Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Depressive and anxiety symptoms in patients with SARS-CoV2 infection

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Dear Editor,

Coronavirus disease 2019 (COVID-19) currently represents a global health concern emerging from China and rapidly spreading worldwide (Chen et al., 2020). COVID-19 is due to severe acute respiratory syndrome (SARS)-Coronavirus2 (SARS-CoV2) infection (Chen et al., 2020). As widely known, SARS-CoCV2 infection primarily causes pneumonia; however, other clinical manifestations have been documented in patients with SARS-CoV2 infection, with various degree of prevalence (Huang et al., 2020). In particular, the affection of cardio-vascular and neurological systems have been well recognized (Mao et al., 2020; Boukhris et al., 2020; Liguori et al., 2020).

In this context, we have recently performed a prospective study in 103 patients with COVID-19 admitted at the University Hospital of Tor Vergata in Rome (Liguori et al., 2020). In this patient group, we documented the frequent occurrence of subjective neurological symptoms (Liguori et al., 2020). Based on the study protocol, all patients underwent an anamnestic interview requiring a dichotomized answer (YES/NO) about 13 neurological symptoms (hyposmia, dysgeusia, auditory dysfunction, headache, confusion, dizziness, numbness/paresthesia, fatigue, daytime sleepiness, sleep impairment, muscle ache, depression, and anxiety). At the time of the interview the following parameters were also evaluated: age, sex, laboratory test (serum levels of white blood cells – WBC - and C-reactive protein – CRP), duration of hospitalization. The study design was approved by the local ethics committee at University Hospital of Tor Vergata in Rome, which approved the procedures, conformed to the Declaration of Helsinki, and informed consents were achieved from all the participants (protocol no. 48.20, version 2020).

In this secondary analysis derived from the previous investigation, (Liguori et al., 2020) we aimed at primarily focusing on the occurrence of depressive and anxiety symptoms in patients with COVID-19, also considering the possible correlation of these symptoms with the other neurological symptoms investigated and the demographic, clinical, and laboratory data achieved.

The main finding of this secondary analysis is the occurrence of anxiety symptoms in 34/103 patients and depressive symptoms in 39/103 patients with COVID-19. In particular, 27 patients complained of both depressive and anxiety symptoms, whereas seven patients experienced only anxiety symptoms and 12 only depressive symptoms (Table 1). We also found that patients with anxiety symptoms presented more frequent muscle ache, higher CRP serum levels and more concomitant neurological symptoms than those without anxiety symptoms. Likewise, patients featured by depressive symptoms showed higher CRP, more concomitant neurological symptoms, and higher rate of anxiety and muscle ache symptoms than those not complaining for depressive symptoms (Table 1). Finally, we did not document sex-based differences related to both anxiety and depressive symptoms.

Neurological manifestations of SARS-CoV2 infection may range from subjective complaints (including headache, muscle ache, hyposmia and dysgeusia) to severe and life threatening conditions, such as encephalitis, stroke, Guillan-Barrè syndrome, and status epilepticus (Boukhris et al., 2020; Liguori et al., 2020). Moreover, psychological distress has been documented in patients with COVID-19 needing hospitalization or quarantine (Guo et al., 2020). Depression, anxiety, and post-traumatic stress symptoms were more frequent in patients with COVID-19 compared to volunteers not affected by SARS-CoV2 infection (Guo et al., 2020). Nationwide on-line or telephonic surveys (mostly performed in China) reported a sex effect on psychological outcomes, with women showing significantly higher psychological distress than men (Bo et al., 2020; Liu et al., 2020; Qiu et al., 2020).

In this study, we did not document differences in anxiety and depressive complaints between men and women. However, we exclusively perform an anamnestic interview with a dichotomized answer to detect anxiety and depression, and not a validated questionnaire or a psychological interview.

We also analyzed white blood cells and CRP in patients with SARS-CoV2 infection. The comparison between patients with and without depressive or anxiety symptoms did not document significant differences in WBC, but showed higher CRP in patients with anxiety or depressive symptoms. Our results partially concord with the data reported by Guo and co-Authors, since in this latter study a correlation between inflammatory markers and psychological distress was evident only in patients with severe depressive symptoms (Guo et al., 2020). Finally, we documented the presence of more concomitant neurological symptoms in patients with anxiety or depressive symptoms. This result can be explained by a higher psychological burden in patients with several neurological symptoms, or by a more severe nervous system involvement also producing depression and anxiety. The neurobiological basis of these symptoms, indeed, have been widely recognized, and SARS-CoV2 seems to affect the nervous system via different mechanisms (Wu et al., 2020). The disproportionate inflammatory response, the direct brain invasion by the virus, or the activation of T cells affecting nervous system have been considered as events leading to nervous system damage in

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Table 1
Demographic, Clinical, Laboratory, and Neurological Data of patients with SARS-CoV2 infection.

