Neurological Manifestations and Complications of Coronavirus Disease 2019 (COVID-19): A Systematic Review and Meta-Analysis

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Systematic Review

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Abstract

**Background:** The spectrum of neurological involvement in COVID-19 is not thoroughly understood. To the best of our knowledge, no systematic review with meta-analysis and a sub-group comparison between severe and non-severe cases has been published. The aim of this study is to assess the frequency of neurological manifestations and complications, identify the neurodiagnostic findings, and compare these aspects between severe and non-severe COVID-19 cases.

**Methods:** A systematic search of PubMed, Scopus, EBSCO, Web of Science, and Google Scholar databases was conducted for studies published between the 1st of January 2020 and 22nd of April 2020. In addition, we scanned the bibliography of included studies to identify other potentially eligible studies. The criteria for eligibility included studies published in English language (or translated to English), those involving patients with COVID-19 of all age groups, and reporting neurological findings. Data were extracted from eligible studies. Meta-analyses were conducted using comprehensive meta-analysis software. Random-effects model was used to calculate the pooled percentages and means with their 95% confidence intervals (CIs). Sensitivity analysis was performed to assess the effect of individual studies on the summary estimate. A subgroup analysis was conducted according to severity. The main outcomes of the study were to identify the frequency and nature of neurological manifestations and complications, and the neuro-diagnostic findings in COVID-19 patients.

**Results:** 44 articles were included with a pooled sample size of 13480 patients. The mean age was 50.3 years and 53% were males. The most common neurological manifestations were: Myalgia (22.2%, 95% CI, 17.2% to 28.1%), taste impairment (19.6%, 95% CI, 3.8% to 60.1%), smell impairment (18.3%, 95% CI, 15.4% to 76.2%), headache (12.1%, 95% CI, 9.1% to 15.8%), dizziness (11.3%, 95% CI, 8.5% to 15.0%), and encephalopathy (9.4%, 95% CI, 2.8% to 26.6%). Nearly 2.5% (95% CI, 1% to 6.1%) of patients had acute cerebrovascular diseases (CVD). Myalgia, elevated CK and LDH, and acute CVD were significantly more common in severe cases. Moreover, 20 case reports were assessed qualitatively, and their data presented separately.

**Conclusions:** Neurological involvement is common in COVID-19 patients. Early recognition and vigilance of such involvement might impact their overall outcomes.

**Background**

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has spread rapidly over the past six months causing the Coronavirus Disease 2019 (COVID-19) pandemic. According to Johns Hopkins Coronavirus Resource Center, as of May 29, 2020, 188 nations and more than 5.8 million people across the globe have been affected (1).

Although SARS-CoV-2 primarily affects the respiratory system causing pneumonia, multiorgan dysfunction and failure are likely to occur in severe cases (2). There is mounting evidence that
coronaviruses can invade the nervous tissue (3,4) resulting in various neurological manifestations (NM) and neurological complications (NC) (5).

The literature about the NM of COVID-19 has been evolving with exponential increase in the number of publications. Multiple studies and case reports described the NM, which vary from being non-specific ones like headache, dizziness, and myalgias to more significant one like ataxia, seizures, anosmia, and ageusia (6–9). Other studies reported NC of COVID-19 like acute ischemic stroke, cerebral venous sinus thrombosis, cerebral hemorrhage, and rhabdomyolysis (6,10). Abnormal findings in neurodiagnostic studies (ND) including neuroimaging (CT and MRI), cerebrospinal fluid (CSF) analysis, and neurophysiological studies (Electroencephalogram (EEG), Nerve Conduction Study (NCS), and Electromyography (EMG)) have also been described (6,11,12).

We conducted a systematic review and meta-analysis of studies addressing the neurological aspects of COVID-19 including NM, NC, and ND findings. In addition, we compared these aspects between severe and non-severe cases. Since the literature is still evolving and not many well designed studies have been published, we also performed a qualitative assessment of the case reports describing some unique NC of COVID-19.

**Methods**

We developed a review protocol (registration number: PROSPERO CRD42020181298) prior to commencing the study. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) were used to ensure the reporting quality of this review (13).

**Literature Search Strategy**

A broad search strategy was conducted through the following databases: PubMed, Scopus, EBSCO, Web of Science, and Google Scholar using terms related to COVID-19 and terms related to neurology; more details about the terms used in the search process are available in the appendix (Additional file 1). Primary search process and secondary search process before the final analysis included studies published between January 1\(^{st}\) 2020 and April 22\(^{nd}\) 2020. Moreover, additional studies referenced in selected papers were identified and included.

**Inclusion and Exclusion Criteria**

Inclusion criteria:

- Randomized controlled trials, non-randomized controlled trials, case-control studies, cohort studies, cross sectional studies, case series, and case reports.
- Studies involving patients diagnosed with COVID-19, regardless of age.
- Studies including clinical features of COVID-19 including NM, NC, or ND studies.
- Articles published in English or are otherwise translated to English.
Exclusion criteria:

- Articles not addressing the neurological aspects of the infection.
- Articles on cases with known neurological conditions before COVID-19 with no major neurological change during the infection (new symptoms or worsening of previous condition).
- Studies addressing any of the other five human coronaviruses.
- Studies published before 2020.

Study Selection

Four reviewers screened the titles and abstracts of retrieved records for eligibility using Rayyan software (14). Individual studies were critically appraised by applying a standardized appraisal form appropriate for the study type. Inter-rater disagreements were resolved following a discussion between the reviewers.

Data Extraction

Two reviewers extracted the following information: date of publication, country, study design, age, gender, previous comorbidities, general and neurological clinical features, laboratory findings, imaging findings, neurophysiological study findings, severity and outcome of the disease. We tried to obtain unpublished missing data by contacting authors.

Risk of Bias Assessment

Two reviewers assessed the risk of bias using the NIH Study Quality Assessment Tools for case series, cross sectional and cohort studies (15,16). Conflicts were resolved by consulting a third reviewer.

Data Synthesis and Analysis

We used a random effects model to calculate the pooled percentages for categorical variables and pooled means for continuous variables with their 95% confidence intervals (CIs) as the effect sizes. For data with median and inter-quartile range (IQR) or median and range, mean and standard deviation (SD) were calculated according to the equations by Luo et.al, Wan et.al, and Hozo et.al (17–19). I² statistic, T² (tau-squared) test, and Cochrane Q were used to assess heterogeneity among studies. Data analysis was done using comprehensive meta-analysis software.

