



Neurological, Neuropsychiatric and Psychiatric Symptoms During COVID-19 Infection and After Recovery: A Systematic Review of Observational Studies

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Abstract

Background: The SARS-CoV-2 virus causes a wide spectrum of disease severity. Initial manifestations include fever, dry cough, and constitutional symptoms, which may progress to respiratory disease. There may also be neurological and psychiatric manifestations, involving both the central and peripheral nervous system.

Methods: We performed a literature search of the databases PubMed, EMBASE, The Cochrane Library and Web of Science for observational studies reporting neurological, psychiatric, and neuropsychiatric effects of COVID-19. This was followed by a narrative synthesis to summarise the data and discuss neuropsychiatric associations, symptom severity, management, and recovery.

Findings: The most frequently reported neurological symptoms were ageusia, hyposmia/anosmia, dizziness, headache, and loss of consciousness. Statistically significant relationships were noted between Asian ethnicity and peripheral neuropathy ($p=0.0001$) and neuro-syndromic symptoms ($p=0.001$). ITU admission was found to have a statistically significant relationship with male sex ($p=0.024$). Depression and anxiety were also identified both during and after infection. The most frequent treatments used were intravenous immunoglobulins, followed by antibiotics, antivirals, and hydroxychloroquine; with mean treatment duration of 6 days.

Interpretation: Various neuropsychiatric symptoms have been associated with COVID-19 infection. More studies are required to further our knowledge in the management of neurological and psychiatric symptoms during and after COVID-19 infection

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Introduction

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a novel virus, initially discovered in the city of Wuhan, China [1]. SARS-CoV-2 causes coronavirus disease (COVID-19), which has led to an ongoing global pandemic. Despite belonging

to the coronavirus family, which usually cause self-limiting upper respiratory tract infections, SARS-CoV-2 is often more virulent than most coronaviruses and may lead to severe respiratory disease [2].

The mechanism of action for SARS-CoV-2 may relate to a specific tropism for respiratory tract mucosal cells through the

attachment of viral surface proteins to angiotensin-converting enzyme (ACE) 2 receptors [3]. After infection, the virus causes a wide spectrum of disease severity, with most patients suffering a mild self-limiting disease. Initial manifestations include fever, dry cough and constitutional symptoms (headache, fatigue, myalgia, arthralgia), progressing to respiratory disease of mild to moderate severity [2,4]. Other disease manifestations include gastrointestinal symptoms (nausea, vomiting, diarrhoea), sore throat, skin rashes, anosmia, ageusia, and chest pain [5]. In patients with underlying comorbidities or advanced age, the infection may be complicated with acute respiratory distress syndrome (ARDS), acute renal failure, sepsis, multi-organ failure and death [6,7].

As the pandemic of COVID-19 persists, the knowledge of the clinical disease spectrum is still unfolding. Medical literature of COVID-19 infected patients reveals a variety of extra-pulmonary organ involvement [8]. Among these, COVID-19 has been associated with several neurological and psychiatric effects, involving both the central and peripheral nervous system [9].

Methods

This systematic review follows the Preferred Reporting Items for Systematic reviews and MetaAnalyses (PRISMA) statement [10] and was registered in the PROSPERO International Prospective Register of Systematic Reviews (number CRD42020203770 at www.crd.york.ac.uk/PROSPERO).

Search Strategy

The literature search was performed in August 2020 using the databases PubMed, EMBASE, The Cochrane Library and Web of Science, from their respective inception dates. The following search terms were used:

(Neuro* OR Nervous OR Psychiatry* OR Mental) AND (COVID OR Corona*)

The search strategies incorporated both medical subject headings (MeSH) and free-text terms, which were adapted according to the database searched. Grey literature was also searched. Reference lists of the identified papers and reviews were hand-searched. Publication languages included English and Greek. There were no publication period restrictions.

Inclusion and Exclusion Criteria

Included studies were observational studies reporting neurological, psychiatric, and neuropsychiatric effects of COVID-19. The included participants were COVID-19 patients of any ethnic origin, sex/gender, age, country, and were either actively infected from COVID-19 at the time of the study or had recovered. We did not include studies examining psychiatric effects on the general population as an indirect result of the pandemic.