	Anxiety		P Value	Depression		P Value
	Yes (*N* = 34)	No (*N* = 69)		Yes (*N* = 39)	No (*N* = 64)	
Sex (M, F)	18, 16	41, 28	NS	19, 20	40, 24	NS
Age (Mean ± SD)	56,71 ± 12,76	54 ± 14,88	NS	57,82 ± 14,45	53,3 ± 13,92	NS
CRP (Mean ± SD)	32,15 ± 45,97	14,05 ± 26,14	***0,039***	34.37 ± 49.41	11.43 ± 16.55	***0,023***
WBC (x10^9/L) (Mean ± SD)	9,71 ± 7,82	7,97 ± 5,31	NS	8,53 ± 4,57	8,55 ± 7,18	NS
Neutrophil, count (Mean ± SD)	5,85 ± 4,51	5,91 ± 5,6	NS	6,4 ± 4,52	5,55 ± 5,69	NS
Lymphocyte, count (Mean ± SD)	3,15 ± 7,57	1,57 ± 0,69	NS	1,41 ± 0,86	2,54 ± 5,56	NS
Neutrophil,%WBC (Mean ± SD)	0,65 ± 0,22	0,66 ± 0,16	NS	0,7 ± 0,15	0,62 ± 0,2	NS
Lymphocyte,%WBC (Mean ± SD)	0,24 ± 0,21	0,24 ± 0,12	NS	0,19 ± 0,12	0,27 ± 0,17	NS
Days of Hospitalization (Mean ± SD)	7,69 ± 7,13	8,53 ± 8,6	NS	8,41 ± 7,09	8,16 ± 8,65	NS
Temperature (Mean ± SD)	36,61 ± 0,84	36,51 ± 0,61	NS	36,55 ± 0,79	36,53 ± 0,64	NS
Hyposmia n	14	24	NS	14	24	NS
Dysgeusia n	16	29	NS	18	27	NS
Auditory Dysfunction n	0	2	NS	2	0	NS
Headache n	17	25	NS	17	25	NS
Confusion n	11	12	NS	11	12	NS
Dizziness n	11	16	NS	12	15	NS
Numbness/Paresthesia n	0	4	NS	1	3	NS
Fatigue n	12	18	NS	11	19	NS
Daytime Sleepiness n	14	18	NS	11	21	NS
Sleep Impairment n	17	30	NS	19	28	NS
Muscle Ache n	16	17	***0,008***	13	20	***0,042***
Depression n	25	11	***0,0001***	NA	NA	NA
Anxiety n	NA	NA	NA	25	10	***0,0001***
N Symptoms (Mean ± D)	5,3 ± 2,17	3,03 ± 2,48	***0,0001***	5,2 ± 2,11	3,04 ± 2,54	***0,0001***

List of Abbreviations: F, female; M, male; n, number; SD, standard deviation; NS, not significant; NA, not admitted; WBC, white blood cells; CRP, C-reactive protein.

patients with COVID-19 (Wu et al., 2020). Hence, the neurotropic activity of the SARS-CoV2 may also explain the occurrence of neuropsychiatric symptoms by activation of immune-inflammatory responses (Wu et al., 2020).

Hence, depression and anxiety are frequent symptoms in patients with SARS-CoV2 infection needing careful medical evaluation and follow-up. Moreover, counteracting these neuropsychological symptoms can improve the reaction to the infection and can need of specific treatments in order to improve the possibility of rehabilitation and recovery.

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Author contributions

NC, MI, JO, GP, EP, OB, GGM contributed with patients' selection and evaluation

CL, MP, MS contributed to data acquisition and analysis

CL, MP contributed to drafting the manuscript and figures

CL, MP, NBM, MA, LS, PR, AM conceived and designed the study, supervised data analysis, contributed to drafting and revising the manuscript

Declaration of Competing Interest

All authors present no conflicts of interest.

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