We assessed the existence of publication bias by the Egger’s test (20). The existence of publication bias was determined by the degree of the funnel plot symmetry and we considered $P < .05$ as an evidence of the existence of publication bias.

Subgroup and Sensitivity Analysis
A subgroup analysis was done to compare clinical and diagnostic neurological features in patients with severe disease compared to patients with non-severe disease; this categorization was determined if the study classified them into these groups. Moreover, we performed a sensitivity analysis, in which the pooled estimates for each variable were recalculated, omitting one study at a time, to ensure that none of the included studies affected the results and to examine whether the overall effect size is statistically robust.

Outcome Measures

The main outcomes of this study were the frequency of NM, NC and ND findings. The main NM included but were not limited to: Headache, myalgia, weakness, dizziness, taste impairment (ageusia), smell impairment (anosmia), altered level of consciousness, behavioral changes, facial weakness, ataxia, abnormal movements (like tremor), hemiparesis, hemiplegia, vision impairment, cranial nerve dysfunction, numbness, paresthesia, and neuropathic pain. The NC included: Ischemic and hemorrhagic strokes, venous sinus thrombosis, meningitis, encephalitis, seizures, and rhabdomyolysis. The ND findings included: Laboratory findings (serum creatine kinase (CK), serum lactate dehydrogenase (LDH), neutrophil count, lymphocyte count, and monocyte count), CSF analysis, neuroimaging (MRI and CT), EEG, NCS, or EMG. Moreover, we examined the treatment associated neurological side effects or complications.

Ratings of the Quality of the Evidence

According to the modified rating scale of Oxford Centre for Evidence-based Medicine for ratings of individual studies(21), the evidence for most of the studies in our meta-analysis was rated as level four (case series without intervention, and cross sectional) and only two were rated as level three (retrospective cohort studies). Moreover, we included case reports in our qualitative assessment (evidence level four; case reports).

Results

Study Selection Results

The primary search yielded 6709 articles, with 41 articles remaining after removal of duplicates and screening titles, abstracts, and full texts. As a result of the rapid growth of the COVID-19 literature, a second search was conducted yielding another 23 articles. Forty-four articles were included in the final meta-analysis and 20 case reports were included in the qualitative descriptive review (Figure 1). Seventeen articles were available on the search databases but they were not yet published in their final form.

Demographics and Characteristics

Forty-four studies were included in the meta-analysis, 14 of which were available as pre-prints at the time of the search (Table 1). A total of 13480 patients were included in our analysis with a mean age of 50.3
(95% CI, 47.7 to 52.9) years, and 53% (95% CI, 50.2% to 55.7%) being males. Thirty-six (81.8%) studies were from China, two (4.5%) were from Italy, and the rest being one from each of Australia, France, Japan, Netherlands, Belgium and the UK. The study sample size ranged from 13 to 6606 patients per study.

The remaining 20 studies were included for the qualitative assessment of case reports (Table 2), three of them were available as pre-prints at the time of the search. These case reports included 57 patients with a mean age of 59.5 (± 20.2) years and 38 (67%) being males.

### Risk of Bias Assessment Results

Of the 44 studies included in the meta-analysis, 39 were considered as case series and they were assessed for risk of bias using the NIH Quality Assessment Tool for Case Series Studies (16). The study quality was rated as good, fair, or poor if the number of “Yes” responses were ≥6, 3 to 5, or ≤2, respectively. Of the 39-case series, 33 received a “fair” rating and 6 studies received a “good” rating.

Two studies were considered cohort studies and three were considered cross-sectional studies. They were assessed using the NIH Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies (15). The study quality was rated as good, fair, or poor if the number of “Yes” responses were ≥9, 4 to 8, or ≤3, respectively. All of the five included cohort and cross-sectional studies were given a “fair” rating.

Moreover, some questions of the previous quality assessment tools were not applicable to all studies. A more detailed illustration of the risk of bias assessment for each study is attached as a table in the supplementary appendix (Additional files 2 and 3).

### Clinical features and laboratory findings

The frequency of NM in COVID-19 patients was as follows: Myalgia (22.2%, 95% CI, 17.2% to 28.1%), taste impairment (19.6%, 95% CI, 3.8% to 60.1%), smell impairment (18.3%, 95% CI, 15.4% to 76.2%), headache (12.1%, 95% CI, 9.1% to 15.8%), dizziness (11.3%, 95% CI, 8.5% to 15.0%), encephalopathy or cognitive dysfunction (9.4%, 95% CI, 2.8% to 26.6%), and ataxia or abnormal gait (2.1%, 95% CI, 0.2% to 23.7%). Nearly, 2.5% (95% CI, 1% to 6.1%) of COVID-19 patients had acute cerebrovascular diseases (CVD); which included ischemic stroke (IS), intracerebral hemorrhage (ICH), and cerebral venous sinus thrombosis (CVT) (Table 3, additional file 4).

About a third of COVID-19 patients were severely affected (31.1%, 95% CI, 21.9% to 42.2%) and 20.6% (95% CI, 14.1% to 29.0%) were admitted to intensive care units. About 37.4% (95% CI, 33.1% to 41.9%) had a pre-existing comorbidity, and 5.7% (95% CI, 3.3% to 9.7%) had a preexisting neurological disease. Detailed characteristics of the pre-existing comorbidities are presented in (Table 3, additional file 5).

Regarding laboratory abnormalities (Table 1, additional file 6), the mean values were as follows: CK: 85.57 U/L (Normal range; 40-200 U/L), LDH: 263.49 U/L (Normal range; 120–250 U/L). The mean lymphocyte, neutrophil, and monocyte count were 1.08, 3.44, and 0.39 (*10^9/L), respectively.
No published data regarding COVID-19 treatment related neurological side effects and complications were found.

Publication Bias

According to Egger et al. (20), publication bias assessment is only reliable for 10 or more pooled studies. Therefore, we presented the results of publication bias for variables that were discussed in 10 or more studies (Additional file 7). Publication bias was observed in the following variables: fever ($p < .001$), headache ($p < .001$), serum LDH ($p = .0015$), Diabetes Mellitus (DM) ($p = .0089$), pre-existing neurological diseases ($p = .0089$), malignancy ($p = .031$), and chronic kidney disease (CKD) ($p = .044$).

