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|  | **Table 1.** Studies Included in Systematic Review |
| Authors | Study Type | Country Location | Study Group | Age, Median (IQR, y) or Mean ± SD | Neurologic Symptoms No. (% of total) | Key Findings | Limitations | Study Quality Level |
| Huang et al,3 2020 | Prospective Cohort | China | 41 patients with RT-PCR positive COVID-19 from throat swab | 49 (41- 58 y) | * Headache, 3 (8%)
* Myalgia, 18 (44%)
 | * Subjects were 13/41 (32%) ICU patients and 28/41 (68%) non-ICU patients
* Headache was more common in non-ICU patients (12% vs 0%)
* Myalgia was more common in ICU patients (54% vs 39%)
* 13/40 (33%) patients had elevated CK levels (> 185 U/L) and more common in ICU patients (46% vs 26%)
 | * Not specifically studied neurological symptoms
* No clear definition of symptoms
* Diagnostic test was limited
 | 2 |
| Guan et al,4 2020 | Cross Sectional | China | 1099 patients with RT-PCR positive COVID-19 from nasopharyngeal and throat swab  | 47 (35-58 y) | * Headache, 150 (13.6%)
* Nausea or Vomiting, 55 (5 %)
* Myalgia or Arthralgia, 164 (14.90%)
 | * Data obtained from 522 hospitals in 30 provinces in mainland China
* Based from disease severity, 926/1099 (84%) were mild and 173/1099 (16%) were severe cases
* In severe cases, patients were more likely to present with headache (15% vs 13.4%), nausea or vomiting (6.9% vs 4.6%), myalgia or arthralgia (17.3% vs 14.5%), and CVD comorbidity (2.3% vs 1.2%)
* 15/1099 (1.40%) patients had CVD comorbidity
* 90/657 (13.7%) patients had elevated CK levels (>200 U/L) and more common in severe cases (19% vs 12.5%)
* 260/560 (46.4%) patients had elevated D-dimer ( ≥ 0.5 mg/L) and more common in severe cases (59.6% vs 43.2%)
 | * No clear definition of symptoms
* Not specifically studied neurological manifestation
* Diagnostic test was limited
 | 4 |
| Mao et al,5 2020 | Retrospective Cohort | Wuhan, China | 214 patients with RT-PCR positive COVID-19 from throat swab | Mean Age (y) ± SD: 52.7y ± 15.5 | Central Nervous Symptoms:* Dizziness, 36 (16,8%)
* Headache, 28 (13.1%)
* Impaired consciousness, 16 (7.5%)
* CVD, 6 (2.8%)
* Ataxia, 1 (0.5%)
* Epilepsy, 1 (0.5%)

Peripheral Nervous Symptoms:* Hypogeusia, 12 (5.6%)
* Hyposmia, 11 (5.1%)
* Hypopsia, 3 (1.4%)
* Neuralgia, 5 (2.3%)
* Muscle injury, 23 (10.7%)
 | * Based from disease severity, 126/214 (58.9%) were mild and and 88/214 (41.1%) were severe cases
* Patients with severe COVID-19 were more likely to present with nervous system symptoms (45.5% vs 30.2%, p<0.05), impaired consciousness (14.8% vs 2.4%, p<0.001), CVD (5.7% vs 0.8%, p<0.05), and muscle injury (19.3% vs 4.8%, p<0.001)
* 78/214 (36.4%) patients had nervous system symptoms classified into: CNS, 53(24.8%); PNS, 19 (8.9%); and skeletal muscular symptoms, 23(10.7%).
