Characteristics of 100 consecutive patients with COVID-19 referred to consultation–liaison psychiatry services in Qatar: A comparison of patients with delirium versus other psychiatric diagnoses

Yousaf Iqbal1,*, Majid Alabdulla1,2, Rajeev Kumar1,2, Javed Latoo1,2, Sultan Albrahim1, Ovais Wadoo1,2, Peter M. Haddad1,2,3

ABSTRACT

Introduction: Coronavirus disease 2019 (COVID-19) can present with various neuropsychiatric manifestations. This study reports on patients with COVID-19 who were referred to the consultation–liaison (CL) psychiatry services in Qatar and compares the clinical and sociodemographic characteristics of those diagnosed with delirium versus other psychiatric diagnoses.

Methods: This is a retrospective review of the first 100 consecutive patients with COVID-19 who were referred to the CL services.

Results: Within the total cohort (n = 100), most patients (92%) were male, and the mean age was 46 years. About 27% of patients had asymptomatic COVID-19, 35% had a past psychiatric history, and 48% reported pandemic related psychosocial stress. Delirium was the most common psychiatric diagnosis (n = 29), followed by acute stress reaction/adjustment disorder, depression, mania, anxiety, non-affective psychosis, and dementia.

Among patients with delirium, agitation was the most common symptom (76%), 86% were treated with psychotropic medications, and 17% died.

Higher age, longer hospital stays, lower oxygen saturation, lower lymphocytic count, and higher C-reactive protein (CRP) values were significantly associated with delirium versus other psychiatric diagnoses. Higher age and lower oxygen saturations predicted delirium.

Address for Correspondence:
Yousaf Iqbal1,*
1Psychiatry Hospital, Hamad Medical Corporation, Doha, Qatar
2College of Medicine, Qatar University, Qatar
3Division of Psychology and Mental Health, University of Manchester, UK
Email: yiqbal@hamad.qa

http://doi.org/10.5339/qmj.2022.28
Submitted: 2 November 2021
Accepted: 24 February 2022
© 2022 Iqbal, Alabdulla, Kumar, Latoo, Albrahim, Wadoo, Haddad, licensee HBKU Press. This is an open access article distributed under the terms of the Creative Commons Attribution license CC BY 4.0, which permits unrestricted use, distribution and reproduction in any medium, provided the original work is properly cited.

Cite this article as: Iqbal Y, Alabdulla M, Kumar R, Latoo J, Albrahim S, Wadoo O, Haddad PM. Characteristics of 100 consecutive patients with COVID-19 referred to consultation–liaison psychiatry services in Qatar: A comparison of patients with delirium versus other psychiatric diagnoses, Qatar Medical Journal 2022(3):28 http://doi.org/10.5339/qmj.2022.28
Conclusion: Delirium was associated with a range of clinical variables and had significant mortality, despite the relatively young age of the patients. COVID-19 should be considered in patients presenting with delirium. Finally, early identification and management of delirium should be integral to COVID-19 protocols.

Keywords: COVID-19, SARS-CoV2, delirium, consultation—liaison psychiatry, hypoxia, inflammatory markers, mortality

INTRODUCTION

Patients with Coronavirus disease 2019 (COVID-19) can present with a range of neuropsychiatric disorders, including delirium. Delirium in COVID-19 can reflect multiple factors, including inflammation, endothelial damage, increased oxidative stress, hypoxemia, iatrogenic factors, and potentially direct infection of the central nervous system by SARS-CoV-2. In fact, delirium has been reported as the presenting and only feature of COVID-19. Delirium in COVID-19 patients identified its prevalence and incidence rates as 24.3% and 32.4%, respectively. A recent systematic review and meta-analysis of delirium in COVID-19 patients identified its prevalence and incidence rates as 24.3% and 32.4%, respectively. Other studies have also demonstrated that delirium associated with COVID-19 is more prevalent in the elderly, who are also more prone to developing severe COVID-19. Delirium in COVID-19 patients has been associated with in-hospital death, increased length of hospital stay, intensive care admission, and ventilator utilization; it has also been reported to be a predictive factor of inhospital death and adverse outcomes in hospitals.