Sensitivity analysis

A sensitivity analysis, in which the meta-analysis was serially repeated after the exclusion of each study, demonstrated that no individual study affected the overall prevalence for each variable except for the following: Taste impairment prevalence was reduced from 19.6% to 10.9% when the study by Spinato et al. was excluded (60); smell impairment prevalence was reduced from 18.3% to 7.5% when the study by Lechien et al. was excluded (53), and increased to 35.2% when the study by Mao et al. was removed (6). After excluding the study conducted by Guan et al., the reported frequency of NC increased from 3% to 5.8% (2). More details can be found in additional file 8.

Subgroup analysis

When comparing severe to non-severe COVID-19 patients, the severe group included older patients [mean age 60 vs 44.7 years-old, $p < .001$] and more males [60.3% vs 48.6%, $p = .001$] than the non-severe group. Myalgia [34.9% vs 4.1%, $p = .045$], acute CVD [34.9% vs 4.1%, $p = .045$], higher CK value [324.9 vs 121.2 U/L, $p = .01$], and higher LDH value (247.6 vs 83.0 U/L, $p = .012$) were more likely in the severe group. While encephalopathy and cognitive dysfunction were more frequent in the severe group [16.9% vs 1.9%, $p = .054$], this was not statistically significant. There was no significant difference for the rest of the variables evaluated (Table 4). Heterogeneity was significant for all the variables and was not resolved by subgroup analysis.

Qualitative assessment

Twenty case reports (57 patients) were identified and their details are summarized in Table 5. Six (10.5%) patients were diagnosed with GBS 5-10 days after the onset of respiratory symptoms (69,72). Their neurological symptoms included numbness, weakness, dysphagia, and facial weakness; four patients (7.0%) had facial weakness including one (1.8%) with facial diplegia. All of these patients had abnormal NCS/EMG findings consistent with an axonal variant in three patients and a demyelinating variant in two.

Besides the above-mentioned EMG/NCS abnormalities, ND findings included neuro-imaging, CSF, and EEG findings. Neuro-imaging utilized were head CT, brain MRI and spinal MRI. Six patients had significant neuroimaging findings, including two patients with cerebral hemorrhage (12,66), one patient
with encephalitis/ventriculitis (11), two GBS patients with enhancement of the caudal nerve roots (72), and one GBS patient with bilateral enhancement of facial nerves (72). Besides, six (10.5%) patients had CSF changes; mainly increased protein in five (8,69,72), and only one with SARS-CoV-2 RNA detected in CSF using RT-PCR assay (11). Lastly, one patient had EEG changes consisting of bilateral and focal slowing in the left temporal region with left temporal sharp waves (8).

Twelve patients received neurology-related management including IVIG in eight patients, and four who used one or more of the following therapies: ceftriaxone, vancomycin, acyclovir, ganciclovir, steroids, levetiracetam, phenytoin, plasma exchange, or vitamin B12.

Of note, some NM and ND findings were reported by a few studies, out of the 44 studies, and were insufficient to be included in the meta-analysis. These included manifestations like visual impairment (6), nerve pain (6), and diffuse corticospinal tract signs with enhanced tendon reflexes, ankle clonus, and bilateral extensor plantar reflexes (52). CSF findings included positive oligoclonal bands with the same pattern in serum, elevated CSF IgG and CSF protein levels, and low albumin level (52). Head CT findings included ischemic stroke, cerebral hemorrhage, and cerebral venous sinus thrombosis (6,10). Brain MRI findings included leptomeningeal enhancement, bilateral frontotemporal hypoperfusion, and acute and subacute ischemic strokes (52). EEG findings included nonspecific changes and slowing consistent with encephalopathy (52).

Discussion

A total of 13480 COVID-19 patients were included in the meta-analysis. NM were frequent with around 20% of patients reporting myalgia, taste impairment, or smell impairment; and around 10% complaining of headache, dizziness, or encephalopathy. Ataxia or abnormal gait was the least reported NM. Five studies reported NC (CVD, seizures, and rhabdomyolysis). CVDs (IS, ICH, CVT) occurred in 2.5% of patients. For those who were tested, high levels of CK and LDH as markers of muscle injury were found, especially in the severe subgroup. About one third of patients included in this study had severe disease course and one fifth of them were admitted to the ICU.

There is a mounting evidence that Angiotensin Converting Enzyme 2 (ACE 2) receptors are expressed throughout the central nervous system, primarily on the surface of neurons (79), and SARS-CoV-2 might use these receptors to gain entry into the nervous system (3,4,80). The result of direct neuronal invasion could explain manifestations such as headache, dizziness, ataxia and encephalopathy, while neuronal death and inflammation could explain complications like meningitis/encephalitis (11,81), as well as seizures or even refractory status epilepticus (82,83). Interestingly, direct invasion of the respiratory centers in the brainstem was proposed as a contributing factor to the respiratory failure in COVID-19 patients (3,84).

Viral entry into the CNS is debatable. This could happen via a hematogenous route in which the virus passes through the blood brain barrier (BBB) by transcytosis or infects endothelial or epithelial cells to
cross the BBB (4,11). Alternatively, the virus could infect and get transported by leukocytes into the CNS, as was shown for SARS-CoV(85).

Moreover, ACE 2 receptor is heavily expressed on the epithelial cells of the mucosa of the oral cavity (86) and a trans-neural transmission of SARS-CoV through the olfactory bulb was seen in a mice model (87). These findings could explain the occurrence of anosmia and ageusia in COVID-19 patients, which at times can be the only presenting features or the very early symptoms of COVID-19(53).

Myalgia and occasionally clinically significant muscle injury in severe disease, as evidenced by elevated CK and LDH, can be either a direct response of viral invasion of the skeletal muscles, which are also known to express ACE2 receptor(80), or an indirect response to the systemic inflammatory reaction manifested by a cytokine storm, subsequently causing muscle injury(88,89).

Multiple mechanisms could explain the increased risk of ischemic strokes and venous sinus thrombosis; these include hypercoagulability (6), high systemic inflammatory response or “cytokine storm” (90), vascular endothelial injury (59), and cardiac injury resulting in cerebral embolism (91).

According to our analysis, myalgia and evidence of muscle injury “elevated CK and LDH” as well as CVD were more likely to occur with severe disease. This might be related to the degree of the inflammatory response and the reported cytokine release syndrome (92) as well as the prothrombotic state (93) that occur with severe cases of COVID-19 and contribute to the multiorgan failure (22,94).