Main Outcomes

The main outcomes included neurological, psychiatric, and neuropsychiatric effects of COVID-19, either based on clinical diagnosis or relevant diagnostic questionnaires. Information about recovery and treatment was reported when available.

Screening

Titles were screened for inclusion, followed by screening of abstracts, and then content. One author (SS) screened the papers, and any disagreements were resolved by discussion with the review's primary author (MS) and the other authors.

Data Extraction

The Cochrane good practice data extraction form was used for data extraction. Data extraction from reviews involved the NICE extraction form, and the data were extracted in an electronic format.

Risk of Bias/Quality Assessment

The quality and risk of bias were assessed by the Mixed Methods tool for Appraisal (MMAT). The guidance from the Centre for Reviews and Dissemination was used for the appraisal of review papers. Discrepancies were resolved by discussion within the authors' team.

Strategy for Data Synthesis

We performed a narrative synthesis review of original studies and reviews reporting neurological, psychiatric, and neuropsychiatric effects in COVID-19 patients.

We summarised the data and discussed:

- a) Neuropsychiatric associations
- b) Symptom severity
- c) Management and
- d) Recovery

Information from the various identified studies was analysed, summarised, and compared.

Results

Following our literature search, we identified a total of 7,460 papers. After removing the duplicated and irrelevant papers, 328 full text articles remained to be assessed for eligibility using the inclusion and exclusion criteria. Of these, 313 studies were included in the final narrative synthesis: specifically, 307 studies for neurological symptoms and 7 studies for psychiatric symptoms, as shown in Figure 1. A total of 15 full text papers were excluded as they were either not relevant (n=4) or unrelated to COVID-19 infection (n=11).

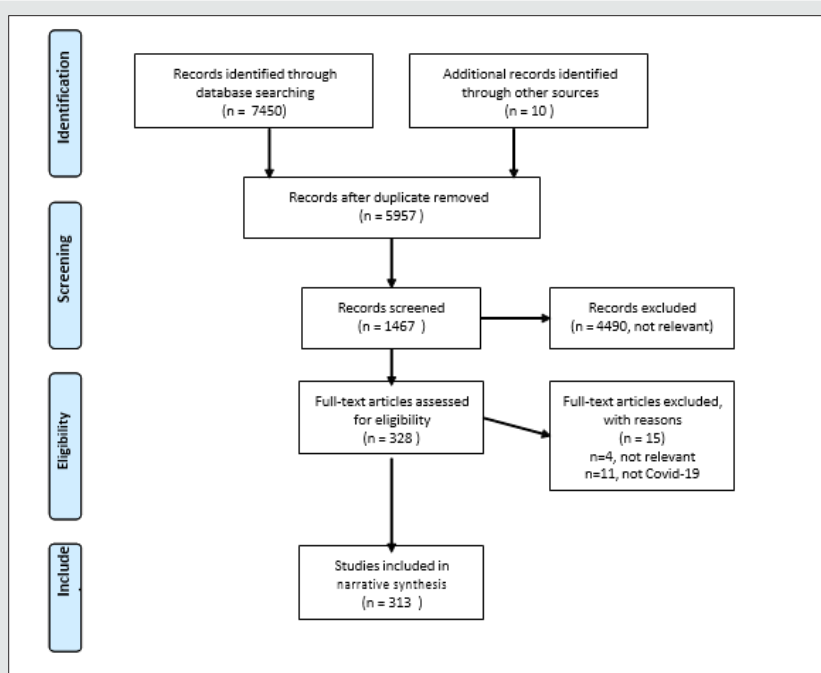


Figure 1: PRISMA flowchart of selected studies.

Neurological Symptoms

A total of 307 studies for neurological symptoms were included in the narrative synthesis, as mentioned above, of which 202 were case reports, 53 case series, 2 retrospective studies, 21 cohort studies, 15 systematic reviews, 8 cross-sectional studies, 3 case-

control studies, and 3 retrospective case series. A summary of the studies included in the systematic review is shown in Table 1, and a complete list of the studies is provided in Supplementary Material 1. The mean age of the patients included was 55.11 (±17.91) years. Most of the patients in our cohort were males (61%) and the majority of the participants were Asians (57%).