* CK levels was higher in severe patients (83 vs 59, p=0.004)
* Most neurologic symptoms occurred in the early stages of disease (median time, 1-2 days), Apart from CVD and impaired consciousness (median time, 8-9 days)
* 40/214 (18.7%) patients were admitted to ICU for severe neurological manifestations.
 | * No clear definition of symptoms
* Incomplete data or observation as the study had ended
* Diagnostic test was limited
 | 3 |
| Wan et al,9 2020 | Retrospective Cohort | Chongqing, China | 135 hospitalized patients with RT-PCR positive COVID-19 from throat swab | 47 (36-55 y) | * Headache, 24 (17.7%)
* Myalgia, 44 (32.5%)
 | * Based from disease severity, 95/135 (70.4%) were mild and 40/135 (29.6%) were severe cases
* In severe cases, headache (27.5% vs 24.2%, p>0.05) and myalgia (47.5% vs 26.3%, p<0.05) were more common.
* 10/135 (7.4%) patients had elevated CK levels (>200 U/L) and more common in severe cases (17.5% vs 3%)
 | * No clear definition of symptoms
* Not specifically studied neurological manifestation
* Diagnostic test was limited
 | 3 |
| Ding et al,10 2020 | Retrospective Case series | Wuhan, China | 5 COVID-19 patients. Diagnosis method was not reported  | (39-66 y) | * Headache, 2 (20%)
* Myalgia, 2 (20%)
 | * 5/5 (100%) all subjects had co-infected with influenza A (60%) and B (40%) virus
 | * Small sample size
* No clear definition of symptoms
* Not specifically studied neurological manifestation
* Diagnostic test was limited
 | 4 |
| Qian et al,38 2020  | Retrospective Cohort  | Zhejiang, China | 88 patients with RT-PCR positive from throat swab and 3 cases of clinical-confirmed COVID-19  | 50 (36.5-57 y) | * Headache, 7 (7.69%)
* Nausea, 11 (12.09%)
* Vomiting, 6 (6.59%)
* Myalgia, 5 (5.49%)
* Back discomfort, 3(3.3%)
 | * Based from disease severity, 82/91 (90%) were mild and and 9/91 (10%) were severe cases
* 3/91 (3.30%) patients had CVD comorbidities
 | * Small sample size
* No clear definition of symptoms
* Not specifically studied neurological manifestation
* Diagnostic test was limited
 | 3 |
| Hu et al,11 2020 | Retrospective case series | Nanjing, China | 24 patients with RT-PCR positive COVID-19 from throat swab | 32.5 (5-95 y) | * Dizziness, 1 (4.2%)
* Arthralgia, 1 (4.2%)
 | * 1/24 (4.2%) patients had CVD comorbidity
 | * No clear definition of symptoms
* Not specifically studied neurological manifestation
* Diagnostic test was limited
 | 4 |
| Wu et al,12 2020 | Cross sectional | Jiangsu, China | 80 patients with RT-PCR positive COVID-19 from throat swab | 46.1 (30.7–61. 5 y) | * Headache, 13 (16.25%)
* Nausea, 1 (1.25%)
* Vomiting, 1 (1.25%)
* Myalgia, 18 (22.50%)
 | * 25/80 (31.25%) patients had CVD comorbidity
* 1/80 (1.25%) patients had nervous system disease comorbidity
* 18/80 (22.5%) patients had CK levels (>310 U/L) above normal range
 | * No clear definition of symptoms
* Not specifically studied neurological manifestation
* Diagnostic test was limited
 | 4 |
| Chen N,13 et al 2020 | Cross Sectional | China | 99 patients with RT-PCR positive COVID-19 from throat swab | Mean Age (y) ± SD: 55.5 ± 13.1 | * Dizziness, 9 (9%)
* Headache, 8 (8%)
* Nausea and Vomiting, 1 (1%)
* Myalgia, 11 (11%)
 | * 40/99 (40%) patients had CVD comorbidities
* 1/99 (1%) patients had nervous system disease
* 13/99 (13%) patients had elevated CK levels (> 185 U/L)
 | * No clear definition of symptoms
* Not specifically studied neurological manifestation
* Diagnostic test was limited
 | 4 |
| Xu et al,14 2020 | Retrospective case series | China | 62 patients with RT-PCR positive COVID-19 from throat swab and sputum | 41 (32-52 y) | * Headache, 21 (34%)
* Myalgia, 32 (52%)
 | * 1/62 (2%) patients had CVD comorbidity
* 5/62 (8%) patients had elevated CK levels (> 185 U/L)
 | * No clear definition of symptoms
* Not specifically studied neurological symptoms
* Diagnostic test was limited
 | 4 |
| Liu et al,15 2020 | Cross sectional | China | 137 patients with RT-PCR positive COVID-19 from throat swab and sputum | 57 (20-83y) | * Headache, 13 (9.5%)
* Myalgia, 44 (44%)
 | * 27/137 (19.7%) patients had underlying disease
 | * No clear definition of symptoms
* Not specifically studied neurological symptoms.
