The Egyptian Journal of Neurology, Psychiatry and Neurosurgery

RESEARCH

Open Access

Neuropsychiatric manifestations of hospitalized patients with coronavirus disease 2019 during the second wave in Egypt

Nahla Nagy[1], Fiby Fayez[1], Reem ElSayed Hashem[1], Marco Antaky[1] and Eman. S. Rabie[1,2*]

Abstract

Background Studies suggested that COVID-19 virus causes neurological and psychiatric manifestations with different mechanisms. However, prevalence of neurological and psychiatric manifestations among COVID-19 patients varies across studies from 18.1%: 82.3%. The objective of this study was to determine neuropsychiatric manifestations in a sample of Egyptian COVID-19 hospitalized patients during the second wave of the pandemic and to detect factors affecting neurological and psychiatric prevalence. This cross-sectional study was conducted at Ain Shams university isolation hospitals and included 110 hospitalized COVID-19 patients, over a 2-month period from June 2021 to August 2021. Patients underwent a careful history taking, full neurological examination including Mini-Mental State Examination, the Structured Clinical Interview for DSM-IV (SCID I), COVID-19 severity criteria. Any available imaging and laboratory tests were recorded.

Results 83 (75.5%) patients had neurological manifestations. The most common neurological manifestations were headache (50.9%), hypogeusia (24.5%), hyposmia, paresthesia (23.6% each) and coma (15.5%). After exclusion of 17 patients who could not be examined by Mini-Mental State Examination, psychiatric manifestations were seen in 56 patients (61.5%) out of the remaining 91 patients. The most prevalent psychiatric disorders were delirium (30.8%), depression (19%), and adjustment disorder (17.5%). Moreover, hypertension, COVID-19 severity, place of admission, and high levels of LDH and ALT affected neurological manifestations prevalence.

Conclusions COVID-19 infection and its immune reaction along with its social and psychological effects have a great impact on mental and physical health. Hence, neuropsychiatric evaluation cannot be ignored in any case with COVID-19 infection.

Keywords Coronavirus, Neurological, Psychiatric, Hospitalized patients, Egypt

Background

Since the end of 2019, pneumonia of unknown cause was diagnosed among a group of patients in Wuhan, China. A new coronavirus was isolated from respiratory system cells among them which was named 2019-nCoV [1]. Egyptian government announced the 1st case in the country on 14th February and declared partial lockdown on March 25th [2].

Corona viruses contain a positive-sense single-stranded RNA which is enclosed in an envelope-like capsid with spikes, which resemble solar corona and COVID-19 is the 7th member of the family of coronaviruses that infect humans [1]. It can be transmitted between humans directly via aerosols, tears, saliva, feco-oral secretions, semen, and mother-to-child or indirectly via fomites [3].

COVID-19 mainly affects respiratory system causing fever, cough, dyspnea but also can affect other systems

*Correspondence:
Eman. S. Rabie
eman.soliman@med.asu.edu.eg
[1] Department of Neuropsychiatry, Ain Shams University, Cairo, Egypt
[2] Okasha's Institute of Psychiatry, Ain Shams University, Abbasseyia, Ramses Street ExtensionDair Al-Malak, P.O. Box: 11657, Cairo, Egypt

including nervous system through neuroinvasion directly by the virus via peripheral nerves, olfactory bulb or systemic circulation, or indirectly via immune response precipitating neuroinflammation causing neurological and psychiatric disorders [4] (Orsini and colleagues, 2020).

Previous studies showed that COVID-19 infection and vaccine are associated with higher prevalence rates of psychiatric and neurological manifestations. Previous studies reported prevalence of neurological manifestations among COVID-19 patients varies from 36.4%: 82.3% [5, 6] and those of psychiatric manifestations vary from 18.1%: 55.7% [7, 8].

COVID-19 infection-associated neurological manifestations include ischemic strokes, transient ischemic attacks, intracranial hemorrhage [9], cerebral venous sinus thrombosis, headache, seizures [10], olfactory and gustatory dysfunction [6], Guillain–Barré syndrome and encephalitis [11].

A study investigated neurological problems in the context of COVID-19 infection in Egypt and found out that most manifestations were optic neuritis, seizures, and ataxia, while in rare cases, acute ischemic stroke, and cerebral venous sinus thrombosis developed [12].

Another study conducted et al.-Azhar University Hospitals reported that neurological manifestations included headache (78.0%) taste and smell impairment (74.0%), myalgia (62.0%) and dizziness (58.0%). It was also shown that 30 patients (60.0%) died among patients with neurological affection while in patients without neurological affection only 13 patients (26.0%) died ($p = 0.001$) suggesting that neurological manifestations are independent predictor of mortality [OR (95% CI): 0.35 (0.14–0.88), p = 0.025] [13].

On the other hand, psychiatric manifestations associated with COVID-19 infection include delirium [14], mood, psychotic and anxiety disorders [15], and stress, adjustment and sleep disorders [16].

According to [15], hospitalized COVID-19 patients showed intracranial hemorrhage in 1.3%, ischemic stroke 4.38%, Guillain–Barré syndrome (GBS) 0.22%, encephalitis 0.24%, mood disorder 14.7%, anxiety disorder 16.4%, and psychotic disorder 2.9%.

An observational cross-sectional study was conducted on 203 COVID-19 patients who attended the COVID-19 outpatient clinic in Kasr Al-Ainy hospital, Egypt, and reported that most of the patients had extremely severe depression, anxiety, and stress (65%, 77.8% and 48.3%, respectively), while insomnia was moderate to severe in 36% of the sample. Anxiety, stress, and depression were positively correlated with insomnia severity index score [17].

There are currently not enough data regarding prevalence of neurological and psychiatric manifestations among Egyptian hospitalized COVID-19 patients.

