

## Neurological manifestations in COVID -19 patients in recovery phase: A retrospective study

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### Abstract

**Background and aims:** The Coronavirus disease 2019 (COVID-19) is a potentially serious condition caused by a novel coronavirus termed as “severe acute respiratory syndrome coronavirus-2. The SARS-CoV-2 virus affects both central and peripheral nervous systems resulting in varied neurological presentations. This study assesses the neurological manifestations in COVID -19 patients in the recovery phase. **Method:** This retrospective study was conducted on 401 patients who were discharged from Government RDBP Jaipuria a hospital Jaipur with COVID negative reverse transcription–polymerase chain reaction (RT-PCR) test for SARS-CoV-2. An individual telephonic interview was conducted after 21-28 days post discharge in post COVID period to assess the neurological manifestations by a self-designed questionnaire. **Results:** In this study conducted from 10<sup>th</sup> September 2020 to 10<sup>th</sup> October 2020, 59 patients refused to participate in the study. So out of 342 patients, 238 (69.60%) were males and 104(30.40%) were females. We found post COVID symptoms with Fatigue - 57.8% ,Myalgia 29% ,Anosmia- 41.5% ,Dysguesia – 35.9% , Headache – 41.0% ,Memory loss 3.2% ,Concentration difficulty – 18.7% ,Sleep disorder – 26.9% ,Psychiatric disorder- 18.12% , 01 patient reported with Right side thigh hematoma and 01 patient with Left side hemiparesis. 48 (14.03%) patients did not reported any of above symptoms, 124(36.25%) patients had one or two symptoms and 174 (58.8%) had three or more persistent symptoms. **Conclusion:** Various neurological presentations occur in the recovery phase of elderly comorbid COVID 19 cases. This recommends a thorough mental evaluation and neurological work up for complete rehabilitation of these patients.

**Keywords:** comorbid, mental evaluation, neurological

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### Introduction

Coronavirus disease 2019 (COVID-19) is a potentially serious condition caused by a novel coronavirus termed as “severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2)”. COVID-19 is clinically characterized by respiratory system involvement. COVID-19 disease was first reported in Wuhan, China, in December 2019, when a series of patients presented with pneumonia of unknown etiology. COVID-19 spread worldwide very rapidly and on March 11, 2020, the World Health Organization officially announced COVID-19 a pandemic. [1] Pathophysiologically , COVID-19 virus targets the angiotensin

converting enzyme via two (ACE-2) receptors which are omnipresent throughout the body, including neural tissues affecting both central and peripheral nervous systems .[2,3] The SARS-CoV-2 virus enters the brain either via a haematogenous route or olfactory system[4].ACE2 receptors are down regulated by the virus leading to endothelial dysfunction with associated hyperinflammation. On-going hyperinflammation and endothelitis causes disruption of the blood-brain barrier, allowing entry of innate immune cells into the brain and further pro-inflammatory cytokine cascades [5,6]. This promotes a hypercoagulable state through mechanisms such as cytokine storm, endothelitis and complement activation. The virus itself causes activation of the coagulation cascade. [7,8]Most patients present with mild flu-like illness. Comorbidities , like diabetes and hypertension, enhance the angiotensin-converting enzyme 2 receptor expression in the brain and neurotropism of the SARS-CoV-2 virus.[9] Neurological complications are frequently reported in severely or critically ill patients with comorbidities like diabetes, chronic obstructive

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pulmonary disease (COPD), cardiovascular diseases (CVD), hypertension, malignancies, HIV, and others.[10]Post-acute COVID-19 seems to be a multisystem disease. After virological recovery, a variety of neurological complications have been reported. COVID -19 patients may present with headache, anosmia,dysgeusia, myalgia, fatigue, lack of concentration, memory loss ,sleep disorder and psychiatric symptoms. The most severe neurological manifestations, altered sensorium ,agitation , delirium, and coma are because of hypoxic and metabolic abnormalities.[2,3]Chang and colleagues[11] described Post COVID-19 Neurological Syndrome (PCNS) in patients with prolonged muscle weakness and other forms of myopathy among SARS-CoV survivors in Hongkong[11].This study was planned to evaluate the neurological manifestations in patients who were discharged from the hospital after recovery from COVID-19. and had a negative reverse transcription–polymerase chain reaction (RT-PCR) test . The objective of this study was to analyze the neurological manifestations in COVID -19 patients in the recovery phase.

**Method**

This retrospective, cross-sectional, observational study was conducted on 401 patients who were discharged from Government

RDBP Jaipuri a hospital Jaipur with COVID negative reverse transcription–polymerase chain reaction (RT-PCR) test for SARS-CoV-2,over a period of one month (Sept 10,2020 to Oct 10,2020) . The demographic profile, risk factors and medical comorbidities of these patients were procured from the hospital medical record . An individual telephonic interview was conducted after 21-28 days post discharge in post COVID period to assess the neurological manifestations by a self designed questionnaire. Approval was obtained from the ethical committee Government RDBP Jaipuri a hospital Jaipur .