* Diagnostic test was limited
 | 4 |
| Wang et al,16 2020 | Retrospective Cohort | China | 138 patients with RT-PCR positive COVID-19 from throat swab and sputum | 56 (22-92 y) | * Dizziness, 13 (9.4%)
* Headache, 9 (6.5%)
* Vomiting, 5 (3.6%)
* Myalgia, 48 (34.8%)
 | * Subjects were 36/138 (26%) ICU patients and 102/138 (74%) non-ICU patients
* Patients admitted to ICU were more likely to present with dizziness (22.2% vs 4.9%, p<0.05) and comorbidity of CVD (16.7% vs 1%, p=0.001)
* 7/138 (5.1 %) patients had CVD comorbidity
* CK levels was higher in ICU patients (102 vs 87, p=0.08)
 | * No clear definition of symptoms
* Not specifically studied neurological manifestation
* Diagnostic test was limited
 | 3 |
| Liu et al,17 2020 | Retrospective Case series | China | 12 patients with RT-PCR positive COVID-19 from throat swab  | 62.5(10-72 y) | * Nausea and Vomiting, 1 (8.3%)
* Myalgia, 4 (33.3%)
 | * 1/6 (16.6%) patients had elevated CK levels (> 185 U/L).
 | * Not specifically studied neurological symptoms
* No clear definition of symptoms
* Diagnostic test was limited
* Insufficient data may result to a biased understanding of the disease.
 | 4 |
| Li et al,18 2020 | RetrospectiveCohort | Wuhan, China | 221 patients with RT-PCR positive COVID-19 from throat swab | 73.5 (57-91 y) | * Cerebrovascular disease, 13/221 (5.9%),
* Ischemic Stroke, 11/13 (84.6%)
* CVST, 1/13 (7.7%)
* Cerebral Hemorrhage, 1/13 (7.7%)
 | * Median durations from first symptoms of infection to CVD onset were 10 days (IQR 1-29)
* The onset of CVD was more likely to present with older age (71.6y vs 52.1y, p<0.05), severe COVID-19 (84.6% vs 39.9%, p<0.01), and underlying diseases such as hypertension (p<0.001) or diabetes mellitus (p<0.01)
* Patients with CVD had more increased in some laboratory findings, including higher white blood cell (p<0.001), and C-reactive protein levels (p<0.01), and D-dimer levels (p<0.001)
 | * Not specifically studied neurological symptoms
* No clear definition of symptoms
* Diagnostic test was limited
 | 3 |
| Chen et al,19 2020 | Cross sectional  | Wuhan, China | 274 patients with RT-PCR positive COVID-19 from throat swab | 62.0 (44.0-70.0 y) | * Dizziness, 21 (7,6%)
* Headache, 31 (11,3 %)
* Myalgia, 60 (21,8%),
* Nausea, 24 (8,7%)
* Vomiting, 16 (5,8%)
 | * 113/274 (41%) died and 161/274 (59%) survives during hospitalization stay.