We aimed in this study to determine neuropsychiatric manifestations in COVID-19 hospitalized patients and to find out possible sociodemographic and clinical risk factors.

Methods

A cross-sectional observational study conducted at Ain Shams university isolation hospitals during the period from June 2021 to August 2021 and included 110 hospitalized COVID-19 patients. The study was approved by the Ethical Committee of faculty of medicine, Ain Shams University, Egypt. The research was completed in accordance with Helsinki Declaration. We included hospitalized Egyptian patients who were positive COVID-19 RT-PCR. Patients who were COVID-19 RT-PCR test negative during examination or those who refused to sign the informed consent were excluded.

The researcher had interviewed patients presented with COVID-19 infection and admitted at Ain Shams university isolation hospitals (ICU, intermediate care unit or ward). ICU admission criteria include oxygen requirements equal or superior to 6–8 l/min to reach a peripheral oxygen saturation ≥ 90–92%, respiratory failure, shock, acute organ dysfunction, and patients at high risk for clinical deterioration [18]. Then the researcher applied the following: careful history taking from patients or from their doctors, full neurological examination, COVID-19 severity criteria scoring system, MMSE (*Mini-Mental State Examination*), SCID1 (*Structured Clinical Interview for DSM-IV)* questionnaire and recording neuroimaging and laboratory tests results (including creatinine, AST, ALT, bilirubin, D-dimer, LDH, CRP, serum ferritin) done to the patient if available to confirm diagnoses.

A short-predesigned sheet including age, gender, education, residency, occupation (health care worker or not), past and current general medical history, past and current psychiatric history, clinical symptomatology of COVID infection, place of admission (ICU, intermediate care unit or ward), duration since admission.

COVID-19 severity criteria scoring system [19, 20]**:** It classifies COVID-19 patients into 4 categories; asymptomatic to mild, moderate, severe and critical: (1) asymptomatic to mild patients may be asymptomatic or have common cold-like symptoms; (2) moderate patients have a cough and fever (≥ 37.5 °C); (3) severe patients have suspected severe pneumonia, that is, a cough and ≥ 38 °C fever lasting over 3 days; and (4) critical patients have suspected critical pneumonia if they have had shortness

of breath for over 1 day and a respiratory rate of 30/min or over.

Structured neurological examination sheet designed by Ain Shams University hospital neuropsychiatry department. We defined neurological problems in the context of COVID-19 as the following: Stroke: we considered stroke in patients with acute onset of a vascular insult. This insult can be diagnosed using CT or MRI. Encephalitis: we defined encephalitis as an altered mental status of more than 24 h. The presence of compatible acute lesions on brain MRI and CSF findings is also diagnostic. Seizures and/or focal neurological signs in the absence of encephalitis are diagnostic. Guillain–Barré syndrome: we defined Guillain–Barré syndrome (GBS) according to the established diagnostic criteria. We defined headache according to The International Classification of Headache Disorders 3rd Edition (ICHD-3).

Mini-Mental State Examination: [21], the Arabic version [22]. A short, standardized form was devised for the serial testing of the cognitive mental state in patients on a neurogeriatric ward, as well as for consecutive admission to a hospital. It was found to be quick, easy to use, and acceptable to patients and testers. The used Arabic version was translated by [22]. Furthermore, according to [23], using the Mini-Mental State Examination to screen for delirium showed an acceptable sensitivity of 88% with a specificity of 54%.

The Structured Clinical Interview for DSM-IV Axis-I Disorders (SCID-I) [24]: the Structured Clinical Interview for DSM-IV Axis-I Disorders (SCID-I) is a clinician-administered, semi-structured interview for use with psychiatric patients or with non-patient community subject, who are undergoing evaluation for psychopathology. The SCID-I was developed to provide broad coverage of psychiatric diagnosis according to DSM-IV. It was designed to be more efficient and simpler to use than other existing instruments and, consequently, to require less time for administration. It was done to demonstrate past co-morbidities of these disorders and to exclude current co-morbidities [24]. It took 30 min in average to be applied.

All data were recorded, and statistical analyses were carried out using the statistical package for the social sciences (SPSS, 25th version). The results were tabulated, grouped, and statistically analyzed using the suitable statistical parameters. For description analysis, data were expressed as mean values and SD for parametric numerical data, while median and interquartile range (IQR) for non-parametric numerical data, and frequency and percentage of non-numerical data. We also used the student T test to assess the statistical significance of the difference between two study group means. *Mann–Whitney test (U test)* was used to assess the statistical significance of the difference of a non-parametric variable between two study groups. *Chi-square test* was used to examine the relationship between two qualitative variables. *Fisher's exact test* was used to examine the relationship between two qualitative variables when the expected count is less than 5 in more than 20% of cells. For all tests, a significance level of P less than 0.05 was predetermined. P value was used to indicate the level of significance (P40.05: insignificant; P 0.05: significant).

Results

A total of 158 patients hospitalized in Ain Shams university isolation hospitals were examined by the researcher, 48 of them were excluded due to having negative RT-PCR on time of examination. The remaining 110 participants had mean age of 56 ± 18 years old, most of the study sample was illiterate, unemployed, tobacco smokers and living in urban areas. 61% of the sample had past medical history of chronic illnesses, with the most common being hypertension followed by diabetes mellitus. Most of the study sample was of severe to moderate infection severity. With regard to place of admission, most of the study sample was admitted at intermediate care unit (IMCU), followed by ward group then intensive care unit (ICU). The rest of clinical characteristics of the sample are shown in Table 1.