Congruent with what Mao et al(6) reported in the first retrospective observational case series describing the NM of COVID-19 in 214 hospitalized patients in Wuhan-China, our meta-analysis shows that myalgia or skeletal muscle injury (with elevated LDH and CK) and acute CVDs are predominantly associated with severe COVID-19.

A recent systematic review of 8 studies (95), not including a meta-analysis, suggested that some patients, particularly those with severe illness, have CNS involvement and NM, which is supported by the results of our study. Montalvan et al (96) concluded that symptoms of hyposmia, headaches, weakness, and altered consciousness, and complications like encephalitis, demyelination, neuropathy, and stroke were associated with coronaviruses infections. Those results are congruent with our findings, although we looked at SARS-CoV-2 exclusively, while they evaluated other human coronaviruses in addition. The authors also suggested that trans-synaptic extension through the cribriform plate and olfactory bulb represents the main mechanism of neuro-invasion, and that invasion of the medulla could contribute to the respiratory failure in critically ill COVID-19 patients. Ahmad et al (97) in a narrative literature review reported that neurological features could occur before the classical features of COVID-19 like fever and cough, and accordingly a high index of suspicion is needed for a timely diagnosis and isolation of cases.

In the 20 case reports we evaluated, the most common NM included fatigue, myalgia, and smell and taste impairment, which is quite similar to our meta-analysis results. NC included GBS (6 cases), encephalitis, seizures, ICH, IS, myelitis and rhabdomyolysis. GBS associated with COVID-19 indicates that SARS-CoV-2
can potentially induce an immune response that results in a delayed neurological complication (98). This association between coronaviruses and GBS was reported before (98,99). In these case reports, the neurological outcome was variable, but one fourth of patients were left with residual deficits after 2 weeks of COVID-19 disease onset, indicating potential severity of the neurological injury.

Quality of the Evidence

We believe that the evidence generated from our meta-analysis is reliable since it is based on fair to good quality studies and well-defined search methods and eligibility criteria. More than 40 studies in varied populations have been included in the final meta-analysis, with emphasis on avoiding overlapping data. In addition, we performed a subgroup analysis to test if there is an association between neurological manifestations of COVID-19 and severity of the disease. We followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist to prepare this study (13).

Limitations

Limitations of our analysis include the heterogeneity among the studies being considerably high both in the overall population and following the subgroup analysis. This is due to the large variation in the sample size among studies, the different study designs and methodologies, and possibly reflecting a true variation between different populations. A random effect model was set a priori since significant heterogeneity was expected. Besides, most of the included studies collected the data retrospectively. Finally, egger test indicated that there is a possible publication bias among the following variables: Fever, headache, serum LDH, DM, pre-existing neurological diseases, malignancy, and CKD. There is a possibility that some unpublished studies were not identified as our meta-analysis was limited to studies published in English-language and since many studies were not yet published at the time of screening. However, we tried to avoid publication bias by including studies translated into English as well as including pre-prints and contacting authors.

Conclusion

In this meta-analysis on the neurological features of COVID-19, we found that several NM and NC are associated with COVID-19, and certain features, such as CVD, muscle injury, and probably encephalopathy, might be associated with severe disease status. Healthcare professional dealing with COVID-19, neurologists, and the general public should be aware of the neurological involvement of the disease. Patients of possible COVID-19 presenting with the previously mentioned neurological features should trigger clinical suspicion. Further studies are required to assess the prevalence of the neurological aspects of COVID-19 in different populations and to directly compare them between severe and non-severe subgroups. More pathophysiological analysis and studies are required as well in order to understand the exact mechanism through which the virus affects the nervous system.

List Of Abbreviations
EEG: Electroencephalography
EMG: Electromyography
CK: Creatine Kinase
CNS: Central Nervous System
COVID-19: Coronavirus Disease 2019
CSF: Cerebrospinal Fluid
CT: Computed Tomography
LDH: Lactate Dehydrogenase
MRI: Magnetic Resonance Imaging
NCS: Nerve Conduction Study
SARS-CoV-2: Severe Acute Respiratory Syndrome Coronavirus 2
PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses
BBB: Blood Brain Barrier
NM: Neurological Manifestations
NC: Neurological Complications
ND: Neurodiagnostic

**Declarations**

*Ethics approval and consent to participate*

Not applicable.

*Consent for publication*

Not applicable.

*Availability of data and materials*

All data synthesized and analyzed are included in this published article.

*Competing interests*
The authors declare that they have no competing interests.

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**Contribution**

AY designed the study, searched the literature, screened the records, assessed the risk of bias, and drafted and revised the manuscript. MN designed the study, searched the literature, extracted and synthesized the data, undertook statistical analyses and interpretation, and drafted the manuscript. AA designed the study, searched the literature, assessed the risk of bias, extracted and synthesized the data, and drafted the manuscript. KA screened the records, interpreted the data, and drafted and revised the manuscript. KE screened the records, interpreted the data, and drafted and revised the manuscript. OS undertook
statistical analyses and interpretation, and revised the manuscript. MA screened the records, assessed the risk of bias, and drafted and revised the manuscript.

Qualifications

- **AY** is an Assistant Professor of Neurology and Neurology Residency Program Director at Jordan University of Science and Technology/ King Abdullah University Hospital. He did his Neurology residency and Clinical Neurophysiology and Epilepsy fellowships in the United States. He has the American Boards in Neurology, Clinical Neurophysiology, Epilepsy and Medical Quality.

