential predictors of discharge in this patient population.

## Methods

### Study Design and Setting

We conducted a retrospective cross-sectional study on inpatients admitted to the post-COVID-19 unit of the AUBMC, an urban tertiary care center in Lebanon. The study was approved by the Institutional Review Board committee of the institution (BIO-2021–0095).

## Study Population

We considered patients eligible if they:

- were adults aged 18 years and above
- were admitted between 3 February 2020 and 23 February 2021
- had an official CLP referral.

Patients were typically admitted or transferred to the post-COVID-19 unit if they had a COVID-19 infection documented on polymerase chain reaction (PCR) analysis of nasopharyngeal swab specimen and followed by a negative PCR test, or if 14 days elapsed since the start of their symptoms, whichever occurred first. The post-COVID-19 unit, therefore, encompassed patients with acute (up to 4 weeks from the onset of symptoms) and post-acute (4 to 12 weeks from the onset of symptoms) COVID-19 infection [20].

## Data Extraction

We retrieved and collected data from patients' Electronic Health Records available on the EPIC Systems at AUBMC. Study outcomes consisted of patients' demographics (age, gender, and marital status), information related to the psychiatric consultation (time of consultation, the reason for referral, psychiatric symptoms on assessment, diagnosis as per Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (DSM-5), and implemented pharmacological and non-pharmacological interventions), other pertinent psychiatric information (past psychiatric history, past psychiatric medications, family history of mental illness), medical comorbidities, course of COVID-19 infection (intensive care requirement during hospitalization, intubation during hospitalization, and receipt of COVID-19 medications), the total length of hospital stay, and outcome at discharge (discharge home, death, or transfer to a chronic care facility).

## Statistical Analysis

We presented descriptive data using absolute numbers and percentages for categorical variables and means with standard deviations for continuous variables. We conducted a Pearson chi-square analysis to examine the associations between our variables and disposition outcome (death versus discharge or transfer to a chronic care facility). We then performed a binary logistic regression for significant associations. For the sake of analysis, antidepressants and antipsychotics were grouped into one variable. A *p*-value of less than 0.05 was used to indicate statistical significance. All data analysis was performed using the Statistical Package for the Social Sciences (SPSS for Windows, version 26.0. SPSS Inc., Chicago, IL, USA).

## Results

Case records of 52 patients seen by the CLP team were retrieved. Table 1 shows their sociodemographic and medical characteristics. The sample consisted of 24 males (46.2%) and 28 females (53.2%) and had a mean age of 57.33. About two-thirds of patients (69.2%)

**Table 1** General sociodemographic and medical characteristics of patients seen by the psychiatry consultation-liaison team on the post-COVID-19 unit

Variable	Count
	<b>Mean ± Standard deviation</b>
Age (years)	57.33 ± 21.64
Length of hospital stay (days)	29.52 ± 55.45
	<b>Frequency (percentage)</b>
Gender	Male 24 (46.2%)
Marital status	Single 10 (19.2%)
	Married 36 (69.2%)
	Divorced 2 (3.8%)
	Widowed 4 (7.7%)
Medical comorbidity	Cardiac 32 (61.5%)
	Pulmonary 15 (28.8%)
	Infectious (not COVID-19) 20 (38.5%)
	Gastrointestinal 5 (9.6%)
	Neurological 8 (15.4%)
	Oncological 13 (25%)
	Other systems 15 (28.8%)
Intensive care unit admission	21 (40.4%)
Intubation	11 (21.2%)
COVID-19 treatment	Steroids 33 (63.5%)
	Convalescent plasma 15 (28.8%)
	Tocilizumab 15 (28.8%)
	Remdesivir 16 (30.8%)
	Ivermectin 18 (34.6%)
	Antibiotics 33 (63.5%)
Discharge outcome	Discharge home 34 (65.4%)
	Death 16 (30.8%)
	Transfer to a chronic facility 2 (3.8%)

were married. The mean length of hospitalization was 29.52 days. Most patients had medical comorbidities; almost half (40.4%) required admission to the intensive care unit and about one-quarter (21.2%) were intubated throughout their stay. The most commonly received treatments for COVID-19 infection included steroids and antibiotics (63.5% of the sample received both). About one-third (30.8%) passed away. Further information is detailed in Table 1.