Moving to the prevalence of neurological manifestations, 75.5% of the study participants had neurological manifestations, central nervous system manifestations seen in 62.7% while peripheral nervous system manifestations seen in 45.5% of the sample. The most common neurological manifestations seen were headache (50.9%), hypogeusia (24.5%), hyposmia, paresthesia (23.6% each) and coma (15.5%), as shown in Fig. 1. After exclusion of 17 patients who could not be examined by MMSE due to being aphasic or in coma, psychiatric manifestations were seen in (61.5%) out of the remaining 91 patients. The most prevalent psychiatric disorders were delirium (30.8%), depression (19%), and adjustment disorder (17.5%), as shown in Fig. 2.

Upon assessing the characteristics of headache, tension headache was the most common type (62.5%), followed by migraine (30.4%), then headache of increased intracranial tension (5.4%) and sinus headache (1.8%). Moving to types of seizures seen, the most common type was generalized tonic clonic seizures (77.8%) followed by focal seizures (22.2%).

The current study showed that factors affecting occurrence of neurological manifestations include hypertension (*P*-value = 0.011), COVID-19 severity (*p*-value = 0.022), place of admission (p-value = 0.002), having myalgia, dyspnea or fever on presentation (p-value = 0.006, 0.016 and 0.036, respectively), and

Table 1 Sociodemographic and clinical data of the study sample

	Mean / n	SD / %
Age	55.96	17.89
Gender		
Male	54	49.1%
Female	56	50.9%
Residency		
Rural	50	45.5%
Urban	60	54.5%
Education		
Illiterate	63	57.3%
Educated	47	42.7%
Employment		
Unemployed/housewife	59	53.6%
Employed	51	46.4%
Substance use		
No	107	97.3%
Yes	3	2.7%
Tobacco smoking		
No	79	71.8
Yes	31	28.2%
Past medical history of chronic illnesses		
No	43	39%
Yes	67	61%
HTN		
No	58	52.7%
Yes	52	47.3%
DM		
No	69	62.7%
Yes	41	37.3%
Dyslipidemia		
No	95	86.4%
Yes	15	13.6%
ISHD		
No	91	82.7%
Yes	19	17.3%
Chronic kidney disease		
No	103	93.6%
Yes	7	6.4%
Past history of psychiatric illness		
No	105	95.5%
Yes	5	4.5%
Duration since admission till the time of examination in days	10.31	8.70
COVID-19 severity		
Asymptomatic with positive RT-PCR	2	1.8%
Mild	6	5.5%
Moderate	38	34.5%
Severe	50	45.5%
Critical	14	12.7%
Place of admission		
Ward	32	29.1%
IMCU	50	45.5%
ICU	28	25.5%
Fever		
No	28	25.5%
Yes	82	74.5%
Cough		
No	26	23.6%
Yes	84	76.4%
Dyspnea		
No	26	23.6%
Yes	84	76.4%
Diarrhea		
No	95	86.4%
Yes	15	13.6%
Myalgia		
No	79	71.8%
Yes	31	28.2%
Temperature	37.98	0.75
Heart rate	89.59	14.34
SBP	126.36	16.18
DBP	74.36	9.34
RR	22.94	5.47
SO2	90.25	6.51
TLC	8.83	4.23
LY	1.00	0.78
PLT	240.24	111.05
HGB	11.95	2.25
Creatinine	1.15	1.14
AST	51.91	58.04
ALT	56.65	61.25
Total bilirubin	0.68	0.42
D-dimer	15.69	88.06
LDH	359.83	203.11
CRP	84.28	73.26
Max serum ferritin	1084.27	963.29

SD standard deviation, *HTN* hypertension, *DM* diabetes mellitus, *ISHD* ischemic heart disease, *IMCU* intermediate care unit, *ICU* intensive care unit, *SBP* systolic blood pressure, *DBP* diastolic blood pressure, *RR* respiratory rate, *SO2 TLC* total leukocytic count, *LY* lymphocytic count, *PLT* platelet, *HGB* hemoglobin, *AST* aspartate transaminase, *ALT* alanine transaminase, *LDH* lactate dehydrogenase level, *CRP* C-reactive protein

having high levels of LDH and ALT (p-value = 0.014 and 0.01, respectively), while other clinical and sociodemographic factors are not statistically significant as shown in Table 2.

In regard to factors affecting occurrence of psychiatric manifestations, the current study showed that

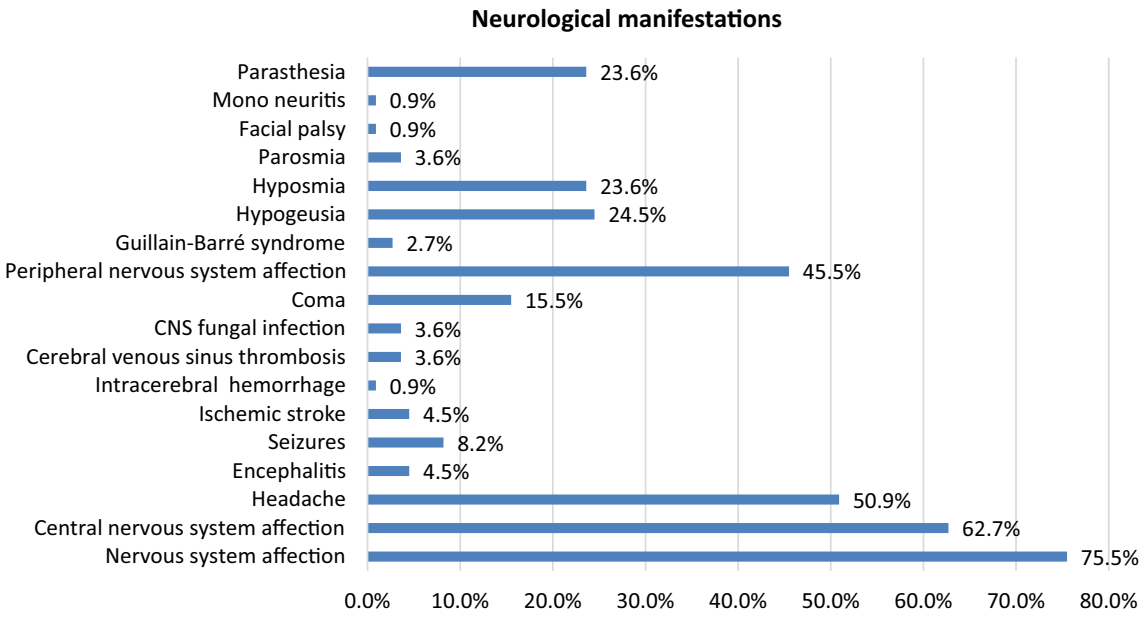

Fig. 1 Shows prevalence of neurological manifestations in the study sample **CNS central nervous system*