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**Tables**

**Table 1:** Characteristics of the Included Studies in the Meta-Analysis of the Neurological Features of COVID-19
| #  | Author                  | Date (DD/MM/Y) | Journal                                         | Study type          | N    | Country | Reference | Study quality |
|----|-------------------------|----------------|------------------------------------------------|---------------------|------|---------|-----------|---------------|
| 1  | Chen and Wu, 2020       | 27-3-2020      | The Journal of Clinical Investigation           | Case series         | 21   | China   | (22)      | Fair          |
| 2  | Liu and Zhang, 2020     | Pre-print: 13-2-2020 | The Lancet Infectious Diseases        | Case series         | 24   | China   | (23)      | Fair          |
| 3  | Wang and Gao, 2020      | Pre-proof: 5-3-2020 | European Respiratory Journal                  | Case series         | 18   | China   | (24)      | Fair          |
| 4  | Giacomelli, 2020        | 26-3-2020      | Clinical Infectious Diseases                  | Cross-Sectional Study | 59   | Italy   | (25)      | Fair          |
| 5  | Mao, 2020               | 10-4-2020      | JAMA Neurology                                 | Case series         | 214  | China   | (6)       | Fair          |
| 6  | Xu and Yu, 2020         | 28-2-2020      | European Journal of Nuclear Medicine and Molecular Imaging | Case series         | 90   | China   | (26)      | Fair          |
| 7  | Jin, 2020               | 24-3-2020      | BMJ                                             | Case series         | 651  | China   | (27)      | Fair          |
| 8  | Chen and Zhou, 2020     | 15-2-2020      | The Lancet                                     | Case series         | 99   | China   | (28)      | Fair          |
| 9  | Li and Li, 2020         | Pre-print:12-2-2020 | MDrxiv                                          | Case series         | 17   | China   | (29)      | Fair          |
| 10 | Qian, 2020              | 17-3-2020      | QJM                                             | Case series         | 91   | China   | (30)      | Fair          |
| 11 | Xu and Wu, 2020         | 10-2-2020      | BMJ                                             | Case series         | 62   | China   | (31)      | Fair          |
| 12 | Huang and Wang, 2020    | 24-1-2020      | Lancet                                          | Case series         | 41   | China   | (32)      | Fair          |
| 13 | Wan, 2020               | 21-3-2020      | Journal of Medical Virology                    | Case Series         | 135  | China   | (33)      | Fair          |
| 14 | Yang and Yu, 2020       | 24-2-2020      | The Lancet Respiratory Medicine                | Cohort - Retrospective | 52   | China   | (34)      | Fair          |
| 15 | Liu and Fang, 2020      | 7-2-2020       | Chinese Medical Journal                         | Case series         | 137  | China   | (35)      | Fair          |
| 16 | Guan, 2020              | 28-2-2020      | The new england journal of medicine             | Case series         | 1099 | China   | (2)       | Fair          |
| 17 | Wang and Hu, 2020       | 7-2-2020       | JAMA                                            | Case series         | 138  | China   | (36)      | Fair          |
| 18 | Qin and Qiu, 2020       | Pre-print: 20-2-2020 | TheLancet                                    | Case series         | 89   | China   | (37)      | Good          |
| 19 | Yang and Cao, 2020      | 26-2-2020      | The Journal of Infection                       | Case series         | 149  | China   | (38)      | Fair          |
| 20 | Qin and Zhou, 2020      | 12-3-2020      | Clinical Infectious Diseases                   | Case series         | 452  | China   | (39)      | Fair          |
| 21 | Liu and Liu, 2020       | 12-2-2020      | Preprint: medRxiv                               | Case series         | 61   | China   | (40)      | Fair          |
| 22 | Easom, 2020             | 29-3-2020      | Influenza Other Respir Viruses                 | Case series         | 68   | UK      | (41)      | Fair          |
| 23 | Deng, 2020              | 20-3-2020      | Chinese Medical Journal                         | Case series         | 225  | China   | (42)      | Good          |
| 24 | Huang and Tu, 2020      | 27-2-2020      | Travel Medicine and Infectious Disease         | Case series         | 34   | China   | (43)      | Fair          |
| 25 | Mo, 2020                | 16-3-2020      | Clinical Infectious Diseases                   | Case series         | 155  | China   | (44)      | Fair          |
| 26 | Li and Wang, 2020       | Pre-print:17-3-2020 | The Lancet                               | Case series         | 221  | China   | (10)      | Good          |
| # | Authors and Year | Date | Journal | Type | Country | Grade |
|---|------------------|------|---------|------|---------|-------|
| 28 | Guo, 2020       | Pre-print: 14-4-2020 | The Lancet | Case series | China | (46) Good |
| 29 | Yan, 2020       | Pre-print: 6-4-2020 | The Lancet | Case series | China | (47) Good |
| 30 | Chang, 2020     | 17-3-2020 | JAMA | Case series | China | (48) Fair |
| 31 | Wang and Pan, 2020 | Pre-proof: 11-4-2020 | International Journal of Infectious Diseases | Case series | China | (49) Fair |
| 32 | Zhou and Sun, 2020 | Pre-print: 16-3-2020 | BMC Infectious Diseases | Case series | China | (50) Fair |
| 33 | Zheng and Xu, 2020 | 10-4-2020 | Journal of Clinical Virology | Case series | China | (51) Fair |
| 34 | Helms, 2020     | 15-4-2020 | NEJM | Case series | France | (52) Fair |
| 35 | Lechien, 2020   | 6-4-2020 | European Archives of Oto-Rhino-Laryngology | Cross-Sectional Study | Belgium, France, Spain, Italy | (53) Fair |
| 36 | Chen and Chen, 2020 | Pre-print: 1-4-2020 | The Lancet | Case series | China | (54) Fair |
| 37 | Jiang, 2020     | Pre-print: 14-4-2020 | medRxiv | Case series | China | (55) Good |
| 38 | Zhang, 2020     | Pre-proof: 9-4-2020 | Journal of Clinical Virology | Case series | China | (56) Fair |
| 39 | Tabata, 2020    | Pre-print: 18-3-2020 | The Lancet | Case series | Japan | (57) Fair |
| 40 | Lei, 2020       | Pre-proof: 9-4-2020 | Travel Medicine and Infectious Disease | Case series | Guangzhou, China | (58) Fair |
| 41 | Zhou and Yu, 2020 | 28-3-2020 | The Lancet | Cohort - Retrospective | China | (59) Fair |
| 42 | Spinato, 2020   | 22-4-2020 | JAMA | Cross-sectional Study | Italy | (60) Fair |
| 43 | Klok, 2020      | 10-4-2020 | Thrombosis Research | Case series | Netherlands | (61) Fair |
| 44 | CNIRST, 2020    | 19-4-2020 | NA | Case series | Australia | (62) Fair |