The characteristics of the psychiatry liaison team consultations are depicted in Table 2. The mean time for a psychiatry consult was 13 days from admission. Agitation/rule out delirium (36.5%), anxiety/panic attacks (30.8%), and low mood (25%) were the most common reasons for the consult of the primary team. The most prevalent DSM-5 diagnoses were delirium (30.8%), major depressive episode (15.4%), and other anxiety disorder (15.4%). Almost half of the participants (46.2%) had a past psychiatric history. About one-third (36.5%) received a psychotropic medication before hospitalization and 21.2% had a positive family history of mental illness. Pharmacological management was implemented in 90.4% of cases and mainly included second-generation antipsychotics (36.5%) and selective serotonin reuptake inhibitors

**Table 2** Characteristics of the psychiatry-liaison team consultations received by patients on the post-COVID-19 unit

Variable	Count	
	<b>Mean <math>\pm</math> Standard deviation</b>	
Day to psychiatry consult	13 $\pm$ 21.51	
	<b>Frequency (percentage)</b>	
Reason for a psychiatry consult	Low mood	13 (25%)
	Suicidality	4 (7.7%)
	Anxiety/Panic attacks	16 (30.8%)
	Agitation/Delirium	19 (36.5%)
Psychiatric symptoms present on assessment	Depressive symptoms	26 (50%)
	Suicidality	20 (38.5%)
	Anxiety symptoms	35 (67.3%)
	Panic symptoms	11 (21.2%)
	Somatic symptoms	2 (3.8%)
	Drug-related symptoms	5 (9.6%)
	Delirium-related symptoms	16 (30.8%)
	Trauma-related symptoms	2 (3.8%)
	DSM-5 diagnosis as per the consulting team	Major depressive episode
Other mood disorder		6 (11.5%)
Adjustment disorder		2 (3.8%)
Panic attack/disorder		3 (5.8%)
Generalized anxiety disorder		1 (1.9%)
Other anxiety disorder		8 (15.4%)
Delirium		16 (30.8%)
Drug intoxication/withdrawal		7 (13.5%)
Serotonin syndrome		2 (3.8%)
Normal reaction to stress		1 (1.9%)
Pharmacological management		Selective serotonin reuptake inhibitor
	Atypical antidepressant	5 (9.6%)
	Tricyclic antidepressant	1 (1.9%)
	1 <sup>st</sup> generation antipsychotic	5 (9.6%)
	2 <sup>nd</sup> generation antipsychotic	19 (36.5%)
	Benzodiazepine	4 (7.7%)
	Cyproheptadine	2 (3.8%)
	Lithium/mood stabilizer	2 (3.8%)
	Melatonin	2 (3.8%)
	Stimulant	1 (1.9%)
None	5 (9.6%)	
Non-pharmacological management	Management of delirium	16 (30.8%)
	Referral to therapy	7 (13.5%)
	Referral to social services	1 (1.9%)
	Suicide precautions	4 (7.7%)
	None	24 (64.2%)
Past psychiatric history	24 (46.2%)	
Previous psychotropic medications	19 (36.5%)	
Psychiatric family history	11 (21.2%)	

(15.4%). Non-pharmacological interventions encompassed those targeting delirium (30.8%), referral to therapy (13.5%) or social services (1.9%), and suicide precautions (7.7%). Restraints were never recommended or used.

Chi-square analysis revealed a significant association between death as disposition outcome and past psychiatric history ( $\chi^2(1)=6.98$ ;  $p=0.008$ ), intensive care unit admission ( $\chi^2(1)=11.50$ ;  $p<0.001$ ), intubation ( $\chi^2(1)=11.53$ ;  $p=0.002$ ), antipsychotic treatment ( $\chi^2(1)=4.74$ ;  $p=0.029$ ), treatment with convalescent plasma ( $\chi^2(1)=5.04$ ;  $p=0.044$ ), treatment with remdesivir ( $\chi^2(1)=7.04$ ;  $p=0.020$ ), treatment with ivermectin ( $\chi^2(1)=4.48$ ;  $p=0.029$ ), and treatment with antibiotics ( $\chi^2(1)=5.28$ ;  $p=0.016$ ). Additionally, the association between disposition outcome and past medical history of cardiac disease was marginally significant ( $\chi^2(1)=3.79$ ;  $p=0.051$ ). Only intubation remained significant in the binary logistic regression ( $p=0.004$ ).