In this study, we conducted a retrospective review of the electronic patient records for the first 100 consecutive patients with COVID-19 referred to the consultation—liaison (CL) psychiatry service in Doha after Qatar recorded its first COVID-19 case (February 2020). The aim was to better understand the psychiatric morbidity associated with acute COVID-19 among patients referred to a CL service.

METHODOLOGY

We have previously reported on the first 50 patients seen in this cohort. In the current report, we describe the full cohort of 100 patients and compare the characteristics of those diagnosed with delirium versus other psychiatric diagnoses. During the pandemic, the Qatar CL service operated across three hospitals in Doha managed by the Hamad Medical Corporation (HMC). The inclusion criteria for the study were individuals aged 18 years and over and a positive real-time polymerase chain reaction test for Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) during the index admission. The 100 cases presented between February 28th and August 3rd, 2020. Psychiatric diagnoses were those recorded by the CL team in the patient records and reflected the team’s clinical judgment. The study was approved by the HMC Institutional Review Board (MRC-05-072).

RESULTS

Table 1 shows the characteristics of the 100 patients. Most (92%) were male, mean age was 46 years, 27% had asymptomatic COVID-19 (i.e., no characteristic physical symptoms of COVID-19), and 35% had a past psychiatric history. Significant recent psychosocial stress, which is largely related to the pandemic, was recorded in the notes of 48 patients. A psychiatric diagnosis was made by the CL team in all but one case. Delirium was the most common psychiatric diagnosis (n = 29), followed by acute stress reaction or adjustment disorder (n = 25), depression (n = 16), mania (n = 15), anxiety (n = 14), non-affective psychosis (n = 13), and dementia (n = 6). Nearly half of the delirium cases (n = 12/29) had a medical comorbidity (i.e., a current medical condition other than COVID-19). Moreover, sleep disturbance was the most common psychiatric symptom (n = 65, 65%), followed by anxiety (n = 52, 52%) among all 100 patients. Recent self-harm thoughts or attempts were present in 24 (24%) of all patients with COVID-19 referred to the CL team. The most common psychiatric symptoms in the delirium cohort were agitation (n = 22, 76%), impaired memory (n = 19, 66%), disorientation (n = 18, 62%), sleep-wake disturbance (n = 11, 38%), and confusion (n = 11, 38%). Recent self-harm thoughts or attempts were present in 2 patients in the delirium cohort. Psychotropic medications were prescribed to 25 out of the 29 (86%) patients with delirium during their admission. The most common medications were haloperidol (n = 17), benzodiazepines (n = 10), and quetiapine (n = 9), and low doses were used in all cases. All patients with delirium were offered non-pharmacological management strategies including advice to the general medical team to assist with orientation, reassurance, and effective communication.
Table 1. Sociodemographic and clinical details of 100 consecutive SARS-CoV-2 positive patients referred to the HMC consultation–liaison psychiatry service.

