International Journal of Health Sciences and Research
[Indexed, Peer-Reviewed Journal]
Volume 15; Issue: 4; April 2025
Website: www.ijhsr.org
Original Research Article *ISSN: 2249-9571*

Immediate and Long-Term Neurological Complications Post COVID-19 Infection and Their Association with Co-Morbidities: A Cross-Sectional Study

Joshi Snehal[1], Kunte Arya P[2]

[1]HOD Department and institution: Department of Neurosciences, [2](Masters in Neurophysiotherapy, Deccan Education Society's Brijlal Jindal College of Physiotherapy (DESBJCOP), Pune

Corresponding Author: Joshi Snehal

DOI: https://doi.org/10.52403/ijhsr.20250406

ABSTRACT

Context: Coronavirus has impacted the health of the world's population. Multiple neurological manifestations have been reported in post infectious phase. The association between the virus and nervous system is unpredictable. This infection is mostly followed by a number of short term and long-term complications.[1]
Aims: To find the immediate and long-term neurological complications in individuals post COVID-19 infection.
Settings and Design: Cross sectional study conducted in community setting
Method: 720 individuals post covid-19 infection were analysed for neurological complications. The association between the neurological complications and the co-morbidities was studied.
The data was analysed using descriptive statistical analysis. The association between the co-morbidities and the neurological complications in individuals with post COVID-19 infection was derived by using Chi – square test.
Results: The immediate and long-term neurological complications were found in 6.38 % and 3.34 % post COVID-19 individuals respectively. GBS, stroke, vision/speech disturbances, memory loss etc. were observed in individuals post COVID-19 infection. Association of diabetes and hypertension was seen with presence of neurological symptoms with χ^2= 121.05 (p= 0.0001) and 62.585 (p= 0.0001) respectively.
Conclusions: The immediate and long-term neurological complications seen in post COVID-19 individuals were GBS, stroke, vision disturbances etc. An association found between co-morbidities like Diabetes Mellitus and/or Hypertension with the neurological complications post COVID-19 infection.

Keywords: post covid-19 infection, neurological manifestations, diabetes, hypertension

INTRODUCTION

India has witnessed three waves of COVID-19 i.e., Coronavirus Disease of 2019 & the infection is not over yet.[2] COVID-19 affects respiratory system is well known but it also has extrapulmonary manifestations. The current study focuses on neurological complications post COVID-19 infection.

The neurological manifestations of COVID-19 have not been of much focus in the literature, but a few published reports are concerning.[3]

The coronavirus has the ability to invade the nervous system i.e., neurotropism. Previous studies have shown the presence of ACE2 receptors (Angiotensin Converting Enzyme 2) in the nervous system and in skeletal muscle, suggesting a mechanism for SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2) related neuromuscular injury. Apart from ACE2, COVID-19-associated nervous system damage may also be caused by direct infection injury, hypoxic injury and immune responses.[4]

COVID-19 can cause both acute and long-term neurological complications in many patients.[5] Now these complications are addressed as nonspecific and specific neurological complications. The non-specific neurological complications are headache, altered mental status, dizziness, depressed level of consciousness, ageusia (loss of taste), anosmia (loss of smell), myalgia and fatigue. The specific neurological complications are cerebrovascular complications such as stroke, subarachnoid haemorrhage, massive cerebral haemorrhage, encephalitis/ meningitis, Acute Haemorrhagic Necrotizing Encephalopathy. Also, there are complications related to demyelination such as GBS (Guillain-Barre Syndrome), Miller-Fischer Syndrome, CNS (Central Nervous System) demyelination. Seizures, Symmetrical Polyneuropathy was also seen.[5]

Neurological complications have emerged as a significant cause of morbidity and mortality in the ongoing COVID-19 pandemic. Beside respiratory insufficiency, many hospitalized patients exhibit neurological manifestations ranging from headache and loss of smell, to confusion and disabling strokes. COVID-19 is also anticipated to take a toll on the nervous system in the long term. [6]