DD/MM/Y, Day, Month, Year. NA, not applicable

Table 2: Characteristics of Included Case Reports
| #  | Author                        | Date (DD/MM/Y)                  | Journal                                               | Study type         | N | Country       | Reference |
|----|-------------------------------|---------------------------------|-------------------------------------------------------|--------------------|---|---------------|-----------|
| 1  | Moriguchi, 2020               | Pre-Print: 25-3-2020            | International Journal of Infectious Diseases          | Case Report        | 1 | Japan         | (11)      |
| 2  | Zhao and huang, 2020          | Pre-Print: 9-4-2020             | medRxiv preprint                                      | Case Report        | 1 | China         | (63)      |
| 3  | Lorenzo Villalba, 2020        | 3-4-2020                        | European Journal of Case Reports in Internal Medicine | Case Report        | 2 | France and Spain | (64)  |
| 4  | Ollarves-Carrero, 2020        | 13-4-2020                       | Travel Medicine and Infectious Disease                | Case Report        | 1 | Spain         | (65)      |
| 5  | Sharifi-Razavi, 2020          | 27-3-2020                       | New Microbes and New Infections                       | Case Report        | 1 | Iran          | (66)      |
| 6  | Marchese-Ragona, 2020         | Pre-print: 7-4-2020             | MedRxiv preprint                                      | Case Report        | 6 | Italy         | (9)       |
| 7  | Novi, 2020                    | 9-4-2020                        | Multiple sclerosis and related disorders              | Case Report        | 1 | Italy         | (67)      |
| 8  | Poyiadji, 2020                | 31-3-2020                       | Radiology                                             | Case Report        | 1 | USA           | (12)      |
| 9  | Karimi, 2020                  | 24-3-2020                       | Iran Red Crescent Med J                               | Case Report        | 1 | Iran          | (68)      |
| 10 | Zhao and shen, 2020           | 1-4-2020                        | Lancet Neurology                                      | Case Report        | 1 | China         | (69)      |
| 11 | Gane, 2020                    | 29-3-2020                       | Rhinology                                             | Case Report        | 1 | United Kingdom | (70)      |
| 12 | Hjelmesæth, 2020              | 5-4-2020                        | Tidsskr Nor Legeforen                                | Case Report        | 3 | Norway        | (71)      |
| 13 | Toscano, 2020                 | 17-4-2020                       | NEJM                                                  | Case Report        | 5 | Italy         | (72)      |
| 14 | Filatov, 2020                 | 21-3-2020                       | Cureus                                                | Case Report        | 1 | USA           | (8)       |
| 15 | Suwanwongse, 2020             | 6-4-2020                        | Cureus                                                | Case Report        | 1 | USA           | (73)      |
| 16 | Wang and Hajizadeh, 2020      | 08-04-2020                      | Journal of Thrombosis and Haemostasis                 | Case Report        | 3 | USA           | (74)      |
| 17 | Wang and Chen, 2020           | 09-02-2020                      | Bioscience Trends                                     | Case Report        | 4 | China         | (75)      |
| 18 | Ren, 2020                     | 05-05-2020                      | Chinese Medical Journal                               | Case Report        | 5 | China         | (76)      |
| 19 | Rothe, 2020                   | 05-03-2020                      | NEJM                                                  | Case Report        | 1 | Germany       | (77)      |
| 20 | Wang and Tang, 2020           | 27-01-2020                      | Journal of Medical Virology                           | Case Report        | 17| China         | (78)      |

DD/MM/Y, Day, Month, Year.

Table 3: Meta-analysis of the clinical characteristics of the study subjects
|                          | Pooled effect size (95% CI) | Heterogeneity | Tau squared | # of studies |
|--------------------------|-----------------------------|---------------|-------------|--------------|
|                          | Q value | P value | I Squared |              |              |
| Mean age (Years)         | 50.3 (47.7-52.9) | 2872.2 | < .001 | 98.50 | 72.58 | 44 |
| Male                     | 53.0 (50.2-55.7) % | 180.71 | < .001 | 77.31 | 8.97 | 42 |
| Clinical features        |                          |              |            |              |              |
| Headache                 | 12.1 (9.1-15.8) % | 989.99 | < .001 | 96.26 | 0.824 | 38 |
| Myalgia                  | 22.2 (17.2-28.1) % | 621.55 | < .001 | 94.85 | 0.740 | 33 |
| Taste impairment         | 19.6 (3.8-60.1) % | 431.04 | < .001 | 99.30 | 3.405 | 4  |
| Smell impairment         | 18.3 (1.54-76.2) % | 853.88 | < .001 | 99.64 | 7.254 | 4  |
| Dizziness                | 11.3 (8.5-15.0) % | 27.85 | .001  | 67.68 | 0.156 | 10 |
| Features of encephalopathy or cognitive dysfunction | 9.4 (2.8-26.6) % | 133.92 | < .001 | 95.51 | 2.70 | 7  |
| Ataxia or abnormal gait  | 2.1 (0.2-23.7) % | 6.59 | .010  | 84.83 | 3.18  | 2   |
| Fever                    | 80.6 (74.9-85.3) % | 1604.55 | < .001 | 97.44 | 1.05  | 42  |
| Cough                    | 64.1 (59.9-68.0) % | 575.30 | < .001 | 93.04 | 0.26  | 41  |
| Neurological complications * | 3.0 (0.9-9.6) % | 50.01 | < .001 | 92.00 | 1.66  | 5   |
| Acute CVD                | 2.5 (1.0-6.1) % | 15.3 | 0.004 | 74.41 | 0.72  | 5   |
| Laboratory findings      |                          |              |            |              |              |
| Serum CK (U/L)           | 85.5 (73.8-97.3) | 369.93 | < .001 | 96.21 | 434.78 | 15  |
| Serum LDH (U/L)          | 263.4 (234.6-292.3) | 648.50 | < .001 | 97.84 | 3026.56 | 15  |
| Lymphocyte (*10^9/L)     | 1.08 (1.02-1.14) | 549.37 | < .001 | 95.08 | 0.024 | 28  |
| Neutrophils (*10^9/L)    | 3.44 (3.21-3.68) | 214.45 | < .001 | 90.67 | 0.244 | 21  |
| Monocytes (*10^9/L)      | 0.39 (0.37-0.42) | 42.66 | < .001 | 78.90 | 0.001 | 10  |
| Severe COVID-19          | 31.1 (21.9-42.2) % | 739.23 | < .001 | 97.02 | 1.16  | 23  |
| ICU admission            | 20.6 (14.1-29.0) % | 231.12 | < .001 | 91.34 | 0.81  | 21  |
| Comorbidities            |                          |              |            |              |              |
| Any previous comorbidity | 37.4 (33.1-41.9) % | 274.90 | < .001 | 89.08 | 0.231 | 31  |
| Diabetes Mellitus        | 10.3 (8.3-12.8) % | 265.15 | < .001 | 88.68 | 0.360 | 31  |
| Hypertension             | 20.4 (17.0-24.2) % | 196.73 | < .001 | 87.292 | 0.253 | 26  |
| Heart diseases           | 9.7 (7.2-12.9) % | 426.59 | < .001 | 93.201 | 0.706 | 30  |
| Neurological diseases    | 5.7 (3.3-9.7) % | 175.60 | < .001 | 90.319 | 1.213 | 18  |
| Condition                     | Rate (95% CI) | \( \chi^2 \)  | \( \text{df} \) | \( p \)  | \( \phi \)  | \text{RR} |
|-------------------------------|---------------|----------------|-----------------|--------|---------|---------|
| Malignancy                    | 2.7 (2.0-3.6) | 61.429         | < .001          | 59.303 | 0.319   | 26      |
| Pulmonary diseases            | 3.4 (2.2-5.0) | 260.24         | < .001          | 89.240 | 0.973   | 29      |
| Chronic kidney disease        | 2.3 (1.3-3.9) | 75.189         | < .001          | 81.380 | 0.858   | 15      |
| Chronic liver disease         | 3.5 (2.6-4.7) | 32.726         | .005            | 54.165 | 0.187   | 16      |
| Smoking                       | 9.2 (6.4-13.0) | 146.643        | < .001          | 89.771 | 0.501   | 16      |