| Characteristic                                      | Number (%) |
|-----------------------------------------------------|------------|
| Age (years)                                         |            |
| Median                                              | 43         |
| Mean                                                | 45.92      |
| Range                                               | 18–91      |
| Male                                                | 92 (92%)   |
| Nationality                                         |            |
| South Asian (Indian, Pakistani, Bangladeshi, Nepalese, Afghan) | 60 (60%)   |
| Qatari                                              | 18 (18%)   |
| Other Arab                                          | 14 (14%)   |
| Filipino                                            | 4 (4%)     |
| Caucasian                                           | 2 (2%)     |
| African                                             | 2 (2%)     |
| Source of psychiatric referral                      |            |
| Ward                                                | 79 (79%)   |
| Emergency Department                                | 21 (21%)   |
| Length of hospital stay (days)                      |            |
| Median                                              | 20         |
| Mean                                                | 26.51      |
| Range                                               | 1–155      |
| Physical comorbidity present                        | 67 (67%)   |
| Includes Cardiovascular Disease, Diabetes, Liver Disease, Lung Disease, Cancer, Chronic kidney disease | |
| Severity of COVID-19 infection¹                    |            |
| Asymptomatic                                        | 27 (27%)   |
| Mild COVID-19                                       | 17 (17%)   |
| Mild COVID-19 pneumonia                             | 21 (21%)   |
| Severe COVID-19 pneumonia                           | 21 (21%)   |
| Critical                                            | 14 (14%)   |
| Details of COVID-19 treatment                       |            |
| Supplementary oxygen                                | 50 (50%)   |
| Steroids                                            | 45 (45%)   |
| Hydroxychloroquine                                  | 50 (50%)   |
| Antibiotics/antivirals                              | 79 (79%)   |
| Past psychiatric history                            | 35 (35%)   |
| Maintenance psychotropic medications prescribed at the time of admission | 17 (17%)   |
| Significant psychosocial stress before admission    | 48 (48%)   |
| Psychiatric diagnosis made by the CL team²         |            |
| Delirium                                            | 29 (29%)   |
| Acute stress reaction/adjustment disorder           | 24 (24%)   |
| Depression (includes 1 case of depressive psychosis) | 16 (16%)   |
| Mania                                               | 15 (15%)   |
| Anxiety disorders                                   | 14 (14%)   |
| Non-affective psychosis                             | 13 (13%)   |
| Dementia (all cases present pre-COVID-19)           | 6 (6%)     |
| No psychiatric diagnosis made                       | 1 (1%)     |
| Miscellaneous (stroke, intellectual disability with challenging behavior, cerebral palsy, epilepsy, metabolic encephalopathy, Herpes Simplex encephalitis, alcohol withdrawal) | 10 (10%)   |
| Psychotropic medication prescribed during admission | 85 (85%)   |
| Psychiatric condition resolved or improved at the time of hospital discharge | 87 (87%)   |

¹Severity of COVID-19 infection related to the most severe illness during the hospital admission and was made by the medical team as per the HMC treatment protocol as below.
(b) asymptomatic: i.e., no characteristic physical symptoms of COVID-19 infection
(b) mild COVID-19: uncomplicated upper respiratory tract viral infection, may have non-specific symptoms, such as fever, cough, sore throat, nasal congestion, malaise, headache, or muscle pain; elderly people and individuals who are immunsuppressed may present with atypical symptoms
(c) mild pneumonia: patients with pneumonia and no signs of severe pneumonia
(d) severe pneumonia: fever or suspected respiratory infection, plus one of the following: (i) respiratory rate > 30 breaths/min, (ii) severe respiratory distress, or (iii) SpO2 < 90% on room air
(e) critical disease: acute respiratory distress syndrome, sepsis, septic shock
²The sum of psychiatry diagnoses exceeds 100, as some patients had more than one psychiatric diagnosis.
About 17% (n = 5) of patients with delirium died during the index admission, while 3% (n = 2) in the non-delirium group died; both patients had metastatic cancer. The 5 patients with delirium who died all suffered from COVID-19 severe pneumonia/critical disease.

A univariate comparison of the characteristics of patients with and without delirium showed older age, a prolonged hospital stay, lower oxygen saturation, higher C-reactive protein (CRP) value, lower lymphocyte count, and a range of treatment variables (use of steroids, antivirals/antibiotics and chloroquine/hydroxychloroquine) as factors that were significantly associated with a diagnosis of delirium (Table 2). Binary logistic regression using a stepwise method, which was employed to control for significant variables in the univariate analysis, revealed higher age and lower oxygen saturations that had statistically significant links with a delirium diagnosis (Table 3).

