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Review Article

**A SYSTEMATIC REVIEW OF ON THE CENTRAL NERVOUS
SYSTEM MANIFESTATIONS OF COVID-19**¹Dr Bushara Gohar Shah, ²Dr Ayesha Khalid, ³Asad Javed¹Associate Professor of Physiology, Sahara Medical College, Narowal²Fatima Jinnah Medical University, Lahore³MBBS Student (Final Year), Sahara Medical College Narowal**Abstract:**

Objective: In this systematic assessment, we determine the involvement of central nervous system (CNS) in Covid-19 affected patients and COVID-19 infected patients were evaluated for neurological manifestation.

Methods: Scopus and MEDLINE (access from PubMed) systematically searched the relevant articles from December 1, 2019 to March 26, 2020. The subsequent exploration policy was implemented in both electronic databases and these keywords (title / summary) were used: "COVID 19 Coronavirus AND "CNS" OR ""brain" neurological" manifestation.

Results: we were able to classify 2 articles on the neurological envelopment of COVID19 by the search tactic. One of these studies was a description analysis, the viewpoint of the Covid-19 was the other study. Though, the writers scanned the available studies reference lists and were able to classify many references. One analysis examined the COVID-19 neurological manifestation and documented CNS symptoms in twenty five percent of the cases. Maximum revisions have generally deal with COVID-19 manifestations.

Conclusion: Although COVID-19 neurological symptoms have not been adequately investigated, some of these patients, especially those with severe disease, probably have neurological symptoms and CNS envelopment. Accurate and detailed certification of electrophysiological evaluation and clinical neurological manifestation of subjects, an attempt to segregate SARS-CoV-2 from CSF, and the role of COVID-19 victims proved in autopsies that causes neurological symptoms

Key words: CNV, COVID-19 manifestation, Neurological involvement, systemic review.

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INTRODUCTION:

Covid-19 is mainly a unique virus that attack the respiratory system in humans, however it too has neuro-invasive ability and can disseminate from the respiratory system to the CNS¹⁻². Earlier outbreaks or coronavirus pandemics were in 2002 with having symptoms of severe acute respiratory syndrome (SARS), and in 2012 there was outbreak of Middle East Respiratory Syndrome (MERS)³⁻⁴. The COVID-19 corona virus is the latest outbreak begin in December 2019 in china and is caused by SARS-CoV-2. The COVID-19 infection symptoms frequently occur after about five days of incubation period. The peak communal COVID-19 disease symptoms are fatigue, cough and fever; Additional signs include hemoptysis, headache and dyspnea. In the utmost serious cases, subjects may advance towards acute respiratory distress syndrome, pneumonia, multi-organ failure and acute heart problems⁵. In December 2019; the first COVID-19 cases was reported in Wuhan city of China however, from December 1, 2019 to March 26,

2020, when searching MEDLINE (access from PubMed) with the keyword "COVID 19", we found 1655 articles surprisingly. This indicates that the COVID-19 outbreak is a serious worldwide community health problem⁶. Covid-19 infections are related with neurological symptoms (for example, convulsions, febrile seizures, encephalitis and altered mental state). Neuroinvasive and neurotropic abilities of coronaviruses have been defined among humans⁷⁻⁸. The CNS access of the corona virus is after the nasal infection through the olfactory bulb, instigating demyelination and inflammation. In this systematic evaluation, we discussed involvement in the CNS and confirmation of neurological manifestation in COVID-19 patients.

METHODS:

The reporting of this systematic review was held in agreement with the commendations of the preferred reporting items for systematic reviews and meta-analysis (PRISMA) (Figure 1).