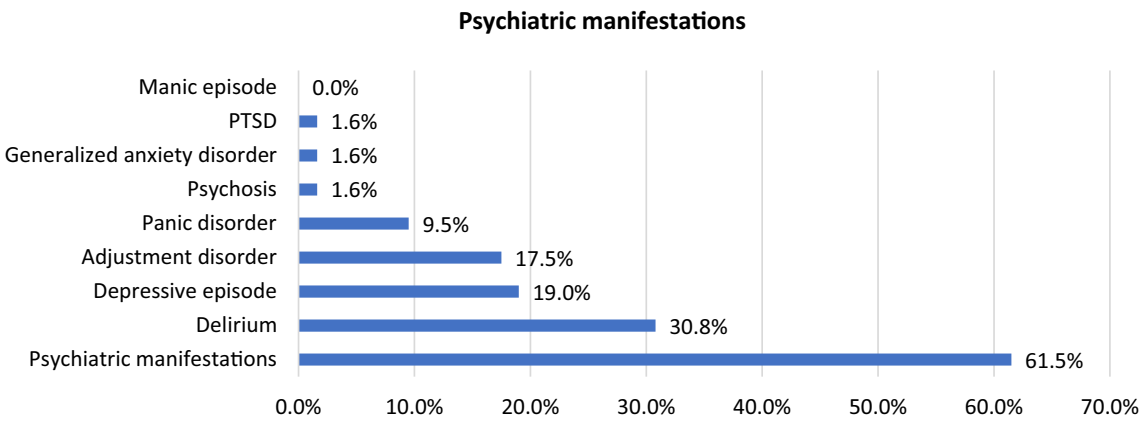

Fig. 2 Shows *prevalence of psychiatric manifestations in the sample of patients. *PTSD post-traumatic stress disorder*

leukocytosis is associated with higher occurrence of psychiatric manifestations (p-value = 0.039). No significant statistical correlation was seen with other sociodemographic and clinical characteristics screened for among the study sample, despite higher percentage of psychiatric disorders among female patients (p-value = 0.569), living in urban areas (p-value = 0.577) with comorbid ischemic heart disease (p-value = 0.093), who were admitted in ward (p-value = 0.197), as shown in Table 2.

Regarding factors affecting COVID-19 severity include patient's age (p-value = 0.019), having fever, dyspnea (p-value = < 0.001, each), cough and diarrhea (p-value = 0.002 and 0.008, respectively), having high body temperature, tachypnea, tachycardia, hypoxia (p-value = < 0.001, each), lower diastolic blood pressure (p-value = 0.014), as shown in Table 2.

It was found that COVID-19 severity is a significant risk factor for developing neurological manifestations among our sample of COVID-19 patients (p-value = 0.002). Thus, patients with severe and critical COVID-19 infection and patients admitted to IMCU and ICU have higher risk to develop neurological manifestations, as shown in Table 3. However, developing psychiatric manifestations is statistically not significantly related to COVID-19 infection severity with (p-value = 0.1743).

Table 2 Correlation between sociodemographic and clinical data, and neurological, psychiatric manifestations and COVID-19 severity

Factors	P-value for neurological manifestations	P-value for psychiatric manifestations	P-value for *COVID-19 severity*
Age	0.183	0.611	0.019
Gender	0.059	0.569	0.576
Residency	0.442	0.577	0.067
Education	0.836	0.679	0.498
Employment	0.263	0.989	0.211
Substance use	0.267	0.326	0.594
Health care worker	1.00	1.00	1.00
HTN	0.011	0.857	0.09
DM	0.16	0.46	0.297
Dyslipidemia	0.351	0.84	0.871
ISHD	0.396	0.093	0.297
Chronic kidney disease	0.191	0.714	0.495
Past history of psychiatric illness	0.094	1.00	0.585
Duration since admission	0.681	0.859	
COVID-19 severity	0.022	0.173	
Place of admission	0.002	0.197	
Fever	0.036	0.445	< 0.001
Cough	0.399	0.215	0.002
Dyspnea	0.016	0.429	< 0.001
Diarrhea	0.518	0.189	0.008
Myalgia	0.006	0.45	0.709
TLC	0.543	0.039	0.072
LY	0.183	0.308	0.678
PLT	0.749	0.599	0.014
HGB	0.19	0.544	0.365
Creatinine	0.405	0.964	0.026
AST	0.605	0.258	0.677
ALT	0.01	0.988	0.566
Total bilirubin	0.125	0.787	0.308
D-dimer	0.978	0.599	0.205
LDH	0.014	0.952	0.037
CRP	0.721	0.867	0.565
Serum ferritin	0.126	0.548	0.423
Body temperature			< 0.001
Heart rate			< 0.001
SBP			0.145
DBP			0.014
RR			< 0.001
SO2			< 0.001

HTN:hypertension, *DM*:diabetes mellitus, *ISHD*:ischemic heart disease, *TLC*:total leukocytic count, *LY*:lymphocytic count, *PLT* platelet, *HGB* hemoglobin, *AST* aspartate transaminase, *ALT* alanine transaminase, *LDH* lactate dehydrogenase level, *CRP* C-reactive protein, *SBP* systolic blood pressure, *DBP* diastolic blood pressure, *RR* respiratory rate, *SO2* oxygen saturation

Discussion

According to previous studies, COVID-19 infection is associated with higher neurological and psychiatric manifestations through neuroinvasion directly by the virus via peripheral nerves, olfactory bulb or systemic circulation, or indirectly via immune response precipitating neuroinflammation as well as psychological effects of unpredicted social and health measures such as quarantine, self-isolation and disruption of personal and social healthcare and lifestyle [19, 25, 26].