**DISCUSSION**

Our data revealed that delirium was the most common psychiatric diagnosis seen by the CL team in COVID-19 patients in the early months of the pandemic. Our cohort of patients with delirium is younger than that reported in other studies of delirium related to COVID-19. This is consistent with Qatar’s relatively young population (median age of 33.7 years). The most prevalent symptoms of delirium in our case series included sleep–wake disturbances and agitation. Hyperactive delirium has been reported to be more common in younger adults with COVID-19, whereas the hypoactive form appears more common in elderly patients. Furthermore, patients with hyperactive delirium may be more likely to be referred to psychiatric services than those with hypoactive delirium.

In our study, over a quarter of COVID-19 patients who were referred to the CL team were physically asymptomatic (i.e., they had no characteristic physical symptoms of COVID-19). These included patients who were transferred from quarantine centers, from psychiatric hospitals, or were admitted following screenings at emergency departments where they first presented with psychiatric symptoms. Nearly one quarter of the patients in the full cohort of 100 patients reported self-harm thoughts or attempts. The diverse psychiatric symptoms seen in the full cohort could reflect the effects of psychosocial stressors, such as quarantine, social distancing, and financial difficulties, the physical effects of SARS–CoV2 including potential direct neurotoxic effects and iatrogenic factors.

Our finding of an association between delirium and raised CRP level suggests that inflammation may be involved in the pathophysiology of COVID-19–associated delirium. Furthermore, raised CRP level has also been found to be independently associated with acute renal failure in COVID-19 patients. Higher age and lowest oxygen saturation were significantly associated with delirium, as previously reported.

In the non-delirium group, patients presented with a range of psychiatric diagnoses, including acute stress reaction/adjustment disorder, depression, anxiety disorders, non-affective psychosis, and first onset mania. Sleep disturbance was the most common psychiatric symptom among all patients with COVID-19 referred to the CL service, and other studies have also highlighted its high prevalence. This underscores the importance of recognition and the management of sleep disturbances in clinical practice. Furthermore, nearly two-thirds of patients in the non-delirium group had no past psychiatric history, thus supporting the view that COVID-19 was likely to be a significant etiological factor in the appearance of these disorders.

The first limitation of this study is that it only assessed patients referred to the HMC CL services. There are likely to be COVID-19 patients who had delirium, especially during intensive care unit (ICU) admissions, who were not referred to CL services because their psychiatric symptoms may not have posed significant management issues. Second, this was an observational study that utilized secondary data. Thus, it is dependent on the quality of the information recorded in the notes.