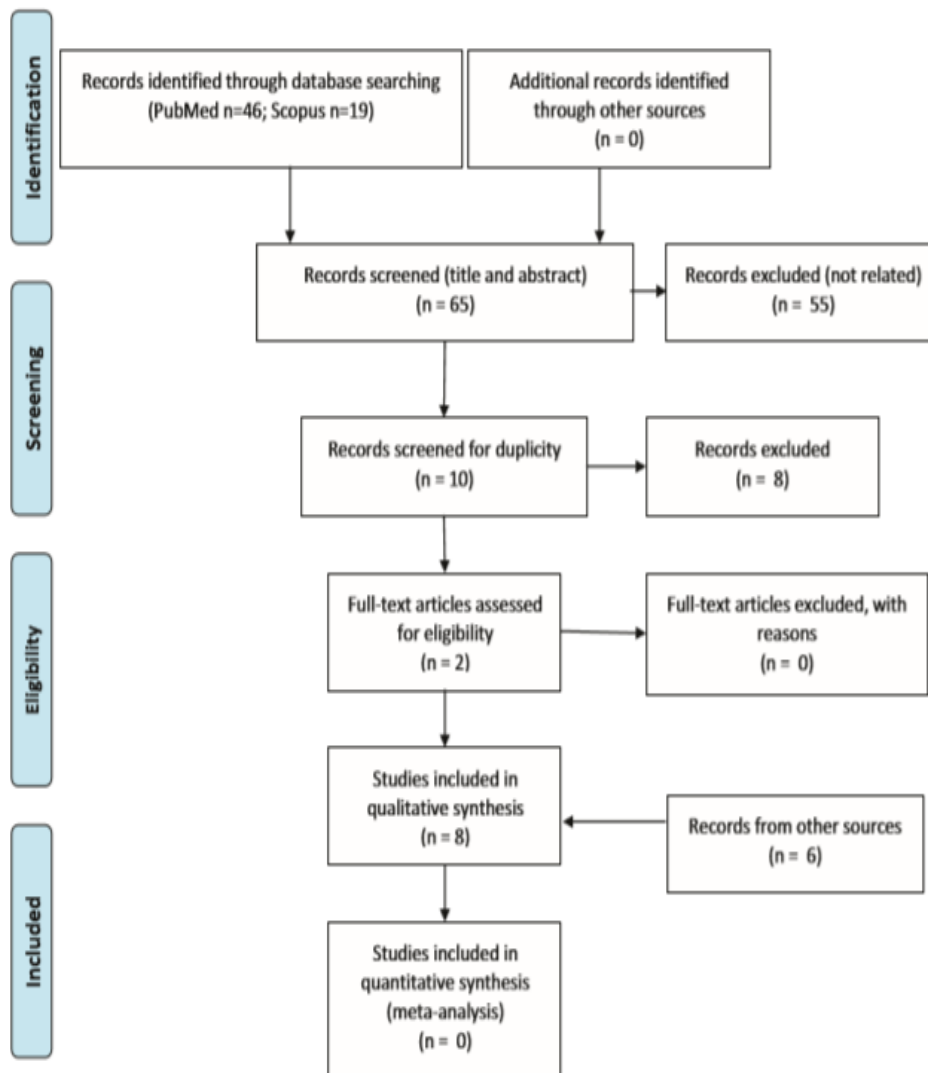


Fig. 1. Preferred reporting items for systematic reviews and meta-analyses (PRISMA) flow diagram of the study.

The audit report has not been recorded before. Scopus and MEDLINE (access from PubMed) systematically searched the relevant articles from December 1, 2019 to March 26, 2020. The subsequent exploration policy was implemented in both electronic databases and these keywords (title / summary) were used: "COVID 19 Coronavirus AND "CNS" OR ""brain" neurological" manifestation. "The search includes articles written in English. To ensure saturation of the literature, the authors scanned their reference letters. Studies or related reviews identified on the basis of the studies. Both writers contributed independently in each stage of the review (inclusion, eligibility, and screening). They analyzed the summaries autonomously in accordance with the criteria of inclusion. They self-reliantly curtailed the abstracts and titles generated by the search in

contradiction of the criteria of inclusion. None of the writers were blind to magazine titles, institutions or research authors. The subsequent informations were obtained from the encompassed analysis: study designs, study authors, limitations and main results. The methodology of the studies involved was evaluated by the authors. The evidence class was defined in accordance with the criteria of the American Academy of Neurology to classify evidence in studies of causation (Annex 1).

RESULTS:

By this research methodology, we were able to recognize 2 articles on the COVID-19 neurological manifestation (Tables 1 and 2). One of these study was a description analysis, the viewpoint of the Covid-19 was the other study.

Table 1

Medline (PubMed)			Scopus (Keywords, Abstract, Article title)	
Keywords	Relevant articles	Primary hints	Relevant articles	Primary hints
CNS	1	1	0	0
Neurologic	1	1	1 (duplicate)	1
Brain	0	17	1 (duplicate)	2
Total	2	19	2 (2 duplicates)	3

Table 2

Medline (PubMed)			Scopus (Keywords, Abstract, Article title)	
Keywords	Relevant articles	Primary hints	Relevant articles	Primary hints
CNS	1 (duplicate)	4	0	3
Neurologic	1 (duplicate)	1	1 (duplicate)	4
Brain	2 (2 duplicates)	22	1 (duplicate)	9
Total	4 (4 duplicates)	27	2 (2 duplicates)	16

Though, the writers scanned the available studies reference lists and were able to classify many references. These studies summary of COVID-19 symptoms in the CNS given in Table III. One analysis examined the neurological symptoms of COVID-19 and documented CNS symptoms in twenty five percent of the cases. Though, the writers did not perform analysis of cerebrospinal fluid (CSF) and electroencephalographic (EEG).