There are also patients who were hospitalized and had a history of stay at intensive care units. Most critically ill COVID-19 patients require mechanical ventilation [6,7] and an agitated state of confusion (delirium) occurs in more than 80% of mechanically ventilated patients in intensive care units. [6,8]

Since the early onset of the pandemic, several treatments have been tested and developed to treat COVID-19. These treatments have reduced the severity of the disease and the time patients spend at the hospital. However, many of those treatments that are being used for COVID-19 have the potential to cause neurological or psychiatric symptoms. [9]

The infected population which has shown neurological complications range from young adults to older adults. In addition, the older adults were having co-morbidities. So, it is still unclear whether there is any co-relation between the pre-existing co-morbidities and COVID-19 infection. So, this study aims at finding the existence of this co-relation.

Since the virus is neurotropic, the neurological manifestations are of a great importance. Not only immediate (short-term) complications but there are long term neurological sequelae which should not go unnoticed.

Limited literature is available which can firmly state the complications of nervous system of this infection. So, the current study aims to find the immediate and long-term neurological complications in individuals post COVID-19 infection.

MATERIALS & METHODS

Objectives of the Study:

1) To find the number of individuals suffering or have suffered any neurological complication post COVID - 19 infection
2) To enumerate the neurological complications that are immediate and long-term in individuals post COVID - 19 infection
3) To find the association between comorbidities and neurological

complications post COVID - 19 infection

Subjects and Methods:

This cross-sectional study, was conducted in community. Individuals both males and females from age 18 – 80 years post COVID-19 infection who were tested and confirmed by RT PCR test (Reverse Transcription-Polymerase Chain Reaction Test) were included in this study. Individuals with pre-existing neurological conditions were excluded from the study. Considering the prevalence of neurological complications in patients suffered from COVID-19 as 1.4 % [10] at type I error of 0.1 and allowable error of 20%, the estimated sample size was 624.

In the first step, the study design and procedure were approved and clearance was taken from the Institutional Ethics Committee (IEC).

Participants were included in the study 2 weeks or 14 days post COVID – 19 infections. [11] The sample records were collected from personal contacts, hospital records & OPD records. Participants were sampled by using simple random sampling. Following data were collected from the participants - demographic data, past history, COVID-19 infection history, history of any diagnosed neurological complication related with COVID infection. Individuals who were falling in the period from recovery of infection up to 6 months post COVID-19 infection were observed for short-term neurological complications and who were falling in the period from 6 months up to one year post COVID-19 infection were observed for long-term neurological complications.

Then the obtained data was analyzed by using descriptive statistical analysis. The association between the co-morbidities and the neurological complications in individuals with post COVID-19 infection was derived by using Chi – square test.

RESULT

Neurological complications were present in 35 (4.9%) patients. (Graph -1)

The neurological complications found in post COVID-19 individuals are – Guillain Barre Syndrome i.e., GBS (0.7%), stroke (0.6%), Weakness in the extremities (0.8%), Vision disturbances (0.6%), Speech disturbances (0.3%), Parkinson's Disease (0.1%), Balance issues (0.1%), polyneuropathies (0.1%), intention tremors in upper limbs (0.3%), altered cognition and sensorium (0.1%), altered sensation in hands and feet (0.3%), memory loss (0.6%), sleep disturbances (0.8%). (Graph – 2)

Total 378 patients were falling in the short-term period (i.e., from recovery of infection up to 6 months post COVID-19 infection) while 329 patients were falling in the long-term period (i.e., from post 6 months up to one year post COVID-19 infection). Out of which 24 were in individuals who suffered short term complications and 11 were in individuals who suffered long term complications. Incidence of neurological complications in individuals who suffered short term complications was 6.38% and in individuals who suffered long term complications was 3.34%. On comparison incidence of neurological complications in individuals who suffered short term complications was almost twice that of neurological complications in individuals who suffered long term complications. The difference was statistically significant. ($Z= 3.03$, $p< 0.001$). (Graph – 3)

Association of Diabetes Mellitus (DM) and Hypertension (HTN) was seen with presence of neurological symptoms (Graph – 4) with $\chi^2= 121.05$ ($p= 0.0001$) and 62.585 ($p= 0.0001$) respectively. It is derived by using Chi-square test and it is statistically significant.