* 4/274 (1%) patients had CVD comorbidity and was more common among deceased patients (4% vs 0%)
* 24/274 (9%) patients had complication of hypoxic encephalopathy and was more common among deceased patients (20% vs 1%)
* CK levels was higher in deceased patients (189 vs 84)
 | * Not specifically studied neurological symptoms
* No clear definition of symptoms
* Diagnostic test was limited
* There are missing data or important tests that might lead to bias of clinical characteristics
 | 4 |
| Guan et al,20 2020 | Retrospective Cohort  | China | 1590 patients with RT-PCR positive COVID-19 from throat swab | Mean Age (y) ± SD: 48.9±16.3 | * Headache, 205/1328 (15.4 %)
* Unconsciousness 20/1421 (1.4%)
* Nausea/vomiting 80/1371 (5.8%)
* Myalgia/arthralgia 234/1338 (17.5%)
 | * 399/1590 (25.1%) had at least one comorbidity.
* Patients with comorbidity were more likely to present with headache (16.6% vs 15.1%), unconsciousness (2.5% vs 1%), nausea/vomiting (10.4% vs 4.3%) and myalgia/arthralgia (18.1% vs 17.3%)
* 30/1590 (1.9%) patients had CVD comorbidity.
 | * Not specifically studied neurological symptoms
* No clear definition of symptoms
* Diagnostic test was limited
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| Zhang et al,21 2020 | Retrospective Cohort  | Zhejiang,China | 645 patients with RT-PCR positive COVID-19 from throat swab | Mean Age (y) ± SD: Normal imaging findings= 34.90±14.20; Abnormal imaging findings = 46.65±13.82  | * Headache, 67 (10.3%)
* Nausea and vomiting, 22 (3.40%)
* Myalgia, 71 (15.2%)

  | * 72/645 (11%) patients had normal imaging, while 573/645 (89%) had abnormal imaging findings
* Headache were more common in those abnormal imaging findings (11.3% vs 2.8%)
* CK levels were higher in those with abnormal imaging findings (73.0 vs 62.5, p<0.05)
 | * Not specifically studied neurological symptoms
* No clear definition of symptoms
* Diagnostic test was limited
 | 3 |
| Zhou et al,22 2020 | Retrospective Cohort  | Wuhan, China | 191 patients with RT-PCR positive COVID-19 from throat swab  | 56 (46.0-67.0 y) | * Myalgia, 29 (15%)
 | * 22/168 (13%) had elevated CK levels (>185 U/L)
* CK levels were more common (21% vs 9%, p<0.05) and higher (73.0 vs 62.5, p<0.05) among non-survivor patients
 | * Not specifically studied neurological symptoms
* No clear definition of symptoms
* Diagnostic test was limited
 | 3 |
| Tian et al,23 2020 | Retrospective Cohort  | Beijing, China | 262 patients with RT-PCR positive COVID-19 from throat swab  | 47.5(1–94 y) | * Headache, 17 (6.5%)
 | * Based from disease severity, 216/262 (82.4%) were common and and 46/262 (17.6%) were severe group
* Headache was present in 3/46 (6.5%) patients with severe group and 14/216 (6.5%) patients with common group
 | * No clear definition of symptoms
* Not specifically studied neurological symptoms
* Diagnostic test was limited
 | 3 |
| Han et al,24 2020 | Retrospective Cohort  | Shaanxi, China | 25 adult patients with RT-PCR positive COVID-19 from throat swab | 44(22-70 y) | * Myalgia, 13 (52%)
 | * In adults, myalgia or fatigue were observed more frequently with no significant difference (52% vs 0%, P=0.25).