Table 3 Correlation between neurological manifestations and COVID-19 severity in the study sample

	Neurological manifestations		OR (95% CI)	Test of significance		
	No	Yes				
	Median (IQR) n (Row %)	Median (IQR) n (Row %)		Value	p-value	Sig
COVID-19 severity						
Asymptomatic	0 (0)	2 (100)		Fisher's exact test	0.022	S
Mild	3 (50)	3 (50)				
Moderate	15 (39.47)	23 (60.53)				
Severe	7 (14)	43 (86)				
Critical	2 (14.29)	12 (85.71)				

IQR interquartile range, *OR* odds ratio, *CI* confidence interval

P value < 0.05: significant

The current study showed higher prevalence rates of neurological manifestations (75.5%) versus 36.4%and 46% in [5] and [27] studies, respectively. In comparison to previous studies done during the first wave of the pandemic, the current study showed almost equal or higher prevalence of altered mental status 40.9% versus 31.8% in [6], stroke 4.5% versus 4.6% in [28], intracranial hemorrhage 0.9% versus 0.5% in [28], cerebral venous sinus thrombosis (CVST) 3.6% versus 3.5% in [12], encephalitis 4.5% versus 3.3% in [27], seizure 8.2% versus 2% in [5], CNS fungal infection 4 cases in 2 months (3.6%) versus 15 cases during 6 months as described by [29], and Guillain–Barré syndrome 2.7% versus 0.1% in [30]. This may be because of the different viral variants between the two waves or because of the preformed immunity toward the virus in the second wave causing more severe cytokines storm and higher immune reaction causing more neurological manifestations [4].

The definite mechanisms for these disorders are still under research, but previous studies reported that COVID-19 patients have exaggerated vascular risk factors, proinflammatory, a prothrombotic state, electrolyte disturbance, multiple drugs use, and immune suppressive drugs [31, 32].

Our study reported headache in 50.9% of the participants versus 37.7% and 13.1% reported by [6]and [5], respectively. [33] study and our study showed that tension headache was the commonest type of headache followed by migraine like headache. Studies suggested fever, hypoxia, and dehydration as causes of headache, in addition to trigemino-vascular system invasion by the virus [34].

Encephalitis resembled 4.5% of our study participants. According to [11], CSF analysis of these patients may be normal or shows pleiocytosis. Moreover, CSF PCR for SARS-CoV-2 is found negative for most of the cases.

COVID-19 causes intracranial hemorrhage in different sites as in addition to [35] and [36] reporting lobar intraparenchymal hemorrhages, subdural hemorrhage and subarachnoid hemorrhage, we reported intraventricular hemorrhage. Compatible with our findings [37] reported that cerebrovascular disorders were more prevalent in the COVID-19 pandemic. Surprisingly, compared to prior times, individuals with autoimmune-mediated neurological diseases had higher hospitalization rates than those with other neurological disorders.

The current study showed that neurological manifestations are more common in elder patients with medical co-morbidities such as hypertension, severely and critically infected patients, patients with fever and dyspnea on presentation, and those admitted to IMCU or ICU which is compatible with [30] *and* [15] studies. This can be attributed to the presence of high viral loads in already immunologically exhausted victims, and they are at risk for infections, electrolyte disturbances, and hypercoagulable state due to immobilization [6]; [27]. Also, this comes in agreement with an Egyptian study which showed that patients with neurological affection are significantly older (54.7 ± 12.8 versus 44.2 ± 18.8 years, p = 0.002) with significantly higher BMI (32.4 ± 7.8 versus 26.3 ± 6.5 kg/m^2, p < 0.001) [13].

The current study showed higher prevalence rates of psychiatric manifestations (61.5%) versus 22.5% and 55.7% in [38] and [7] studies, respectively.

Our study showed higher or almost equal prevalence of delirium 30.8% versus 24.3% in [39], depression 19% versus 14.7% in [15], psychotic disorder 1.6% versus 1.4% in [15] and panic disorder 9.5%versus 4.3% in [40], as our study was done on hospitalized patients who are more prone to suffer from psychiatric disorders especially patients in ICU with severe infection [8].

However, it showed lower prevalence of adjustment disorder17.5% versus 27% in [16], generalized anxiety disorder 1.6% versus 4.5% in [40] and post-traumatic stress disorder 1.6% versus 7% in [41]. This may be because our study was done during the acute infection phase and the criteria of diagnosis of some of these disorders are affected by time [24].

However, a study carried out by [42] where a total of 382 participants with mean age of 41.5 ± 15.0 years old, of whom 72.5% were males were included in the study. 91.6% of participants had all the three studied psychological disorders; depression, anxiety, and stress with most of participants had either severe or extremely severe conditions (13.9 and 75.7 for anxiety, 22.8 and 46.3% for depression, 38.5 and % 19.6 for stress, respectively).

Also a study held in Kasr-Al-Ainy outpatient clinic found that the majority of the sample had extremely severe depression, anxiety and stress (65%, 77.8% and 48.3%, respectively) while insomnia was moderate to severe in 36% of the sample.