**Inclusion Criteria**

- 1.All patients were hospitalized for COVID-19 treatment.
- 2. Patients discharged from hospital with COVID-19 negative report .

**Exclusion Criteria**

- 1. Who didn't attended telephone.
- 2.Unwilling to answer questionnaire.

**Results**

**Sample size**

From Sept 10 to Oct 10, 2020, 401 patients were potentially eligible for the interview; 59 individuals (14.7%) didn't attended telephone. Thus, 342 patients were included.

**Table 1:Sample size**

	N	%
Total number of patients	401	100
Drop out rate	59	14.7
Final total patients	342	85.28

**Area distribution**

In this study,78.36% patients belongs to urban area and 21.64% belongs to rural area.(Table 2)

**Table 2 :Area distribution**

	N=342	%
Urban	268	78.36
Rural	74	21.64

**Demographic Profile**

In this study, out of 342 patients 238 (69.60%)were males and 104(30.40%)were females. Among 238 males,0.42% were <20 years,23.94% were between age group of 21-40 years ,36.97% were of age group 41-60 years and 38.65% were of >60 years .Among 104 females,1.92% were <20 years,17,30% were between age group of 21-40 years ,53.84% were of age group 41-60 years and 26.92% were of >60 years .

**Table 3:Demographic Profile**

Age	Male(N =238/342)	Percentage = 69.60%	Female(N=104/342)	Percentage =30.40%
<20 years	01/238	0.42%	02/104	1.92%
21-40 years	57/238	23.94%	18/104	17.30%
41-60 years	88/238	36.97%	56/104	53.84%
>60 years	92/238	38.65%	28/104	26.92%

**Personal History**

In the study,14.3% patients were alcoholic ,22.9% patients were active smoker,26.9% were former smokers and 50.2% didn't reported any personal history of alcohol and smoking.

**Table 5:Personal History**

	N=342	%
Alcoholics	49	14.3%
Smoker		
a)Active	78	22.9%
b)Ex-Smoker	92	26.9%
c)None	172	50.2%

**Neurological Symptoms**

**Table 6:Neurological symptoms**

S.No.	Symptoms	No.	Percentage
1.	Fatigue	198	57.8%
2.	Myalgia	99	29%
3.	Anosmia	142	41.5%
4.	Dysgeusia	123	35.9%
5.	Headache	140	41.0%
6.	Memory loss	11	3.2%

7.	Concentration difficulty	64	18.7%
8.	Sleep disorder	92	26.9%
9.	Psychiatric symptoms	62	18.12%
10.	Others	2*	0.58%

\*01- Right sided thigh hematoma ,01- Left sided hemiparesis

Figure 1 shows that Neurological symptoms with Fatigue - 57.8% ,Myalgia – 29%,Anosmia- 41.5%,Dysgnesia – 35.9%, Headache – 41.0%,Memory loss – 3.2%,Concentration difficulty – 18.7%,Sleep disorder – 26.9%, Psychiatric symptoms- 18.12% , 01 patient reported with Right sided thigh hematoma and 01 patient with Left sided hemiparesis.

Figure 1

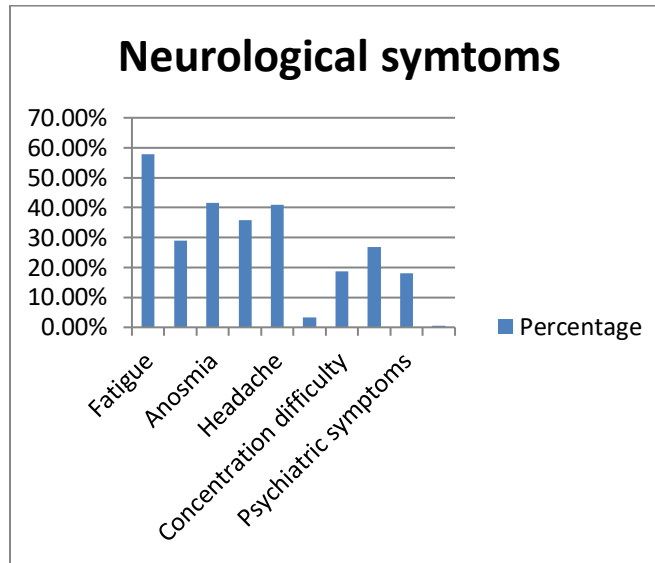


Fig 1:Neurological symptoms

Post COVID- 19 Persistent symptoms

Table 7: Post COVID- 19 Persistent symptoms

Persistent symptoms	N= 342	Percentage
a)None	48	14.03%
b) 1 or 2	124	36.25%
c)More > or = 3	174	50.8%