Table 3

Authors / years	Method	Neurological-manifestations	Limitations	Levels of evidence
Chen/ 2020 [14]	99 hospitalized patients; Retrospective case series study	Headache in 8%; Confusion in 9%	No CSF or EEG studies. Not specifically studied neurological manifestations.	II
Wang/ 2020 [13]	138 hospitalized patients; A Retrospective case series	Headache in 7%; Dizziness in 9%	No CSF or EEG studies. Not specifically studied neurological manifestations.	II
Yang/ 2020 [12]	52 critically ill mature subjects; A Retrospective study	6% have Headache	No CSF or EEG studies. Not specifically studied neurological manifestations.	II
Huang/ 2020 [11]	41 patients were admitted; A Prospective study	8% have Headache	No EEG or CSF studies. Not specifically studied neurological manifestations.	I
Li/ 2020 [10]	221 admitted patients; A Retrospective case series	acute ischemic stroke in 5%, cerebral venous sinus thrombosis in 0.5% and 0.5% have cerebral hemorrhage	Other associated neurological manifestations were not studied.	II
Mao/ 2020 [9]	214 admitted patients; A Retrospective case series	Headache (13%), CNS indices: in 25%, impaired consciousness (8%), dizziness (17%), ataxia (0.5), seizures (0.5%) and acute cerebrovascular problems (3%)	No clear definition of symptoms; No EEG study; No CSF analysis	III

In other retrospective analysis concerned the onset of acute cerebrovascular disease after COVID-19. Additional researches have generally focused the COVID-19 symptoms; they haven't pay much consideration to neurological manifestations.

DISCUSSION:

In this literature, we determined the confirmation of involvement in the CNS and the COVID-19 neurological manifestations is of low quality and scarce⁹⁻¹⁰. Though, the only analysis that precisely investigates this problem has acknowledged that 1/4th of admitted patients in hospitals due to Covid-19 infection and have symptoms of severe acute respiratory syndrome have some CNS envelopment¹¹⁻¹². Some COVID-19 patients may experience nonspecific neurological signs like headache and confusion. Some COVID-19 infected patients had more precise neurological symptoms such as cerebrovascular and convulsions problems (Table 3). Moreover, neuroinvasion of SARS-CoV2 may explain partially why few cases have respiratory failure, whereas others do not¹³. Most coronaviruses have same route of infection and viral structures; therefore, pathomechanisms found previously for other coronaviruses can also be used

for SARS-CoV2. The coronavirus in humans are is not only affect respiratory tract; they can attack CNS. Increasing evidence suggests that neurotropism and neuroinvasion are a communal feature of human coronaviruses. SARS-CoV infection is associated with neurological symptoms¹⁴⁻¹⁵. It has been positively tested for the presence of CSF virus in patients reported with SARS-CoV. In study 183 children with clinical suspicion of acute encephalitis had coronavirus infection (unspecified) in 22 (12%) with anti-CoV IgM. In MERS-CoV infection study on 70 patients, 26% of patients and 9% of patients with seizures experienced psychological changes¹⁶. Therefore, if you look closely, and especially COVID-19 infected patients, you will see neurological symptoms.

Lastly, Cases of severe COVID-19 may exhibit multiorgan failure, hypoxia, electrolyte and

metabolic disorders, and may necessitate complex therapeutic interventions and treatment regimens¹⁷⁻¹⁸. Therefore, these patients are expected to develop status epilepticus, acute subclinical or clinical symptomatic attacks. Mental disorders have been testified in cases of COVID-19 with severe form; however, in previous studies; these manifestations has never been studied adequately (Table 3). When visiting a patient with a change in mental and critical status, ensure that non-convulsive epilepsy (NCSE) is not covered by clinical conditions¹⁹. NCSE diagnosis is often ignored and critical patients have other serious problems. To quickly diagnose NCSE, it is essential to constantly monitor EEG in every subject with a serious health situation with changes in the mental state. Salzburg Consensus Criteria for Non-Convulsive Status Epilepticus is a supportive monitor to confirm the NCSE in critically ill patient's diagnosis²⁰.

CONCLUSION:

Although the COVID-19 neurological manifestations have not been adequately studied, some of these patients, especially those with serious illnesses, probably have neurological manifestation and CNS involvement. Accurate and detailed certification of neurological symptoms (e.g. dizziness, headache etc.) and signs (e.g. meningeal symptoms, altered mental status etc.), electrophysiological investigation (especially in altered mental status), neurological and clinical tests must be ensured, efforts to isolate SARS-CoV-2 from CSF, and COVID-19 victims autopsies may illuminate the roles played by this virus in instigating neurological manifestations.

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