This wide range of prevalence can be explained by many factors, starting with the assessment tools, where many studies had different cutoff points for their tools. In addition, COVID-19 related factors should be considered, like the time of assessment (first wave was associated with more stress), the severity of the illness, and the restrictive measures (more measures in winter are associated with more insomnia). Another aspect is the healthcare system in each country, where better systems can detect milder or earlier cases and have better outcomes [43].

In contrast to neurological manifestations, psychiatric manifestations in our study showed no statistical correlation with sociodemographic and clinical data of the patients except leukocytosis (p-value = 0.039) which is partially compatible with previous studies [44]. This shows that psychological and social factors such as fear of death, loneliness, uncertainty about the treatment and coronaphobia play a great role in developing psychiatric manifestations in these patients [45].

However, although both our study and [16] showed similar mean age among patients with psychiatric diagnoses and patient without (55.5 and 54.9 years, respectively), the latter showed that delirium was associated with older age (73.8 ± 15 years). Moreover, [46] reported that COVID-19 patients with depressive or adjustment disorders shows higher IL-6 and CRP levels which means that inflammation associated with COVID-19 infection plays a major role in developing depressive or adjustment disorders. Also, ICU survivors and patients receiving mechanical ventilation show high rates of anxiety, depression, and PTSD [47].

Our study shows that COVID-19 infection is more severe in elder patients, patients presenting with fever, cough or dyspnea and those with tachypnea, tachycardia or hypoxia. However, previous studies reported other factors such as gender, medical co-morbidities as hypertension, leukocytosis, impaired kidney and liver functions [5, 48].

Reliable estimates of neurological and psychiatric prevalence during COVID-19 patients' hospitalization are important for informing efforts to prevent, treat, and identify causes of these disorders especially in light of recent work revealing a high prevalence of neurological and psychiatric disorders among them.

Although adverse events are not necessarily predictable or preventable, strategies to change or decrease their impact on the COVID-19 patients are available. So, screening for neurological and psychiatric disorders during hospitalization of COVID-19 patients is mandatory for shortening the duration of hospital stay along with improving the outcome and post-infection quality of life. Intervention studies are needed, as screening tools, virtual support groups, family visits through video calls, and treatment protocols adjustment.

The limitation of this study was that it took a snap-shot view of the studied outcomes; therefore, it is difficult to be generalized as there might be other factors affecting the results. Second, including only a small sample size of hospitalized patients in a tertiary health care center to decrease risk of spread of the infection to investigator and others, limits generalization of its findings. Third, high percentage of patients had altered mental status on time of examination (40.9%), hindering further psychiatric assessment of them.

We did not consider medications used in management of COVID-19 patients as a confounding factor for the underlying neurological and psychiatric manifestations due to the over crowdedness of the isolation hospitals and the burn out of health care workers at that time which hindered comprehensive data collection.

Finally, studying patients during isolation where they are still infectious along with the affordability of the hospital hindered the performance of some needed investigations to confirm some of the diagnoses such as electroencephalogram (EEG), nerve conduction velocity (NCV), MRI brain and CSF analysis.

Conclusion

There is high evidence that prevalence of neurological and psychiatric manifestations is high in COVID-19 hospitalized patients. Multiple sociodemographic and medical factors affect their prevalence. Second wave of the pandemic is associated with higher prevalence of neurological and psychiatric disorders. So, early

detection and treatment of such disorders improve the quality of life of COVID-19 survivors. It is crucial to increase awareness of the problem of psychiatric and neurological consequences of COVID-19 infection and to screen for COVID-19 infection in patients with neurological or psychiatric disorders even without its common respiratory symptoms.

Abbreviations

ALT	Alanine transaminase
AST	Aspartate transaminase
CNS	Central nervous system
COVID-19	Corona virus disease 2019
CoVs	Corona viruses
CRP	C-reactive protein
CT	Computed tomography
CVS	Cerebrovascular stroke
CVST	Cerebral venous sinus thrombosis
DM	Diabetes mellitus
DSM-V	Diagnostic and statistical manual-fifth edition
HGB	Hemoglobin level
HTN	Hypertension
ICU	Intensive care unit
ICHD-3	International classification of headache disorders 3rd edition
IL	Interleukin
IMCU	Intermediate care unit
ISHD	Ischemic heart disease
LDH	Lactate dehydrogenase level
LY	Lymphocytic count
mmHg	Millimeters of mercury
MRI	Magnetic resonance imaging
PLT	Platelet count
PNS	Peripheral nervous system
PTSD	Post-traumatic stress disorder
RT-PCR	Reverse transcriptase polymerase chain reaction
SARS-CoV-2	Severe acute respiratory syndrome corona virus 2
SCID I	Structured clinical interview for DSM-IV
SD	Standard deviation
SPO2	Peripheral oxygen saturation
SPSS	Statistical package for social sciences
TLC	Total leukocytic count

Acknowledgements
The authors would like to thank medical staff in Ain Shams University Hospitals for their kind help.

Author contributions
NN: main idea, revised paper; MA: collect clinical data, data analysis, write paper; NN, FF, RH, MA and ER had access full responsibility for all data associated with this study; ER wrote the manuscript. All authors contributed to reviewing and editing the manuscript. All authors read and approved the final manuscript.

Funding
This study had no funding from any resource.

Availability of data and materials
The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
The study was performed in accordance with the Declaration of the Helsinki. It was approved by the Ethics Committee of Faculty of Medicine, Ain Shams University (29 June 2021); each participant signed a written informed consent.

Consent for publication
Not applicable.

Competing interests
All authors declare no conflict of interest.