Comorbid conditions

Table 8:Comorbid conditions

Comorbid condition	N=342	Percentage %
Respiratory distress	67*	19.60%*
Diabetes mellitus	118	34.5%
Hypertension	70	20.46%
Cardiovascular Disease	12	3.50%
Acute kidney injury (AKI)	4	1.17%
Thyroid disease	13	3.80%
Others	10**	2.92%

\*67 = 47(Bilateral pneumonitis), 13(Asthma), 3(Chronic obstructive pulmonary disease),4(Pulmonary tuberculosis- Treated)

\*\*10 = 01(Carcinoma of breast ),01(Carcinoma ovary),01 (HIV),02(Septic shock), 01(Seizure disorder),01(left side hemiparesis),03(Arthritis)

48 (14.03%) patients did not report any of above symptoms, 124(36.25%) patients had one or two symptoms and 174 (50.8%) had three or more persistent symptoms.

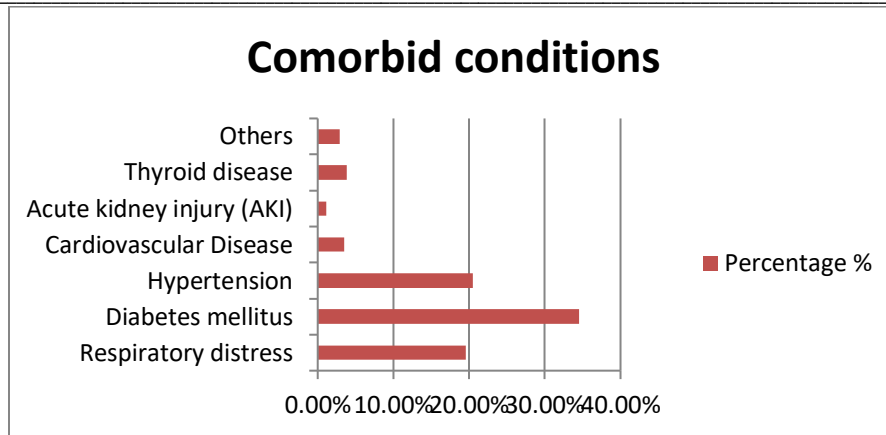


Fig 2:Comorbid conditions

**Discussion**

COVID-19 is a highly infective respiratory viral disease that can lead to respiratory, physical, and neurological dysfunction in patients. In this study conducted between Sept 10, 2020 to Oct 10, 2020, 401 patients were found to be potentially eligible for the interview with drop out rate of 14.7%. Eventually, 342 patients were included (table -1). The demographic profile of the present study showed that out of 342 patients, 238 cases (69.60%) were male and 104 cases (30.4%) were female. Out of 238 males the majority of males 92 (38.65%) were >60 years of age . Out of 104 females, 56 (53.84%) were of age group 41-60 years (table-3). A total of 48 (14.03%) patients were completely free of any COVID -19 related symptoms while 124(36.25%) patients had one or two symptoms and 174 (58.8% ) had three or more persistent symptoms (table-7) . A significant number of individuals still had post COVID symptoms like fatigue (57.8%), and myalgia (29%) (table 6). According to the study by Angelo Carfi, MD *et al*, [12] out of 143 patients , the mean age was found to be 56.5 years(SD, 14.6 , range 19-84 years), and 53 patients (37%) were women. Only 18 cases(12.6%) were completely free of any Covid-19–related symptoms, while 32% had 1 or 2 symptoms and 55% had 3 or more. Worsened quality of life was observed among 44.1% of patients. A high proportion of individuals reported fatigue (53.1%), dyspnea (43.4%), joint pain, (27.3%) and chest pain (21.7%) (table-6). These results were quite coinciding with our study. In the study done by Yvonne M.J [13] out of 2113 respondents , a large number of patients(85%)were women with a median age of 47 (39-54) years had fatigue (94.9%) and dyspnoea (89.5%) as the most prevalent symptoms . In contrast, our study found the percentage of females affected to be much less(30.4%). In our study, the other common post COVID symptoms were anosmia-41.5%, dysgeusia – 35.9% and headache – 41.0% (table -6). According to Timothée Klopfenstein *et al* [14] ,out of 70 patients , the mean age was found to be 57.0 years and 29 patients (41%) were men . Neurologic symptoms were present in more than half of the patients: Fatigue (93% [65]), anosmia (53% [37]) and dysgeusia (48% [34]). These results are almost in concordance with the result of our study. A recent European study by Lechien JR [15] noted a different clinical profile of younger (median 37 years) COVID-19 patients. In 1,420 patients with mild-to-moderate COVID-19 disease, headache (70%) was the most prevalent symptom. Other common neurological symptoms were loss of smell (70%), asthenia (63%), myalgia (63%), and loss of taste (54%).In a French study, Lechien and co-workers [16] reported that out of 417 COVID-19 patients, 86% and 88% of patients, respectively, reported anosmia and ageusia. Anosmia in many patients was the first manifestation of Covid-19.In the commencing days of COVID-19 pandemic ,a case study conducted