Table 1: Summary of studies included in the systematic review for neurological symptoms.

Type of Study	Number of studies	Total sample size	Average sample size	Average female %	Averagemale %
Case report	202	2,104	18	38	62
Cross-sectional	8	10,623	1,328	48	52
Retrospective study	2	223	112	46	54
Case series	53	3,447	75	27	73
Retrospective caseseries	3	578	193	40	60
Systematic review	15	36,724	3,023	41	59
Cohort study	21	6,180	294	34	66
Case control	3	218	73	37	63
Total of all studies	307	60,097	640	39	61

Clinical Presentation

A total of 107 studies (42.7%), involving 26,758 patients, included a full account of neurological symptoms experienced by the participants following COVID-19 infection. Table 2 presents the

frequency of symptoms and their resolution. The most reported symptoms were ageusia (n=390), hyposmia/anosmia (n=480), dizziness (n=230), headache (n=860), and loss of consciousness (n=310).

Table 2: Frequency and recovery rates of different COVID-19 neurological presentations.

Clinical Presentation	n patients	n patients resolved	% of patients whose symptoms resolved
Headache	860	690	80%
Skeletal symptoms	730	700	100%
Acute CVA	500	370	74%
Hyposmia/anosmia	480	420	87%
Ageusia	390	360	92%
Meningitis-encephalitis	380	330	86%
Encephalopathies	380	300	78%
Neurological syndromes	320	230	71%
Loss of consciousness	310	290	93%
Dyspnoea	280
Seizure	260	230	88%
Dizziness	230	200	86%
Fatigue	130
Fever	110
Peripheral nervous system	90	60	66%
Dry cough	81
Cerebellar symptoms	70	60	85%
Spinal cord syndromes	30	10	33%
Flu-Like symptoms	30
Dysphagia/odynophagia	30
Anorexia	30
Abdominal pain	20
GI symptoms	18
Haemoptysis	10

Moreover, a significant number of patients experienced severe neurological manifestations, such as seizures (n=260), acute cerebrovascular events (n=500), cerebellar syndromes (n=70), peripheral neuropathies (n=90), meningitis/encephalitis (n=380), encephalopathies (n=380), neurological syndromes such as Guillain-Barre syndrome (n=320), and spinal cord syndromes (n=30).

A statistically significant relationship was noted between ethnicity and peripheral neuropathy (p=0.0001) as well as between ethnicity and neuro-syndromic symptoms (p=0.001), with Asian patients being more likely to experience these symptoms. Both sexes were statistically as likely to present with symptoms of ageusia (p=0.0001), dizziness (p=0.033), gastrointestinal symptoms (p=0.0001), and anorexia (p=0.0001). However, flu-like symptoms were statistically more prevalent in females (p=0.008), whereas hyposmia (p=0.037) and haemoptysis (p=0.0001) was more frequent in males.

Following recovery from COVID-19 infection, a large proportion of patients demonstrated a complete resolution of their symptoms.

Specifically, patients presenting with loss of consciousness and ageusia reported the highest resolution rates (93% and 92% respectively), while the patients that experienced spinal cord syndromes had the lowest resolution rates of their symptoms (33%).

Treatments

The most frequent treatments used in the studies analysed were intravenous immunoglobulins (IVIG) (20.17%), followed by antibiotics such as azithromycin (19.29%), antivirals (14.91%), and hydroxychloroquine (10.52%). However, a combination of therapies was required for treatment in some patients. Figure 2 illustrates the different types of drugs that the COVID-19 patients received during their admission and how the drug therapy is markedly heterogeneous among this group of patients.

The most common route of drug administration was intravenous (65%), although oral drug administration and intramuscular injections were also utilised. Patients received treatment for a mean duration of 6 (±4) days.