Received: 16 December 2023 Accepted: 20 July 2024
Published online: 12 September 2024

References

1. Zhu N, Zhang D, Wang W, Li X, Yang B, Song J, et al. A novel coronavirus from patients with pneumonia in China, 2019. N Engl J Med. 2020;382(8):727–33.
2. Situation Report-26 SITUATION IN NUMBERS total and new cases in last 24 hours China Very High Regional Level High Global Level High.
3. Karia R, Gupta I, Khandait H, Yadav A, Yadav A. COVID-19 and its modes of transmission. SN Compr Clin Med. 2020. https://doi.org/10.1007/s42399-020-00498-4.
4. Orsini A, Corsi M, Santangelo A, Riva A, Peroni D, Foiadelli T, et al. Challenges and management of neurological and psychiatric manifestations in SARS-CoV-2 (COVID-19) patients. Neurol Sci. 2020. https://doi.org/10.1007/s10072-020-04544-w.
5. Mao L, Jin H, Wang M, Hu Y, Chen S, He Q, et al. Neurologic manifestations of hospitalized patients with coronavirus disease 2019 in Wuhan. China J Neurol. 2020;77(6):683–90.
6. Liotta EM, Batra A, Clark JR, Shlobin NA, Hoffman SC, Orban ZS, et al. Frequent neurologic manifestations and encephalopathy-associated morbidity in Covid-19 patients. Ann Clin Transl Neurol. 2020;7(11):2221–30.
7. Mazza MG, de Lorenzo R, Conte C, Poletti S, Vai B, Bollettini I, et al. Anxiety and depression in COVID-19 survivors: role of inflammatory and clinical predictors. Brain Behav Immun. 2020;1(89):594–600.
8. Taquet M, Luciano S, Geddes JR, Harrison PJ. Bidirectional associations between COVID-19 and psychiatric disorder: retrospective cohort studies of 62 354 COVID-19 cases in the USA. Lancet. 2021;8(2):130–40.
9. Meppiel E, Peiffer-Smadja N, Maury A, Bekri I, Delorme C, Desestret V, et al. Neurologic manifestations associated with COVID-19: a multicentre registry. Clin Microbiol. 2021;27(3):458–66.
10. Hameed S, Wasay M, Soomro BA, Mansour O, Abd-Allah F, Tu T, et al. Cerebral Venous thrombosis associated with COVID-19 infection: an observational. Multicenter Study Cerebrovasc Dis Extra. 2021;11(2):55–60.
11. Ellul MA, Benjamin L, Singh B, Lant S, Michael BD, Easton A, et al. Neurological associations of COVID-19. Lancet Neurol. 2020;19:767–83.
12. Azab MA, Azzam AY, Salem AE, Reda A, Hassanein SF, Sabra M, et al. Neurological problems in the context of COVID-19 infection in Egypt. A Multicenter Retrospective Analysis Interdiscip Neurosurg. 2021;1:26.
13. Essmat A. Neurological manifestations in Egyptian Covid-19 patients. AIMJ. 2021. https://doi.org/10.21608/aimj.2021.49994.1352.
14. Rebora P, Rozzini R, Bianchetti A, Blangiardo P, Marchegiani A, Piazzoli A, et al. Delirium in patients with SARS-CoV-2 infection: a multicenter study. J Am Geriatr Soc. 2021;69(2):293–9.
15. Taquet M, Geddes JR, Husain M, Luciano S, Harrison PJ. 6-month neurological and psychiatric outcomes in 236 379 survivors of COVID-19: a retrospective cohort study using electronic health records. Lancet Psychiat. 2021;8(5):416–27.
16. Turan Ş, Poyraz BÇ, Aksoy Poyraz C, Demirel ÖF, Tanrıöver Aydın E, Uçar Bostan B, et al. Characteristics and outcomes of COVID-19 inpatients who underwent psychiatric consultations. Asian J Psychiatr. 2021;1:57.
17. Atef M, Abdel-Haleem H, Abdalaziz RA, Ramadan A, Hegazy MT, El-Korashy RIM, et al. Psychiatric symptoms screening among patients suffering from COVID-19 infection attending Kasr-Al-Ainy outpatient clinic: a cross sectional study. Microbes Infect. 2023;4(3):741–53.
18. Hajjar LA, da Costa IBS S, Rizk SI, Biselli B, Gomes BR, Bittar CS, et al. Intensive care management of patients with COVID-19: a practical approach. Ann Intensive Care. 2021. https://doi.org/10.1186/s13613-021-00820-w.
19. Clinical management [Internet]. 2021. https://apps.who.int/iris/bitstream/handle/10665/338871/WHO-2019-nCoV-clinical-web_annex-2021.1-eng.pdf