An important finding from our study is that delirium can occur in relatively young and otherwise healthy patients with COVID-19. Moreover, delirium is not invariably associated with severe COVID-19 illness but can present in people who are physically asymptomatic or have mild physical symptoms of COVID-19. Therefore, it is important to consider a diagnosis of COVID-19 in patients presenting with delirium. In our results, we recorded a 17% (n = 5/29) mortality in the delirium cohort despite the relatively young mean age of these patients (59.4 years).
| Characteristic                                | Clinical Diagnosis | \( P \) value (2-tailed) |
|----------------------------------------------|-------------------|--------------------------|
|                                              | \( n = 29 \) | \( n = 71 \) |
| Age                                          | 59.45 (17.49)     | 40.39 (13.25) | 0.000 |
| Gender                                       |                   |                      |
| Male                                         | 28 (30.4)         | 64 (69.6)           | 0.430 |
| Female                                       | 1 (12.5)          | 7 (87.5)            |      |
| Ethnicity                                    |                   |                      |
| Qatari                                       | 2 (11.1)          | 16 (88.9)           | 0.119 |
| Non-Qatari                                   | 27 (32.9)         | 55 (67.1)           |      |
| Referral source                              |                   |                      |
| Emergency department                         | 2 (9.5)           | 19 (90.5)           | 0.052 |
| Inpatient units                              | 27 (34.2)         | 52 (65.8)           |      |
| Physical comorbidity                         |                   |                      |
| Yes                                          | 24 (35.8)         | 43 (64.2)           | 0.056 |
| No                                           | 5 (15.2)          | 28 (84.8)           |      |
| Current smoker                               |                   |                      |
| Yes                                          | 2 (13.3)          | 13 (86.7)           | 0.349 |
| No                                           | 26 (31.7)         | 56 (68.3)           |      |
| Current alcohol or substance use             |                   |                      |
| Yes                                          | 1 (16.7)          | 5 (83.3)            | 0.669 |
| No                                           | 28 (29.8)         | 66 (70.2)           |      |
| Past psychiatric history                     |                   |                      |
| Yes                                          | 7 (20.0)          | 28 (80.0)           | 0.222 |
| No                                           | 22 (33.8)         | 43 (66.2)           |      |
| Maintenance psychotropics medication on      |                   |                      |
| admission                                     |                   |                      |
| Yes                                          | 1 (5.9)           | 16 (94.1)           | 0.020 |
| No                                           | 28 (33.7)         | 55 (66.3)           |      |
| Psychosocial stress                          |                   |                      |
| Yes                                          | 6 (12.5)          | 42 (87.5)           | 0.001 |
| No                                           | 23 (44.2)         | 29 (55.8)           |      |
| Severity of COVID-19                         |                   |                      |
| Non-severe disease                           | 11 (16.9)         | 54 (83.1)           | 0.001 |
| Severe disease                               | 18 (51.4)         | 17 (48.6)           |      |
| Oxygen administered                          |                   |                      |
| Yes                                          | 25 (50.0)         | 25 (50.0)           | 0.000 |
| No                                           | 4 (8.0)           | 46 (92)             |      |
| Treatment with antibiotics/antivirals        |                   |                      |
| Yes                                          | 28 (35.4)         | 51 (64.6)           | 0.013 |
| No                                           | 1 (4.8)           | 20 (95.2)           |      |
| Treatment with chloroquine/hydroxychloroquine|                 |                      |
| Yes                                          | 18 (36.0)         | 32 (64.0)           | 0.019 |
| No                                           | 11 (22.0)         | 39 (78.0)           |      |
| Treatment with steroids                      |                   |                      |
| Yes                                          | 21 (46.7)         | 24 (53.3)           | 0.001 |
| No                                           | 8 (14.5)          | 47 (85.5)           |      |
CONCLUSION

Delirium was the most common psychiatric disorder seen in patients with acute COVID-19 who were referred to CL services in Qatar—a country with a young, predominantly migrant population. Furthermore, the data showed that delirium was not invariably associated with severe COVID-19 illness but can also present in people with COVID-19 who were physically asymptomatic or had mild physical symptoms of COVID-19. In our population, delirium was associated with a range of variables, including hypoxia, older age, elevated CRP, and a prolonged hospital length of stay compared to patients with other psychiatric diagnoses. In addition, delirium was associated with significant mortality (17%). This is consistent with the findings of other studies, which show that delirium is associated with poor outcomes, including mortality, in COVID-19 patients. The early recognition of delirium may improve the management and outcomes of a subgroup of COVID-19 patients at high risk of poor outcomes. Furthermore, clinicians caring for COVID-19 patients should be aware of the risks associated with delirium. The early identification and management of delirium should be integral to COVID-19 clinical protocols. We hope that this study may assist with resource allocation and the planning of CL services. Further studies are needed to investigate the longer-term psychiatric sequelae of COVID-19.

DECLARATIONS

Ethical approval and consent to participate

This study was approved by the Institutional Review Board of Hamad Medical Corporation (MRC-05 – 072).
Availability of data and materials
The data that support the findings of this study are available from the corresponding author upon reasonable request and pending additional ethical approval.

Competing interests
Competing interests: PMH reports personal fees from Janssen, NewBridge Pharmaceuticals, and Otsuka, outside the submitted work.

Funding
This study did not receive any specific grant from funding agencies in the public, commercial, or non-profit sectors.

Acknowledgments
We are thankful to Prem Chandra who provided statistical analysis assistance to the research team.