*Neurological complications include: Cerebrovascular diseases (ischemic stroke, cerebral hemorrhage, and venous sinus thrombosis), rhabdomyolysis, and seizures.

P < .05 indicates the presence of heterogeneity.

**Table 4: Subgroup analysis between severe and non-severe groups**
| Study                              | Subgroup   | Pooled effect size (95% CI) | Heterogeneity | Tau squared | Mixed effects analysis |
|------------------------------------|------------|-----------------------------|---------------|-------------|------------------------|
|                                    |            |                             | Q value       | Df (Q)      | P value†               | I Squared | P value             |
| Age (Years)                        | Total      | 56.9 (55.1-58.8)            | 1443.18       | 34          | < .001                 | 97.64     | 107.603             | < .001    |
|                                    | Non severe | 44.4 (40.1-48.7)            | 585.98        | 16          | < .001                 | 97.26     | 77.40               |
|                                    | Severe     | 60.0 (57.9-62.1)            | 78.77         | 17          | < .001                 | 78.418    | 13.35               |
| Male                               | Total      | 53.1 (49.5-56.6) %          | 108.58        | 31          | < .001                 | 71.45     | 0.104               | .001      |
|                                    | Non severe | 48.6 (44.2-53.1) %          | 54.23         | 15          | < .001                 | 72.34     | 0.082               |
|                                    | Severe     | 60.3 (54.7-65.7) %          | 36.90         | 15          | < .001                 | 59.36     | 0.104               |
| Clinical features                  |            |                             |               |             |                        |          |                    |
| Headache                           | Total      | 14.8 (12.4-17.5) %          | 187.25        | 30          | < .001                 | 83.97     | 0.474               | .308      |
|                                    | Non severe | 12.2 (7.9-18.2) %           | 170.26        | 15          | < .001                 | 91.19     | 0.730               |
|                                    | Severe     | 15.4 (12.7-18.5) %          | 16.27         | 14          | .296                   | 14.003    | 0.025               |
| Myalgia                            | Total      | 24.4 (18.2-32.0) %          | 167.89        | 18          | < .001                 | 89.279    | 0.468               | .045      |
|                                    | Non severe | 19.4 (13.1-27.9) %          | 102.34        | 9           | < .001                 | 91.206    | 0.463               |
|                                    | Severe     | 34.9 (22.3-49.9) %          | 58.061        | 8           | < .001                 | 86.221    | 0.651               |
| Dizziness                          | Total      | 11.9 (8.7-16.0) %           | 16.073        | 7           | .024                   | 56.449    | 0.106               | .506      |
|                                    | Non severe | 10.9 (7.4-16.1) %           | 10.27         | 4           | 0.036                  | 61.076    | 0.145               |
|                                    | Severe     | 13.5 (8.2-21.5) %           | 5.619         | 2           | .06                    | 64.409    | 0.152               |
| Features of Encephalopathy / cognitive dysfunction | Total      | 3.2 (1.2-8.4) %            | 116.97        | 6           | < .001                 | 94.87     | 4.753               | .054      |
|                                    | Non severe | 1.9 (0.6-5.8) %            | 2.266         | 2           | .322                   | 11.743    | 0.167               |
|                                    | Severe     |                             |               |             |                        |          |                    |           |
|                          | Total          | Non severe     | Severe          | **p-value** | **95% CI**  |
|--------------------------|----------------|----------------|-----------------|-------------|------------|
| **Fever**                |                |                |                 |             |            |
| Total                    | 79.8 (71.6-86.2) % | 313.83         | 238.40          | < .001      | 93.708     | 2.63       |
| Non severe               | 76.9 (66.3-85.0) % | 141.37         | 135.46          | < .001      | 89.66      | 0.734      |
| Severe                   | 86.5 (72.6-93.9) % |                 |                 |             |            |            |
| **Cough**                |                |                |                 |             |            |
| Total                    | 59.2 (52.8-65.3) % | 285.48         | 141.37          | < .001      | 89.39      | 0.302      |
| Non severe               | 55.8 (48.2-63.2) % | 171.78         | 135.46          | < .001      | 89.39      | 0.302      |
| Severe                   | 67.4 (55.9-77.2) % |                 |                 |             |            |            |
| **Neurological Complications** |          |                |                 |             |            |
| Total                    | 3.8 (1.3-10.0) % | 82.532         | 37.55           | < .001      | 89.34      | 1.607      |
| Non severe               | 1.3 (0.2-8.8) % | 17.18          | 7               | < .001      | 88.35      | 2.663      |
| Severe                   | 5.6 (1.7-17.1) % |                 |                 |             |            |            |
| **Acute CVD**            |                |                |                 |             |            |
| Total                    | 2.6 (1.1-5.8) % | 33.02          | 15.38           | < .001      | 74.00      | 0.797      |
| Non severe               | 0.6 (0.1-3.1) % | 4.57           | 4               | < .001      | 89.34      | 1.607      |
| Severe                   | 4.1 (1.6-10.0) % |                 |                 |             |            |            |
| **Laboratory findings**  |                |                |                 |             |            |
| **Serum CK**             |                |                |                 |             |            |
| Total                    | 91.5 (79.3-103.7)     | 90.95         | 15              | < .001      | 83.505     | 377.38     |
| Non severe               | 83.0 (69.1-96.8) % | 53.346        | 7               | < .001      | 86.87      | 276.03     |
| Severe                   | 121.2 (95.4-147.1)  |                 |                 |             |            |            |
| **Serum LDH**            |                |                |                 |             |            |
| Total                    | 270.6 (243.1-298.1) | 494.931       | 66.42           | < .001      | 89.462     | 4195.36    |
| Non severe               | 247.6 (214.8-280.4) | 272.42        | 7               | < .001      | 97.43      | 1997.9     |
| Severe                   | 324.9 (274.4-375.4) |                 |                 |             |            |            |
| **Preexisting neurological diseases** |          |                |                 |             |            |
| Total                    | 4.5 (2.8-7.0) %   | 101.58         | 36.692          | < .001      | 78.19      | 0.970      |
| Non severe               | 2.6 (1.2-5.5) %   | 36.692         |                 | < .001      | 78.19      | 0.970      |