* 1/25 (4%) adult patients had elevated CK levels (>200 U/L)
 | * Small sample size
* No clear definition of symptoms
* Not specifically studied neurological symptoms
* Diagnostic test was limited
 | 3 |
| Poyiadji et al,25 2020 | Case Report | Detroit, United States  | A female airline worker patients with RT-PCR positive COVID-19 from throat swab  | 50 year old  | * 3 days history of fever, cough, and altered mental status
 | * This is the first reported case of COVID-19–associated acute necrotizing hemorrhagic encephalopathy
* Imaging findings: Noncontrast head CT images, symmetric hypoattenuation within the bilateral medial thalamic; Images from brain MRI, hemorrhagic rim enhancing lesions within the bilateral thalami, medial temporal lobes, and subinsular regions
* CSF finding were normal and negative for bacterial culture, HSV-1 and 2, Varicella zoster, and West Nile virus
 | * Diagnostic test was limited
 | 5 |
| Moriguchi et al,26 2020 | Case Report | Japan | A man with RT-PCR positive COVID-19 from spinal fluid, and negative from nasopharyngeal swab | 24 year old | * Headache, fever, fatigue (day 1)
* Unconsciousness followed by seizure (day 9)
 | * This is the first reported case of COVID-19 associated meningitis/encephalitis
* Durations from first symptoms of infection to unconsciousness were 9 days
* Clinical findings were GCS of 6 and neck stiffness
* Imaging findings: chest CT, ground glass opacity on pulmonary lobes indicates pneumonia; brain MRI, right lateral ventriculitis and encephalitis mainly on right mesial lobe and hippocampus
* Cerebrospinal fluid was clear, colorless, initial pressure > 320 mmH2O, cell count was 12/μL (10 mononuclear and 2 polymorphonuclear cells without red blood cells )
 | * Patient outcome was not reported as the study was still ongoing
 | 5 |
| Wang et al,27 2020 | Retrospective Cohort | China | 339 patients with RT-PCR positive COVID-19 from throat swab | 65 (65-76 y) | * Dizziness, 13 (3.8%)
* Headache, 12 (3.5%)
* Myalgia, 16 (4.7%)
* Nausea, 13 (3.8%)
 | * 21/339 (6.2%) patients had CVD comorbidity and more prevalent in deceased patients 10/65 (15.6%)
* In survivors, patients were more likely to present with dizziness (4% vs 3.1%), headache (3.5% vs 0%), myalgia (5.5% vs 1.6%), and nausea (4.4% vs 1.6%)
* CVD comorbidity was predictive factor of poor outcomes (HR 3.26, CI 1.66-6.40, P = 0.001)
* CK levels were higher among deceased patients (84 vs 60 , p=0.005)
 | * Not specifically studied neurological symptoms
* No clear definition of symptoms
* Diagnostic test was limited
 | 3 |
| Cai et al,28 2020 | Retrospective Cohort | China | 298 patients with RT-PCR positive COVID-19 from throat swab | 47 (33-61y) | * Headache, 5 (2.08%)
 | * Based from disease severity, 240/298 (80.5%) were common and and 58/298 (19.5%) were severe group
* Headache was more common among non-severe group compared to severe group (5/240 [12%] vs 0/58 [0%], p >0.05)
* Compared to non-severe patients, CK levels significantly increased among severe patients (64.5 vs 87, p=0.006).
 | * Not specifically studied neurological symptoms
* No clear definition of symptoms
* Diagnostic test was limited
 | 3 |
| Cao et al,29 2020 | Prospective Cohort  | China | 102 patients with RT-PCR positive COVID-19 from throat swab | 54 (37-67 y) | * Myalgia, 35 (34.4%)
 | * Myalgia was more common among non-survivors group (34.6% vs 29.4%, p=0.641)
* 6/102 (5.9 %) patients had CVD comorbidity and more common among non-survivors group 3/17 17.6 % vs 3.5%, p=0.090)
 | * Not specifically studied neurological symptoms
* No clear definition of symptoms
* Diagnostic test was limited
 | 2 |
| Yang et al,30 2020 | Retrospective Cohort | Wenzhou, China | 149 patients with RT-PCR positive COVID-19 from throat swab | Mean Age (y) ± SD: 45.11 ± 13.35 | * Headache, 13 (8.72%)
* Nausea and Vomiting, 2 (1.34%)
* Myalgia, 5 (3.36%)
 | * 28/149 (18.79%) have cerebrovascular underlying disease
* 12/149 (8.05%) patients had elevated CK levels (>200 U/L)
 | * Not specifically studied neurological symptoms
* No clear definition of symptoms
* Diagnostic test was limited
* Incomplete data or observation as the study had ended
 | 3 |
| Zhao et al,31 2020 | Case Report | Shanghai, China | A female with RT-PCR positive COVID-19 from throat swab | 61 year old | * Patient presented with acute weakness in both legs and severe fatigue progressing within 1 day
 | * Patient had travel history returned from Wuhan, China 4 days earlier before the weakness onset
* Neurological examination showed symmetrical weakness grade 4/5 and areflexia in both legs and feet
* Nerve conduction studies (day 5) showed delayed distal latencies and absent F waves in early course, supporting demyelinating neuropathy and was diagnosed with GBS
* Fever and respiratory symptoms occurred after GBS symptoms (day 8)
* All symptoms resolved and patient discharged at day 30
 | * Diagnostic test was limited
 | 5 |
| Filatov et al,32 2020 | Case Report | United States of America | A man with COVID-19 with RT-PCR positive COVID-19  | 74 year old | * The patient presented with fever and cough, and then was discharged with suspicion of the COPD exacerbation.
