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ORIGINAL ARTICLE

Neuro-Psychiatric Manifestations in COVID-19 Recovered Patients

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Abstract

Background: Viral infections of respiratory system affect the central nervous system (CNS), causing a spectrum of psychiatric and neurological disorders. **Aim**: To investigate neuropsychiatric manifestations in patients with COVID-19 RT-PCR positive. **Methods**: 140 consecutive patients of different age groups who were positive for COVID-19 RT-PCR during 12 months were included. Neurological symptoms, MRI findings, and CSF findings were recorded. Subjects were assessed with the Mini Mental State Examination (MMSE)scale, Mental Health Inventory (MHI), Fatigue Impact Scale-5-item Version (MFIS-5). **Results**: Anxiety, Depression and Fatigue are significantly associated with the total score, it was found that Anxiety was significantly associated with Depression and Fatigue was associated with both Anxiety and Depression. **Conclusion**: Patients suffering from COVID-19, mostly suffer from neuropsychiatric manifestations. Attention to the neuropsychiatric consequences of COVID-19 may help in early detection and better management.

Keywords: COVID-19, Depression, Anxiety, Stress.

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Introduction

The World Health Organization has declared the coronavirus disease (COVID-19) a pandemic, on March 11, 2020. More than six million confirmed cases, more than 366,000 fatalities, and more than two million recoveries were reported globally as of May 2020. Physical signs of COVID-19 include fever, chills, lethargy, coughing, breathing problems, coryza, vomiting and diarrhoea, as well as neurological signs including headache and vertigo. Numerous mental and neurological conditions are brought on by respiratory virus infections that have an impact on the central nervous system (CNS).

There are several hypotheses to support why patients with COVID-19 may experience neuropsychiatric manifestations. One such study demonstrated that COVID-19 attacks regions of the cerebral cortex, basal ganglia and midbrain that are closely related to the olfactory bulb after being intracranially injected through the trigeminal or peripheral olfactory nerve [1,2].

From a psychological standpoint, COVID-19 patients may experience emotional disturbances like rage, fear, hysteria, depression, anxiety, and other psychological issues due to the severity of the disease, physical discomfort, loneliness, and psychosocial stress. Release of several inflammatory markers, such as IL-6, IL-12, and tumour necrosis factor alpha and cell-mediated immune activation through them can lead to aetiology of depression. These psychosocial factors can, in turn, compromise innate immunity. Therefore, it can be considered as a common pathogenesis of immune disorders in the infection of COVID-19 and mental disorders [2]. Despite considerable study on the social and psychological

repercussions, it is uncertain how SARS-CoV-2 directly affects the central nervous system and psychological neuroimmunity. A negative association between lymphocyte count, C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), and severity of infection is one piece of evidence pointing to the immune system's involvement in the aetiology of COVID-19 and psychiatric disorders. Antibody levels that fight infection are related to mortality [3].

The high frequency of COVID-19 and its unusually asymptomatic and atypical presentation provide a challenge to the international health community. For the treatment and prevention of COVID-19, like with any pandemic, it is essential to increase our understanding of the demography, transmission mechanisms, clinical manifestations, and complexity of the condition [4]. The current study was conducted to examine neuropsychiatric manifestations in COVID-19 recovered patients due to the paucity of Indian studies in this field.

Materials & Methods

This prospective, cross-sectional study done in a tertiary health care hospital, for a duration of 12 months from January 2021 to December 2021.

Before the study began, the institutional Ethics Committee granted ethical clearance to the study. All subjects provided their written informed consent.

Sample Size

According to a study, prevalence of Neuro-psychiatric manifestations in COVID recovered patients was 10.4% (p)(3) Using the formula, Sample Size = Z 2 * (p) * (1-p)/ c 2, sample size was calculated to be140.

Sample

140 consecutive patients of all age groups and both sex who were positive for COVID-19 RT-PCR, currently recovered and attending OPD of tertiary health care centre formed the study sample. Among these patients those who meet inclusion criteria but not exclusion criteria were taken as cases.

Inclusion Criteria for Cases

COVID-19 RT-PCR positive patients who are symptomatic.