by Alpana Garg [17] in a middle aged woman found that she initially presented with myalgia, fatigue, loss of taste and smell, and non-specific memory impairment.Two months later she suffered a stroke and reported with acute onset of right-sided weakness, sensory loss, and worsening cognitive impairment. In our study, other neurological symptoms were memory loss 3.2%, concentration difficulty 18.7% and sleep disorder 26.9%. Hopkins *et al* [18,19 ] studied long-term outcomes for adults requiring ventilation for multiple causes and observed impairments in attention, memory, verbal fluency, processing speed and executive functioning in 78% of patients 1 year after discharge and in around half of patients up to 2 years. Gary Joseph Ordog [20] after compiling the various studies done across the world commented on the most common symptoms of post covid 19. Studies conducted in Wuhan found that 40% of the patients experienced confusion and disturbance in consciousness while recovering from coronavirus.. This is commonly referred to as "brain fog". In another survey of 924 people, 46% reported the symptom of difficulty in Concentrating or Focusing[20]. Another survey of 782 people, 39% reported the symptom of difficulty sleeping. . This lack of sleep may be due to anxiety or worry about the virus or may be ascribed to other persisting symptoms, such as muscle pain or cough.Another survey reported 35% patients with memory problem out of 714 people. Critical cases presented with memory problems and cognitive decline as potential side effects [20].In our study , 18.12% patients had psychiatric symptoms (table 6). In the study by Maxime Taquet [21] , the incidence of all psychiatric disorders was higher after COVID-19 diagnosis than after control health events. The estimated probability of having been diagnosed with any psychiatric illness in the 14 to 90 days after COVID-19 diagnosis was 18.1% (95% CI 17.6–18.6), significantly higher than for all control health events (HRs 1.24–1.49).In study by Que *et al* [22]2020; Psychological symptoms including anxiety, depression, insomnia are prevalent in up to 60 % among physicians, nurses and medical residents during COVID-19 pandemic , which are likely to persist for several years.In study by Natarajan Kathirvel [23] , symptoms of emotional disturbance, irritability, insomnia, depression and post-traumatic stress appeared in the post quarantine period. The mental morbidity of the society is expected to rise during the post-pandemic time as a result of the long term effects of the restrictive measures such as social distancing and quarantine and the socio-economic effects. In present study patients also reported with right sided thigh hematoma in one patient and with Left sided hemiparesis in one patient.In this study, 20.4% patients were hypertensive ,34.5% patients were having diabetes mellitus ,3.5% patients had a cardiovascular disease (CVD) and 67(19.6%) patients had

respiratory distress (with 47 cases of bilateral pneumonitis, 13 cases of asthma, 3 cases of COPD and 4 patients were treated cases of pulmonary tuberculosis) as a comorbid condition (table 8). In a meta-analysis done by Yang J [24], hypertension was prevalent in approximately 21.1% of the patients quite similar to our study; diabetes, cardiovascular disease, and respiratory system disease were present in 9.7%, 8.4%, and 1.5% of the cases, respectively. Another study by F.Zhou et al [25] in Wuhan in 191 patients (135 from Jinyintan Hospital and 56 from Wuhan Pulmonary Hospital) reported that 91 (48%) patients had a comorbidity, with hypertension being the most common (58 [30%] patients), followed by diabetes (36 [19%] patients) and coronary heart disease (15 [8%] patients). In China, W.W. Chen [26] observed that 23% uncontrolled blood pressure is associated with COVID-19 infection and also with a high case fatality rate of 6%. In study by Emami A [27], Li B [28], comorbidities in patients of Asian origin with COVID-19 of (16 studies, N = 78 520), a relatively low prevalence of hypertension and diabetes mellitus (16–17% and 12–16%, respectively) was reported compared to our study. Qiu H reported that COVID-19 illness can lead to the development of hypoxemia in 15–20% of the patients requiring ventilator support in adversity. A better understanding of this entity and multidisciplinary approach including Physician, Anesthesiologist, Psychiatrist, Chest physician, a Neurologist and other super specialities might help to propose an adequate treatment.

#### Conclusion

Various neurological presentations occur in the recovery phase of elderly comorbid COVID-19 cases. This recommends a thorough mental evaluation and neurological work up for complete rehabilitation of these patients. Advanced age, male sex, diabetes mellitus, hypertension, respiratory disease and cardiovascular disorders were independent markers of poor prognosis and increased severity of the disease. Although vaccine is a lifeboat but still long term regular monitoring after discharge will improve prognosis of the patients.

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