DISCUSSION

Current study included 707 post COVID-19 individuals who matched inclusion criteria. In this study there were 390 female and 317 male participants. Out of which immediate complications were assessed in 378

individuals and 329 individuals were assessed for long term neurological complications. 6.34 % of individuals developed immediate and 3.34 % of individuals developed long term neurological complications. This study also found association between the co-morbidities seen (which are Diabetes Mellitus and Hypertension) and the neurological complications seen in the patients post COVID-19 infection.

In the current study, neurological complications were seen in 4.9 % of patients affected with COVID-19 infection. Bauer et. al. stated that, SARS CoV-2 has neuro-invasive potential and has also shown neurotropism and neurovirulent property in at least a subgroup of patients.[12] Neuronal and glial cells and endothelial cells in the central nervous system express ACE 2 receptor.[13] ACE 2 receptor is used by SARS-CoV-2 to gain entry into human cells.[14] As a result of respiratory failure, patients develop shortness of breath which leads to hypoxemia. Pathological changes consisting of brain congestion, oedema, and degeneration of a part of the neurons in hypoxia makes severe hypoxia as the major risk factor for hypoxic encephalopathy and ischemic stroke, causing serious damage to the nervous system. [15,16] Infection with SARS-CoV-1 also causes the surge of cytokines that are released in response to these infections cause endothelial damage and alteration of microvascular permeability; this results in hypercoagulability leading to cerebrovascular accidents. [17,18,19] Cytokine storm is one of the possible underlying causes of CNS & PNS (Peripheral Nervous System) complications in COVID-19 infection.[20] Immune dysfunction after this infection can result in a series of post-infectious diseases, such as ADEM (Acute Disseminated Encephalomyelitis), GBS and its variants etc.[16]

Following are the neurological complications seen in individuals having post infectious status of COVID-19 – GBS (0.7%), stroke (0.6%), Weakness in the extremities (0.8%), Vision disturbances (0.6%), Speech disturbances (0.3%), Parkinson's Disease (0.1%), Balance issues (0.1%), polyneuropathies (0.1%), intention tremors in upper limbs (0.3%), altered cognition and sensorium (0.1%), altered sensation in hands and feet (0.3%), memory loss (0.6%), sleep disturbances (0.8%). (Graph - 2)

In this study, association of diabetes and hypertension was seen with presence of neurological symptoms in post COVID-19 individuals, and it is found statistically significant. One meta-analysis demonstrated that the prevalence of diabetes and hypertension is lower in survivors than in non-survivors of COVID-19 patients.[21] The immune system of diabetes patients might be altered by the abnormal blood glucose level, resulting in dysregulation and reduced responses of immune components. Consequently, these patients are susceptible to SARS-CoV-2 and various other types of bacteria.[22] Hypertension is treated with ACE inhibitors and ARBs, which results in an upregulation of ACE2 and SARSCoV-2 binds to their target cells through ACE2. This increases the susceptibility for infection with COVID-19.[23] The above hypothesis could possibly explain that, why people with pre-existing co-morbidities are more susceptible to develop neurological complications post covid. So, this suggests that more attention can be given while screening these individuals with history of COVID and preventing the consequences of neurological complications. On comparison incidence of neurological complications in individuals who suffered short term complications (6.38%) was almost twice that of neurological complications in individuals who suffered long term complications (3.34%). The difference was statistically significant.