REFERENCES
1. A. Varatharaj, N. Thomas, M.A. Ellul, N. Davies, T.A. Pollak, E.L. Tenorio, et al. Neurological and neuropsychiatric complications of COVID-19 in 153 patients: a UK-wide surveillance study. Lancet Psychiatry 2020; 7(10): 875 – 882. PMID: 32593341; PMCID: PMC7316461. https://doi.org/10.1016/S2215-0366(20)30287-X.
2. A. Ticinesi, N. Cerundolo, A. Parise, A. Nouvenne, B. Prati, A. Guerra, et al. Delirium in COVID-19: epidemiology and clinical correlations in a large group of patients admitted to an academic hospital. Aging Clin Exp Res 2020; 32: 2159 – 2166 (2020). https://doi.org/10.1007/s40520-020-01699-6.
3. D. Emmerton & A. Abdelhafiz, A. Delirium in older people with COVID-19: clinical scenario and literature review. SN Compr Clin Med, 1 – 8. Advance online publication. https://doi.org/10.1007/s42399-020-00474-y.
4. MA. Oldham, A.J.C. Slooter & C. Cunningham. Characterising neuropsychiatric disorders in patients with COVID-19. Lancet Psychiatry. 2020; 7: 932 – 933.
5. M. Taquet M, S. Luciano, JR. Geddes, PJ. Harrison. Bidirectional associations between covid-19 and psychiatric disorder: retrospective cohort studies of 627354 covid-19 cases in the USA. Lancet Psychiatry 2020 (published online 9 Nov). doi:10.1016/s2215-0366(20)30462-4.
6. Y. Iqbal, M. Alabdulla, J. Latoo, R. Kumar, S. Albrahim, O. Wądo, et al. Mania and hypomania associated with COVID-19: a series of 15 cases seen by the consultation-liaison psychiatry service in Qatar. Qatar Med J 2021; 65: http://dx.doi.org/10.5339/qmj.2021.65.
7. S. R. Beach, N.C. Praschan, C. Hogan, S. Dotson, F. Meredith, N. Kontos, et al. Delirium in COVID-19: a case series and exploration of potential mechanisms for central nervous system involvement. Gen Hosp Psychiatry 2020; 65: 47 – 53. doi: 10.1016/j.genhosppsych.2020.05.008. Epub 2020 May 22. PMID: 32470824; PMCID: PMC7242189.
8. Z. Wu & J.M. McGoogan. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72 314 cases from the Chinese Center for Disease Control and Prevention. JAMA. 2020; 323(13): 1239 – 1242.
9. W. A. Alkeridy, I. Almaghlouth, R. Alrashed, K. Alayed, K. Binkhamis, A. Alsharidi, et al. A unique presentation of delirium in a patient with otherwise asymptomatic COVID-19. J Am Geriatr Soc. 2020; 68(7): 1382 – 1384. https://doi.org/10.1111/jgs.16536.
10. S.-C. Shao, C.-C. Lai, Y.-H. Chen, Y.-C. Chen, M.-J Hung, S.-C Liao. Prevalence, incidence and mortality of delirium in patients with COVID-19: a systematic review and meta-analysis, Age and Ageing, 2021; 50: 1445 – 1453. https://doi.org/10.1093/ageing/afab103.
11. M. Kennedy, B.K.I. Helfand, R.Y. Gou, S.L. Gartaganis, M. Webb, J.M. Moccia, et al. Delirium in older patients with COVID-19 presenting to the emergency department. JAMA Netw Open. 2020; 3(11): e2029540. doi: 10.1001/jamanetworkopen.2020.29540.
12. F. B. Garcez, M.J. Aliberti, P.C. Poco, M. Hiratsuka, S.D. Takahashi, V.A. Coelho, D.B. Salotto, et al. Delirium and adverse outcomes in hospitalized patients with COVID-19 presenting to the emergency department. JAMA Netw Open. 2020; 3(11): 2440 – 2446. doi: 10.1111/jgs.16803. Epub 2020 Sep 5. PMID: 32835425; PMCID: PMC7460960.
13. N. Alwahaibi, M. Al Maskari, B. Al Dhahli, H. Al Issaei and S. Al Bahlani. One-year review of COVID-19 in the Arab World. Qatar Med J 2021; 2021(3).https://doi.org/10.5339/qmj.2021.66.
14. Y. Iqbal, M.A. Al Abdulla, S. Albrahim, J. Latoo, R. Kumar & P.M. Haddad. Psychiatric presentation of patients with acute SARS-CoV-2 infection: a retrospective review of 50 consecutive patients seen by a consultation-liaison psychiatry team. BJPsych Open. Cambridge University Press 2020; 6 (5): e109.
15. J. Helms, S. Kremer, H. Merdji, M. Schenck, F. Severac, R. Clere-Jehl et al. Delirium and encephalopathy in severe COVID-19: a cohort analysis of ICU patients. Crit Care BioMed Central. 2020; 24: 1 – 11.