## Discussion

In this study, we summarize cases seen by the CLP service on a post-COVID-19 unit. To the best of our knowledge, similar studies focus on the acute, rather than post-acute, period of the infection. Thus, we highlight the vulnerability of patients in both the acute and post-acute periods of hospitalization for COVID-19.

Most reasons for consulting the psychiatry team were low mood, anxiety and panic, and delirium-related symptoms such as aggression and disorientation. In general, the identified reasons for requesting a consult did not diverge from those of recent studies conducted on COVID-19 wards [21, 22]. However, one study by Arbelo et al. had psychiatric drug dose adjustment as the most common reason for psychiatry referral (38.8%) [23]. This can be explained by the large number of participants who had one previous psychiatric diagnosis (74.6% compared to 46.2% in our sample) and were taking at least one psychiatric drug (63.4% compared to 36.5% in our sample) [23].

When looking into provided diagnoses, our results also replicate other international studies [21]. We found delirium (30.8%) to be the most common diagnosis. Similarly, other studies found a high prevalence of delirium in patients on COVID-19 wards [23, 24], ranging from 26% [22] to 38.2% [21]. It is important to note that our sample had high rates of comorbid medical illnesses, a factor well known to predispose to the development of delirium. In hindsight, it can be hypothesized that delirium develops at increased rates during COVID-19 and that physicians should more rigorously screen for it [25, 26].

Furthermore, the mortality rate in our sample was high, with intubation, as expected, identified as a significant risk factor. Other relevant risk factors include age, medical comorbidities, and a diagnosis of delirium [27, 28]. This is of relevance as CLP, often-times, is approached for difficult extubation; this may particularly occur secondary to agitation in the setting of hyperactive delirium [29]. Delirium is known to be a negative prognostic predictor of hospitalization [30]. Studies done at the start of the pandemic showed that delirium in elderly patients with COVID-19 infection was, in fact, strongly associated with in-hospital mortality [26, 31]. Similar more recent studies confirmed that patients with COVID-19 diagnosed with delirium have a more severe infection, longer hospital stay, more admissions and transfers to intensive care units, difficult weaning, and subsequent higher mortality rates during their hospitalization [21, 23]. In one study, one-quarter of patients with COVID-19 died approximately one week after the onset of delirium [23]. Collaborative efforts should, therefore, target early and aggressive delirium treatment, with the goal at the very least of shortening its duration if not resolving it.

One should keep in mind that the use of antipsychotics to treat delirium remains controversial and can be another risk factor for increased mortality. A recent randomized-controlled trial showed that the use of haloperidol or ziprasidone, compared to placebo, in patients with acute respiratory failure or shock and hypoactive or hyperactive delirium in the intensive care unit did not significantly alter one- or three-month survival [32]. Despite a systematic review and meta-analysis found no differences in outcomes of delirium when using antipsychotics, some of the included trials reported more frequent potentially harmful cardiac effects with antipsychotic use [33]. Notably, in our sample, one patient with hyperactive delirium responded to valproic acid. As the management of delirium in individuals with COVID-19 infection has variations across the globe [34], there is a dire need to develop guidelines that ensure best clinical practices in this vulnerable group. Future studies should also explore alternative treatment options, such as valproic acid [35], in case antipsychotics fail.

Anxiety and panic symptoms were also commonly observed on the consultation service. One of the earliest cross-sectional surveys of COVID-19 inpatients in two isolation wards in Wuhan found that, of 85 participants, 38.8% had symptoms of anxiety [36]. A consultation-liaison service in Morocco identified anxiety symptoms in two-third of hospitalized infected patients [37]. In the current study, the consults for anxiety required a psychological intervention, more commonly so than on regular consultation-liaison floors, focusing on breathing exercises and relaxation techniques. Our service found these tools, employed to help with “difficulty breathing” and forgetting how to “normally breathe”, to be a cornerstone in the patients’ treatment. This is not surprising as a strong association between post-COVID-19 fatigue and anxiety, with no associated symptoms of autonomic dysfunction, was recently reported [38]. Many post-COVID-19 patients continue to experience panic-like symptoms in the post-acute period, including dysfunctional breathing and palpitations, which typically become superimposed with – and sometimes difficult to differentiate from – other respiratory organic symptoms [39]. As such, these patients should receive close follow-up and an early tailored intervention combining pulmonary rehabilitation with psychological support [39, 40]. Mindfulness and diaphragmatic breathing exercises are particularly beneficial in this population, mainly when conducted before or during occupational and physical therapy sessions [41]. Yogic breathing was also suggested to be helpful [42, 43].