In the recovery phase of covid-19, the immune hyper-inflammatory response declines in the long-term phase. Phase of cytokine storm also diminishes by the time of long-term phase of COVID-19 infection. Blood also achieves its proper viscosity, so

thereby avoiding the chances of thrombus formation leading to infarcts. But there is a clinical evidence of a long-lasting antibody response in recovered COVID-19 patients while highlights the immune evasiveness of SARS-CoV-2 variants, this can predispose the individual to develop long term complications.[24]

Implication

The data obtained from the current study can be used for early detection and rehabilitation of neurological complications which are seen in the post infectious phase. Also, special attention can be given to the patients with pre-existing co-morbidities (DM &/ HTN), as there is established association between these co-morbidities and post COVID neurological complications. Maximum precaution regarding patient's health should be taken in first 6 months post infection, as the immediate complications are more likely to occur within this period. Routine checkup and maintenance of BSL, lipid profile and BP within advisable limit is crucial for these specific patients.

Limitations

Association of neurological complications with other co-morbidities such as asthma, obesity etc. could not be established due to poorer incidence of these conditions found in these patients. This study couldn't analyze the para infectious neurological complications, so only post infectious neurological complications were studied.

Future Scope

Even pediatric population is seen to develop neurological consequences of COVID-19 infection. So, neurologic manifestations in post COVID pediatric population can be studied. Association between respiratory manifestations resulting into neurological complications in the post COVID phase can also be found out in future studies. Effect of treatment given during COVID-19 (invasive/non-invasive, effect of hydro-chloroquine toxicity, etc.) on producing neurological complications could also be the interest of future studies

CONCLUSION

Immediate and long-term neurological complications post COVID-19 infection were found in 6.68% and 3.34% individuals respectively. The immediate and long-term neurological complications seen in post COVID-19 individuals are GBS, stroke, vision or speech disturbances, Parkinson's Disease, balance issues, polyneuropathies, intention tremors in upper limbs, altered cognition and sensorium, altered sensation in hands and feet, memory loss (especially short-term), etc. There is an association between co-morbidities like Diabetes Mellitus and/or Hypertension with the neurological complications post COVID-19 infection.

Declaration by Authors

Ethical Approval: Approved
Acknowledgement: None
Source of Funding: None
Conflict of Interest: The authors declare no conflict of interest.

REFERENCES

1. Werner C., Scullen T., Mathkour M., Zeoli T., Beighley A. Neurological impact of coronavirus disease (COVID-19): Practical considerations for the Neuroscience community. Journal of Neurological Sciences 2020.
2. Arnab Sarkar, Alok Kumar Chakrabarti, Shanta Datta. Covid-19 Infection in India: A Comparative Analysis of the Second Wave with the First Wave. Pathogens (MDPI). September 2021.
3. Mary Kathryn Bohn, Alexandra Hall, Lusia Sepiashvili, Benjamin Jung, Shannon Steele, Khosrow Adeli. Pathophysiology of COVID-19: Mechanisms Underlying Disease Severity and Progression. Journal of applied physiology. August 2020.
4. Chih-Cheng Lai, Wen-Chien Ko, Ping-Ing Lee, Shio-Shin Jeand, Po-Ren Hsueh. Extra-respiratory manifestations of COVID-19. International Journal of Antimicrobial Agents. May 2020.
5. Ali Al-Ramadan, Omar Rabab'h, Jawad Shah, Abeer Gharaibeh. Acute and Post-Acute