Exclusion Criteria for Cases

Patients with past history of psychiatric disorders or on psychotropic medications were excluded from the study.

Tools Used

Socio-demographic pro-forma: This self-made proforma was used in all patients to record their demographic data, neurological symptoms, MRI findings and CSF results.

Mini Mental State Examination (MMSE): Subjects were assessed with the MMSE scale, which tells the current cognitive status. It has multiple questions which create a total score of 30. Those scoring higher than 23 on MMSE are taken as normal.

Mental Health Inventory (MHI) to find out prevalence of anxiety and depression, behavioral issues and positive effect. In this scale, For Anxiety questions 4,6,11,18 is taken, for Depression questions 2,9,12,14 is taken, for behavior control questions 5,8, 16,17 are taken, for positive effect questions 1,7,13,15 is taken. Each question is scored from 1-6, yielding a total score of 108 [5]. A total MHI score of 67 or more, indicates good mental health and score of 61 or less, indicates poor mental health [5].

Modified Fatigue Impact Scale -5- Item Version (MFIS-5) was applied to find out prevalence of sleep disorders and Fatigue in COVID-19 positive patients. It is a 5-item questionnaire, each question is scored from 0-4, giving a total score of 20 [6].

Procedure

All the patients recovered from COVID-19 and attending post COVID-19 OPD were approached for study. All the patients who met the inclusion and exclusion criteria, were included in the study and a written informed consent was obtained from them. Aim and objective of the study was explained to them. The socio-demographic data sheet was filled and then the MHI and fatigue scale were applied.

Statistical Analysis

The IBM SPSS 20 statistical analysis was used. The Mann-Whitney U test, Pearson's correlation, chi-square test, and t-test were used where required.

Results

In our study, a total of 140 COVID Positive recovered patients were taken, their age ranged from 10–87 years, mean (±SD) was 42.9 (19.25) years. Most of the patients, 64 out of 140 belonged to 20 – 40 years age, remaining 7 were in 0-20 years, 34 were in 20-40 years, 30 were in 60-80 years and 5 were in 80-100 years age group. Among 140 cases, 80 were male and remaining 60 were female. The duration of illness of the cases ranged from 10–21 days, mean (±SD) was 14.18 (3.24).

On Mini Mental State Examination, mean was 28.66, Median was 30, range of scores was 26 – 30. Standard Deviation was 2.47. <1 % patients had abnormal findings in MRI. Among 140 cases, 98-99.9% had an MMSE score between 24 to 30, with majority having a 30/30 score. A total of 44.2 % patients scored a total of more than 67 on MHI, which indicates good mental health in them. In MFIS-5, A maximum score of 20 indicates moderate amount of fatigue on MFIS-5 scale as

this is a screening tool, surprisingly in our study, 99 % patients scored less than 10 which indicates low levels of fatigue in these patients.

The scores of the subjects on MHI and fatigue scale are given in Table 1. Correlations were calculated through Spearman's correlations and a positive correlation was found between anxiety, Depression and Fatigue. This indicated that a higher the levels of anxiety and depression greater would be the fatigue and vice versa (Table 2).

cognitive impairment. This was in agreement to a 10-month long case control study in covid survivors in Italy which reported the mean of MMSE in both cases and control to be in range of 28.1-29.4 [7]. On the contrary, certain studies found the cognitive impairment to be upto 65 % after several weeks in covid recovered patients [8].

More than 99 % showed normal MRI findings which was in agreement to earlier studies who found no discernible differences between COVID-19 patients and healthy controls

Table 1: Scores of recovered COVID-19 patients on Mental Health Inventory and Fatigue

	Mean	SD	Variance	Skewness	Kurtosis
MHI - Total	67.43	11.09	123.2	0.184	-0.91
MHI- Anxiety	31.4	19.4	377.7	1.22	1.56
MHI- Depression	66.54	26.02	677.11	-.596	-0.49
MHI- Behavior Control	66.143	17.76	315.59	-0.048	-1.01
MHI- Positive Affect	63.7	21.08	444.55	-0.191	-0.70
Fatigue	5.70	2.43	5.95	-0.019	-0.25