16. G. Bellelli, J.S. Brathwaite & P. Mazzola. Delirium: a marker of vulnerability in older people. Front Aging Neurosci. 2021; 13: 626127. doi:10.3389/fnagi.2021.626127. PMID: 33994990; PMCID: PMC8119654.

17. Qatar Demographic Profile, Index Mundi, accessed 19/5/2020. https://www.indexmundi.com/qatar/demographics_profile.html.

18. T. E. Poloni, A.F. Carlos, M. Cairati, C. Cutaia, V. Medici, E. Marelli, et al: Prevalence and prognostic value of delirium as the initial presentation of COVID-19 in the elderly with dementia: an Italian retrospective study. EClinical-Medicine 2020; 26: 100490. doi:10.1016/j.eclinm.2020.100490. PMCID: PMC7392565, PMID: 32838241.

19. J. S. Generoso, J.L. Barichello de Quevedo, M. Cattani, B.F. Lodetti, L. Sousa, A. Collodel, et al. Neurobiology of COVID-19: how can the virus affect the brain? Braz J Psychiatry 2021; 43(6): 650 – 664. doi: 10.1590/1516-4446-2020-1488. PMID: 33605367; PMCID: PMC8639021.

20. A. Oussalah, S. Gleye, I.C. Urmes, E. Laugel, F. Barbé, S. Orlowski, et al. The spectrum of biochemical alterations associated with organ dysfunction and inflammatory status and their association with disease outcomes in severe COVID-19: a longitudinal cohort and time-series design study. EClinicalMedicine. Elsevier. 2020; 27: 100554. doi: 10.1016/j.eclinm.2020.100554. Epub 2020 Sep 20. PMID: 32984786; PMCID: PMC7502281.

21. Y. R. Guo, Q.D. Cao, Z.S. Hong, T. Yuan-Yang, C. Shou-Deng, J. Hong-Jun, et al. The origin, transmission and clinical therapies on coronavirus disease 2019 (COVID-19) outbreak – an update on the status. Mil Med Res 2020; 7(1): 1 – 10. https://doi.org/10.1186/s40779-020-00240-0.

22. O. Semiachkina-Glushkovskaya, A. Mamedova, V. Vinnik, M. Klimova, E. Saranceva, V. Ageev, et al. Brain mechanisms of COVID-19-sleep disorders. Int J Mol Sci 2021; 22(13): 6917. doi: 10.3390/ijms22136917. PMID: 34203143; PMCID: PMC8268116.

23. T. I. Hariyanto, C. Putri, J.E. Hananto, J. Arisa, V. Fransisca, R. Situmeang, & A. Kurniawan. Delirium is a good predictor for poor outcomes from coronavirus disease 2019 (COVID-19) pneumonia: a systematic review, meta-analysis, and meta-regression. J Psychiatr Res 2021; 142: 361 – 368. doi: 10.1016/j.jpsychires.2021.08.031.