Neurological Complications of COVID-19. Neurology international. March 2021.
6. Costantino Iadecola, Josef Anrather, Hooman Kamel. Effects of COVID-19 on the Nervous System. Cell 183; October 2020.
7. Cummings M.J., Baldwin M.R., Abrams D., Jacobson S.D., Meyer B.J., Balough E.M., Aaron J.G., Claassen J., Rabbani L.E., Hastie J. Epidemiology, clinical course, and outcomes of critically ill adults with COVID-19 in New York City: a prospective cohort study. Lancet. 2020.
8. Ely E.W., Inouye S.K., Bernard G.R., Gordon S., Francis J., May L., Truman B., Speroff T., Gautam S., Margolin R. Delirium in mechanically ventilated patients: validity and reliability of the confusion assessment method for the intensive care unit (CAM-ICU) JAMA. 2001.
9. García C.A.C., Sánchez E.B.A., Huerta D.H., Gómez-Arnau J. Covid-19 Treatment-Induced Neuropsychiatric Adverse Effects. Gen. Hosp. Psychiatry. 2020.
10. Liotta EM, Batra A, Clark JR, Shlobin NA, Hoffman SC, Orban ZS, Koralnik IJ. Frequent neurologic manifestations and encephalopathy-associated morbidity in Covid-19 patients. Ann Clin Transl Neurol. 2020 Nov;7(11):2221-2230.
11. https://www.who.int/news-room/commentaries/detail/criteria-for-releasing-covid-19-patients-from-isolation
12. Lisa Bauer, Brigitta M. Laksono, Femke M.S. de Vrij, Steven A. Kushner, Oliver Harschnitz, Debby van Riel. The neuroinvasiveness, neurotropism, and neurovirulence of SARS-CoV-2; Trends in neurosciences. May 2022 Vol. 45, No. 5.
13. Francisco J. Barrantes; Central Nervous System Targets and Routes for SARS-CoV-2: Current Views and New Hypotheses. ACS Chemical Neuroscience. August 2020.
14. Samavati L, Uhal BD. ACE2, much more than just a receptor for SARS-COV-2; Frontiers in Cellular and Infection Microbiology. June 2020.
15. Li YC, Bai WZ, Hashikawa T. The neuroinvasive potential of SARS-CoV2 may play a role in the respiratory failure of COVID-19 patients. Journal of medical virology. February 2020.
16. Haiyang Yu, Tong Sun, Juan Feng. Complications and Pathophysiology of COVID-19 in the Nervous System; Frontiers in Neurology. December 2020.
17. Patrick Moore, Fatema Esmail, Shuai Qin, Sucha Nand, Stephanie Berg. Hypercoagulability of COVID-19 and Neurological Complications: A Review; Journal of Stroke and Cerebrovascular Diseases, Vol. 31, No. 1. January 2022.
18. Cantan B, Luyt CE. Martin-Loeches I. Influenza infections and emergent viral infections in intensive care unit. Seminars in Respiratory and Critical Care Medicine Vol. 40 No. 4; 2019.
19. Marc J Kahn. Hypercoagulability as a cause of stroke in adults. Southern Medical Journal. April 2003.
20. Parisorn Thepmankorn, John Bach, Ahmed Lasfar, Xilin Zhao, Sami Souayah, Zhao Zhong Chong, Nizar Souayah. Cytokine storm induced by SARS-CoV-2 infection: The spectrum of its neurological manifestations. Cytokine 2021.
21. Parveen R, Sehar N, Bajpai R, Agarwal NB. Association of diabetes and hypertension with disease severity in covid-19 patients: A systematic literature review and exploratory meta-analysis. Diabetes Res Clin Pract. 2020 Aug; 166:108295.
22. Wu J., Li W., Shi X., et al. Early antiviral treatment contributes to alleviate the severity and improve the prognosis of patients with novel coronavirus disease (COVID-19) J Intern Med. 2020.
23. Fang L., Karakiulakis G., Roth M. Are patients with hypertension and diabetes mellitus at increased risk for COVID-19 infection? Lancet Respir Med.
24. Yan Zhan, Yufang Zhu, Shanshan Wang, Shijun Jia, Yunling Gao, Yingying Lu, Caili Zhou, Ran Liang, Dingwen Sun, Xiaobo Wang, Zhibing Hou, Qiaoqiao Hu, Peng Du, Hao Yu, Chang Liu, Miao Cui, Gangling Tong, Zhihua Zheng, Yunsheng Xu, Linyu Zhu, Jin Cheng, Feng Wu, Yulan Zheng, Peijun Liu, Peng Hong. SARS-CoV-2 immunity and functional recovery of COVID-19 patients 1-year after infection. Signal Transduction and Targeted Therapy. October 2021.

How to cite this article: Joshi Snehal, Kunte Arya P. Immediate and long-term neurological complications post COVID-19 infection and their association with co-morbidities: a cross-sectional study. *Int J Health Sci Res.* 2025; 15(4):42-47. DOI: *10.52403/ijhsr.20250406*

******