* Within 24 hours, Patient returned with worsening symptoms, including headache, altered mental status, fever, and cough
 | * Patient had travel history returned from Europe 7 days earlier before the symptoms onset
* Patient had history of atrial fibrillation, cardioembolic stroke, Parkinson’s Disease, COPD, and cellulitis
* EEG shows diffuse slowing and focal slowing sharply contoured waves in the left temporal region indicate encephalopathy
* Head CT-Scan showed no acute changes, other than the presence of hypodensity area indicates prior history of embolic stroke
* the CSF findings showed no signs of infection
 | * Diagnostic test was limited
 | 5 |
| Korea Centers for Disease Control and Prevention,33 2020) | Case Series | South Korea | 28 patients with laboratoryconfirmed COVID-19.  | Mean Age (y) 42.6 (20-73 y) | * Headache, 3 (10.7%)
* Myalgia, 4 (14.3%)
 | * 18/28 (64.3%) patients are tested positive pneumonia by imaging
 | * Not specifically studied neurological symptoms
* No clear definition of symptoms
* Diagnostic test was limited
 | 4 |
| Zhao et al,34 2020 | RetrospectiveCohort | China | 101 patients with RT-PCR positive COVID-19  | 43 (17–75 y) | * Nausea and Vomiting, 2 (2%)
* Myalgia, 17 (16.8%)
 | * 16/101 (15.8%) patients have cerebrovascular underlying diseases
 | * Not specifically studied neurological symptoms
* No clear definition of symptoms
* Diagnostic test was limited
 | 3 |
| Xu et al,35 2020 | Retrospective Cohort | China | 50 patients with RT-PCR positive COVID-19 | Mean Age (y) ± SD: 43.9 ±16.8 | * Headache, 5 (10%)
* Myalgia, 8 (16%)
 | * Headache was mostly found in patients with moderate disease 3/50 (6%)
* Myalgia was mostly found in patients with moderate disease 4/50 (8%)
 | * Not specifically studied neurological symptoms
* No clear definition of symptoms
* Diagnostic test was limited
 | 3 |
| Li et al,36 2020 | Retrospective Cohort | China | 131 patients with RT-PCR positive COVID-19 | Mean Age (y) ± SD: 47 ± 15  | * Myalgia, 2 (2%)
 | * Not available
 | * Not specifically studied neurological symptoms
* No clear definition of symptoms
* Diagnostic test was limited
 | 3 |
| Wang et al,37 2020 | Retrospective Cohort | China | 1012 patients with RT-PCR positive COVID-19 from sputum or nasoharyngeal swab | 50 (16-89 y) | * Headache, 152 (15%)
* Myalgia, 170 (16.8%)
* Vomiting, 30 (3.3%)
 | * Patients included in the study were non critically ill patients.
* 100/1012 patients had aggravation of illness during follow up
* headache (19% vs 14.6%), myalgia (17% vs 16.8%), and vomiting (6% vs 3.3%) were more common among patients with aggravation of illness during follow up
 | * Not specifically studied neurological symptoms
* No clear definition of symptoms
* Diagnostic test was limited
 | 3 |