20. Kim SW, Lee KS, Kim K, Lee JJ, Kim JY. A brief telephone severity scoring system and therapeutic living centers solved acute hospital-bed shortage during the COVID-19 outbreak in Daegu. Korea J Korean Med Sci. 2020. https://doi.org/10.3346/jkms.2020.35.e152.
21. Folstein MF, Folstein SE, Mchugh PR. 1975 Mini-mental state" A practical method for grading the cognitive state of patients for the clinician Related papers "mini-mental state" a practical method for grading the cognitive state of patients for the +clinician*. J gsychiaf Res Pergamon Press 12
22. El-Okl M. prevalence of Alzheimer dementia and other causes of dementia in Egyptian elderly MD thesis Ain Shams University faculty of medicine Cairo. [Cairo] 2002.
23. Ringdal GI, Ringdal K, Juliebø V, Wyller TB, Hjermstad MJ, Loge JH. Using the mini-mental state examination to screen for delirium in elderly patients with hip fracture. Dement Geriatr Cogn Disord. 2012;32(6):394–400.
24. First MB, Spitzer RL, Gibbon M, Williams JBW. The structured clinical interview for. J. Pers. Disord: The Guilford Press Widiger and Frances; 1995.
25. Wu Z, McGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in china: summary of a report of 72314 cases from the Chinese center for disease control and prevention. JAMA. 2020;323:1239–42.
26. Dantzer R. Neuroimmune interactions: from the brain to the immune system and vice versa. Physiol Rev. 2018;98:477–504.
27. Nersesjan V, Amiri M, Lebech AM, Roed C, Mens H, Russell L, et al. Central and peripheral nervous system complications of COVID-19: a prospective tertiary center cohort with 3-month follow-up. J Neurol. 2021;268(9):3086–104.
28. Li Y, Li M, Wang M, Zhou Y, Chang J, Xian Y, et al. Acute cerebrovascular disease following COVID-19: a single center, retrospective, observational study. Stroke Vasc Neurol. 2020;5(3):279–84.
29. Fouad YA, Abdelaziz TT, Askoura A, Saleh MI, Mahmoud MS, Ashour DM, et al. spike in rhino-orbital-cerebral mucormycosis cases presenting to a tertiary care center during the COVID-19 pandemic. Front Med. 2021;28:8.
30. Frontera JA, Sabadia S, Lalchan R, Fang T, Flusty B, Millar-Vernetti P, et al. A prospective study of neurologic disorders in hospitalized patients with COVID-19 in New York City. Neurology. 2021;96(4):e575–86.
31. Bhatia R, Pedapati R, Komakula S, Padma Srivastava MV, Vishnubhatla S, Khurana D. Stroke in coronavirus disease 2019: a systematic review. J Stroke Korean Stroke Society. 2020;22:324–35.
32. Sharma S, Grover M, Bhargava S, Samdani S, Kataria T. Post coronavirus disease mucormycosis: a deadly addition to the pandemic spectrum. J Laryngol Otol. 2021;135(5):442–7.
33. López JT, García-Azorín D, Planchuelo-Gómez Á, García-Iglesias C, Dueñas-Gutiérrez C, Guerrero ÁL. Phenotypic characterization of acute headache attributed to SARS-CoV-2: An ICHD-3 validation study on 106 hospitalized patients. Cephalalgia. 2020;40(13):1432–42.
34. Caronna E, Pozo-Rosich P. Headache as a symptom of COVID-19: narrative review of 1-year research, vol. 25. Current Pain and Headache Reports: Springer; 2021.
35. Rothstein A, Oldridge O, Schwennesen H, Do D, Cucchiara BL. Acute cerebrovascular events in hospitalized COVID-19 patients. Stroke. 2020. https://doi.org/10.1161/STROKEAHA.120.030995.
36. Siegler JE, Cardona P, Arenillas JF, Talavera B, Guillen AN, Chavarría-Miranda A, et al. Cerebrovascular events and outcomes in hospitalized patients with COVID-19: The SVIN COVID-19 multinational registry. IJS. 2021;16(4):437–47.
37. Sayed SS, El-Khatib MES, Abdelghaffar M, Metwally FEO, ElSary AY, Daker LI. The pattern of neurological disorders requiring hospitalization during the COVID-19 era: an experience from Fayoum University Hospital Egypt. Egypt J Neurol Psych. 2024. https://doi.org/10.1186/s41983-024-00831-x.
38. Nalleballe K, Reddy Onteddu S, Sharma R, Dandu V, Brown A, Jasti M, et al. Spectrum of neuropsychiatric manifestations in COVID-19. Brain Behav Immun. 2020;1(88):71–4.
39. Shao SC, Lai CC, Chen YH, Chen YC, Hung MJ, Liao SC. Prevalence, incidence and mortality of delirium in patients with COVID-19: a systematic review and meta-analysis. Meta-Analysis. 2021. https://doi.org/10.1093/ageing/afab103.
40. Alonso J, Vilagut G, Mortier P, Ferrer M, Alayo I, Aragón-Peña A, et al. Mental health impact of the first wave of COVID-19 pandemic on Spanish healthcare workers: a large cross-sectional survey. Rev Psiquiatr Salud Ment. 2021;14(2):90–105.
41. Liu N, Zhang F, Wei C, Jia Y, Shang Z, Sun L, et al. Prevalence and predictors of PTSS during COVID-19 outbreak in China hardest-hit areas: gender differences matter. Psychiatry Res. 2020;1:287.
42. Gad BK, Arafa MA, Attia AF, Farahat AH, Abdou MS. Depression, anxiety, and stress among COVID-19 patients in South Sinai, Egypt: prevalence and associated predictors. Sci Rep. 2023. https://doi.org/10.1038/s41598-023-45775-z.
43. Morin CM, Bjorvatn B, Chung F, Holzinger B, Partinen M, Penzel T, et al. Insomnia, anxiety, and depression during the COVID-19 pandemic: an international collaborative study. Sleep Med. 2021;1(87):38–45.
44. Li X, Cai Q, Jia Z, Zhou Y, Liu L, Zhou Y, et al. The correlation between mental health status, sleep quality, and inflammatory markers, virus negative conversion time among patients confirmed with 2019-nCoV during the COVID-19 outbreak in China An observational study. Medicine. 2021. https://doi.org/10.1097/MD.0000000000026520.
45. Usher K, Bhullar N, Durkin J, Gyamfi N, Jackson D. Family violence and COVID-19: increased vulnerability and reduced options for support. IJMHN. 2020;29:549–52.
46. Iglesias-González M, Boigues M, Sanagustin D, Giralt-López M, Cuevas-Esteban J, Martínez-Cáceres E, et al. Association of serum interleukin-6 and C-reactive protein with depressive and adjustment disorders in COVID-19 inpatients. Brain Behav Immun Health. 2022;19: 100405.
47. Hendrickson MA, Melton GB, Pitt MB. The review of systems, the electronic health record, and billing. JAMA. 2019;322:115–6.
48. Nazar T, Aziz B, Shabbir B, Saeed F, Nawaz K, Nabeel M. Predictors of disease severity in adult covid-19 patients admitted in mayo hospital, Lahore, Pakistan. JCPSP. 2021;31(6):638–43.

Publisher's Note