MHI= Mental Health Inventory; SD=Standard Deviation

Table 2: Spearman's correlations of scores of recovered COVID-19 patients on Mental Health Inventory and fatigue

		MHI total	MHI Anxiety	MHI Depression	MHI Behavior control	MHI Positive affect
MHI-Anxiety	CC	0.821**				
	Sig.	0.000				
MHI-Depression	CC	0.749**	0.556**			
	Sig.	0.000	0.000			
MHI-Behavior	CC	0.035	0.012	0.012		
control	Sig.	0.679	0.890	0.892		
MHI-positive affect	CC	0.147	0.164	0.050	0.055	
	Sig.	0.083	0.052	0.561	0.518	
Fatigue	CC	0.220**	0.170*	0.203*	0.062	0.113
	Sig.	0.009	0.045	0.016	0.464	0.184

CC= Correlation Coefficient; Sig=Sig. [2-tailed)

Discussion

There has been a daily upsurge in cases of COVID-19 in the past two to three years. The public health systems of nations all over the world including India were ill prepared for a pandemic of such global proportions. The primary focus of treatment in COVID-19 infection have always been pulmonary symptoms which contributed to the immediate mortality. However, prevalent literature suggests that these outbreaks have demonstrated that the known and unknown neuropsychiatric symptoms that result from COVID-19 infection can significantly increase the health burden leading to a negative impact on mental health in covid survivors and their quality of life [1].

In this study, the current mental status using MMSE was normal in round 98-99 % of the patients indicating no possible

in total brain volume [7]. <1 % of patients in our study reported neurological manifestations such as acute cerebritis, chronic subdural hematoma, brain abscess and degenerative changes in spine. Contrary to our findings, several studies quote significant brain changes in COVID-19 infection [9-12]. Acute cerebrovascular illness, such as cerebral bleeding, acute ischemic stroke, major vessel occlusion, dural venous sinus thrombosis, etc., may be associated with COVID-19, according to some new reports [13]. Existing literature suggests that the most common brain change found in covid infection was acute stroke whose prevalence varied between 1.9 and 52 percent, with a mean of 22.7 % across studies [13].

In this study 55.8 % of the patients had poor mental health on MHI in subscales of depression, anxiety, positive affect and behavior control and had scores below 67 which was in agreement to an Indian study done on pre and post

psychological intervention in patients suffering from COVID-19. They found out that MHI showed lower scores for Depression, anxiety, positive affect and behavior control. Their scores on MHI improved post intervention in their study [14]. Anxiety and depression were found to be present in 34.5% and 32%, respectively, of covid survivors, according to a study [15]. Another meta-analysis revealed that 47% and 45%, respectively, of COVID-19 patients reported having anxiety and depressed symptoms [16]. Around 99% of patients in this study did not report fatigue on MFIS scale which was contrary to an earlier study done in a study done in Egypt which evaluated fatigue 3 to 4 months post COVID and 64.2% of participants were fatigued and 35.8% didn't show symptoms of fatigue on MFIS scale [17]. This suggests that fatigue is usually visible 3 to 4 months post recovery. With proper psychological intervention, these symptoms can be taken care of, in COVID-19 recovered patients.

Limitations

In our study, small sample size was taken, larger sample size could give better co-relations. In the absence of suitable control group, the study could not compare COVID positive cases with healthy people. Duration of study being one year only, it could be another limitation.

Conclusion

This study focused on the neuropsychiatric signs of fatigue, anxiety, and depression in COVID-19 patients who were recovering from viral infections. In this study, COVID-19 survivors reported elevated levels of anxiety and depression but not fatigue. As neuropsychiatric involvement is linked with a higher risk of morbidity as well as mortality, doctors should be aware of these manifestations in COVID-19 patients. These neuropsychiatric symptoms potential long-term effects are still unknown. Future research in this area will be necessary. Effective patient care for COVID survivors requires early detection, appropriate treatment, and long-term follow-up, and it is necessary to have a better understanding of the COVID-19 consequences.

Conflict of Interest:	All authors declare no COI
Ethics:	There is no ethical violation as it is based on voluntary anonymous interviews
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