Suicidality, as assessed by the CLP team, was alarmingly present in 38.5% of cases. Interestingly, at the beginning of the pandemic, several mental health experts warned of a possible increase in suicide, describing it as a “tsunami of suicide”, “dual pandemic of suicide and COVID-19”, and “suicide mortality and COVID-19: a perfect storm” [44]. Multiple studies looked into changes in suicide rates following the pandemic. One study assessing the early effects of the COVID-19 pandemic in 21 high- and middle-income countries found that suicide rates were unchanged or even declined [45]. A systematic review looking at COVID-19-related suicide trends in Bangladesh found the prevalence of suicidal ideations to range between 5–19% and to increase as the pandemic progressed [46]. Another study found that the risk of COVID-19-related suicide increased within the first week of diagnosis, particularly during the acute phase while receiving treatment in a hospital [47]. This sheds light on the possible difference in suicide trends according to the phase of illness, namely between the acute phase of the infection and the post-COVID-19 phase. In our study, the high prevalence of suicidality emphasizes the need for a diligent suicide risk assessment in post-COVID-19 patients. Symptoms of psychiatric, neurological, and physical illnesses, as well as inflammatory damage to the brain in individuals with post-COVID-19 syndrome, might synergistically increase suicidal ideations and behaviors

in this population [48]. Understanding the role of these different factors can help develop appropriately tailored interventions.

An important differential diagnosis in our study was serotonin syndrome. Our two cases of serotonin syndrome, initially consulted on to rule out agitation in the setting of delirium, were prescribed several medications that increased their risk of the illness (fentanyl, linezolid, ondansetron, and selective serotonin reuptake inhibitors). Recently, serotonin syndrome was described in two patients with COVID-19 infection who received several medications with additive serotonergic activity [49]. Zaid et al. showed that platelets are potentially hyperactivated in individuals with COVID-19, leading to increased plasma serotonin levels [50]. This was particularly noted in patients with COVID-19 experiencing diarrhea [51]. This highlights the importance of keeping a broad differential for agitation in the setting of COVID-19 infection, particularly when patients are receiving multiple serotonergic medications, as management in the case of serotonin syndrome would diverge from standard agitation treatment guidelines.

To note, one patient in our sample required stimulants for the management of post-COVID-19 brain fog and fatigue. Several emerging reports described a new and common entity of “long haulers”, where patients experience brain fog, fatigue, cognitive changes, and poor concentration among other symptoms months following the resolution of the infection [52, 53]. The patient in our study responded to atomoxetine, which goes along with the results of a case series that reported modafinil, another stimulant, as an avenue to combat fatigue and maintain wakefulness in patients with COVID-19 infection [54].

This study has many limitations. First, it has a sample size limiting the power of the statistical analysis. Recruitment was restricted to one institution and individuals in the acute and post-acute periods of COVID-19 infection. Therefore, results cannot be generalized and should be carefully interpreted. Also, we did not compare our participants to those on the post-COVID-19 unit who did not have CLP on board. Future studies looking into this would help identify at-risk individuals who would benefit from a psychiatry consultation.

To conclude, hospitalized individuals recovering from COVID-19 infection are at risk of developing psychiatric symptoms and disorders. Diligent screening and appropriate referral to the CLP team are essential. Having a tailored approach to this category of patients is also necessary, including checking for less common differentials and providing appropriate and timely psychological interventions. Subsequent outpatient monitoring should be kept in mind as these individuals could be at increased risk of suffering from long-term psychiatric sequelae.

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**Availability of Data and Material (data transparency)** Available upon request.

**Code Availability (software code or custom code)** Available upon request.

## Declarations

**Ethics Approval** This retrospective chart review study involving human participants was in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The Human Investigation Committee (IRB) of the American University of Beirut Medical Center (AUBMC) approved this study.

**Consent to Participate** Not applicable.

**Consent for Publication** Not applicable.

**Conflict of Interest/Competing Interests** The authors declare that they have no conflicts of interest.

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