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**Table 5: Patients characteristics and findings of the included case reports**

| Severe | 6.2 (3.5-10.9) | 42.959 | 11 | < .001 | 74.39 | 0.772 |
|--------|----------------|--------|----|--------|-------|-------|

*CVD (Cerebrovascular diseases): Ischemic stroke, cerebral hemorrhage, and venous sinus thrombosis.
†P < .05 indicates the presence of heterogeneity.
| Variable                              | N (%) or Mean± SD |
|---------------------------------------|-------------------|
| Number Cases                         | 57                |
| Articles                             | 20                |
| Countries of the cases reported      |                   |
| China                                 | 28 (49.1%)        |
| Italy                                | 12 (21.0%)        |
| USA                                  | 6 (10.5%)         |
| Norway                               | 3 (5.3%)          |
| Iran                                 | 2 (3.5%)          |
| Spain                                | 2 (3.5%)          |
| France                               | 1 (1.8%)          |
| Germany                              | 1 (1.8%)          |
| Japan                                | 1 (1.8%)          |
| UK                                   | 1 (1.8%)          |
| Age (Years)                          | 59.5 ± 20.2       |
| Gender                               |                   |
| Male                                 | 38 (66.6%)        |
| Female                               | 19 (33.3%)        |
| Comorbidities                         |                   |
| Any                                  | 24 (42.1%)        |
| DM                                   | 7 (12.3%)         |
| Hypertension                         | 13 (22.8%)        |
| Cardiovascular diseases              | 9 (15.7%)         |
| Neurological diseases                | 8 (14.0%)         |
| Chronic liver diseases               | 3 (5.2%)          |
| Pulmonary diseases                   | 5 (8.8%)          |
| Malignancy or cancer                 | 1 (1.8%)          |
| Chronic kidney disease               | 4 (7%)            |
| ICU                                  |                   |
| Yes                                  | 16 out of 28 (57.1%) |
| No                                   | 12 out of 28 (42.8%) |
| Onset (Days) *                       | 7.7 ± 2.9         |
| Ventilator                           |                   |
| Yes                                  | 11 out of 31 (35.4%) |
| No                                   | 20 out of 31 (64.5%) |
| Clinical features                    |                   |
| Fever                                | 41 (71.9%)        |
| Cough                                | 34 (59.6%)        |
| Fatigue                              | 14 (25.6%)        |
| Myalgia                              | 12 (21.0%)        |
| Headache                             | 5 (8.8%)          |
| Dizziness                            | 2 (3.5%)          |
| Taste impairment                     | 11 (19.3%)        |
| Smell impairment                     | 13 (22.8%)        |
| Encephalopathy features              | 5 (8.8%)          |
| Weakness/ paralysis                  | 7 (12.3%)         |
| Altered reflexes                     | 3 (5.3%)          |
| Altered sensation**                  | 5 (8.8%)          |
| Ataxia or abnormal gait              | 1 (1.8%)          |
| Facial weakness                      | 4 (7%)            |
| Neck pain/ rigidity                  | 2 (3.5%)          |
| Number of neurological manifestations |                   |
| None                                 | 20 (35.0%)        |
| 1-2                                  | 27 (47.3%)        |
| >3                                   | 10 (17.5%)        |
| Neurological complications           |                   |
| Any                                  | 12 (21.0%)        |
| GBS                                  | 6 (10.5%)         |
| Encephalitis                         | 2 (3.5%)          |
| Seizure                              | 2 (3.5%)          |
| Cerebral Hemorrhage                  | 1 (1.8%)          |
| Myelitis                             | 1 (1.8%)          |
| Rhabdomyolysis                       | 1 (1.8%)          |
| Onset (Days)*                        | 7.25 ± 2.43       |
| Imaging                              |                   |
| CT/MRI changes                       | 6 (10.5%)         |
| CSF                                  |                   |
| Increased protein                    | 5 (8.8%)          |
| SARS-CoV-2 RNA in CSF                | 1 (1.8%)          |
| Severity of COVID-19 | Onset (Days) * | 7 ± 2.49 |
|---------------------|----------------|----------|
| Asymptomatic        | 3 (5.3%)       |          |
| Non-severe          | 19 (33.3%)     |          |
| Severe              | 30 (52.6%)     |          |

| Nerve conduction study/EMG | EEG                   | Temporal slowing and sharp waves | 1 (1.8%) |
|----------------------------|-----------------------|---------------------------------|----------|
| Demyelinating or Axonal patterns |                      |                                 |          |

| Neurology-related management | Neurological outcome | Morbidity/ disability | 4 out of 16 (25%) |
|-----------------------------|----------------------|-----------------------|-------------------|
| Demyelinating or Axonal patterns |          |                      |                   |

| COVID-19 disease outcome | Death | 20 out of 45 (44.4 %) |
|--------------------------|-------|-----------------------|
| Discharged/ Recovery     | 18 out of 45 (40 %) |
| Still hospitalized       | 7 out of 45 (15.5 %) |

Some data are missing or not reported. All patients in the aforementioned case reports were confirmed to have COVID-19.

GBS; Guillain–Barré Syndrome

* Onset in relation to the onset of COVID-19 symptoms

**Altered sensation included paresthesia, numbness, loss of pain, temperature, or tactile sensations of the lower limbs, upper limbs, or trunk.

Figures
Figure 1
Flow diagram of study selection

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