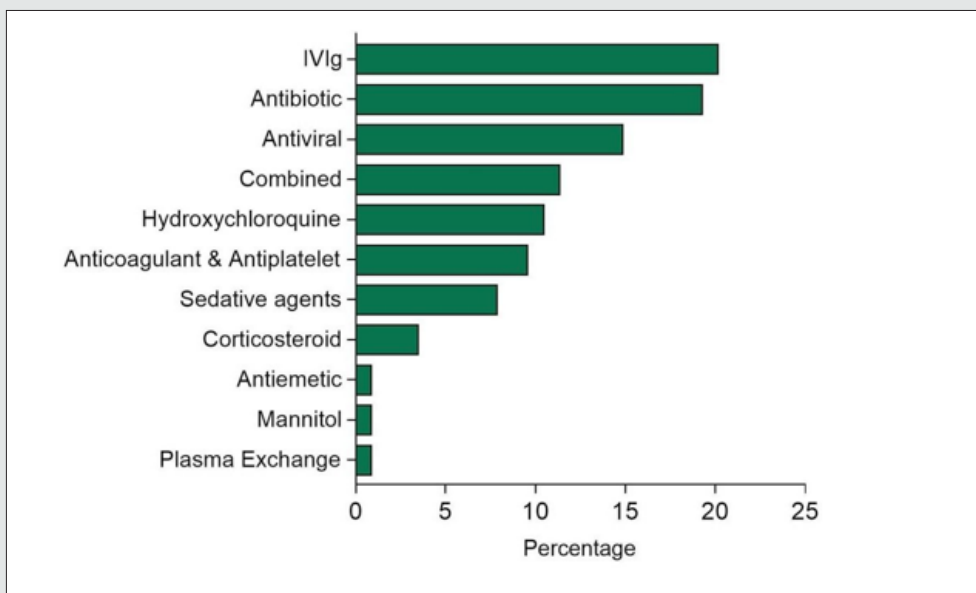


Figure 2: Drug type administered to COVID-19 patients.

Prognosis

Patients admitted to an Intensive Therapy Unit (ITU) were reported in 126 studies. Figure 3 shows the different types of

management that patients received when admitted to ITU and illustrates that the most common cause of ITU admission was the need for respiratory support with intubation and mechanical ventilation (84% of the cases).

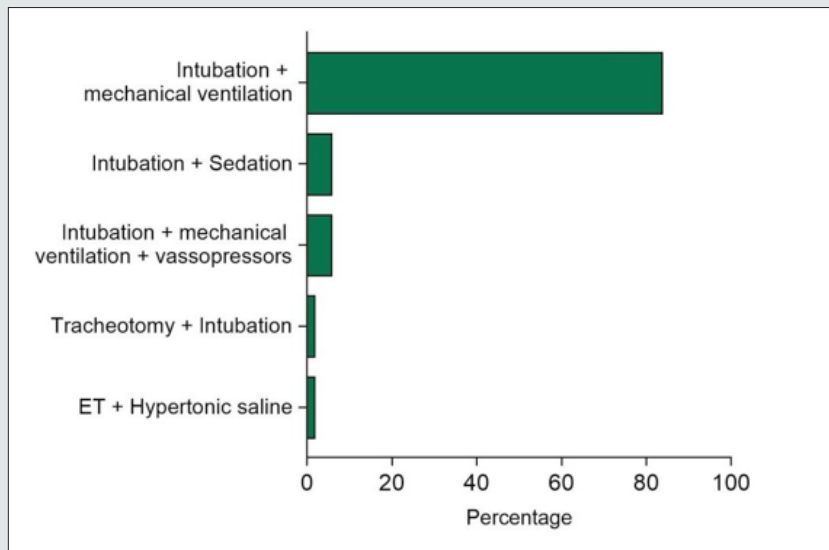


Figure 3: Types of ITU management received by patients.

ITU admission was found to have a statistically significant relationship with males ($p=0.024$), but not age. Interestingly, there was a statistically significant relationship with ITU admission and symptoms of hyposmia/anosmia ($p=0.0001$), headache ($p=0.035$), acute CVA ($p=0.0001$), seizure ($p=0.001$), meningitis ($p=0.034$), and encephalopathies ($p=0.0001$).

Psychiatric Symptoms

We identified seven studies reporting psychiatric effects, of which five were cross-sectional studies, one was a retrospective cohort study, and one was a case report. Details of the six studies are reported in Table 3. The studies involved 299,000 patients in total, of which 44% were male and 56% were female. Half of the

studies were reported in China. Three studies involved 171 patients in hospital settings while having active COVID-19 infection, three studies involved 498 patients at home after recovery, and one study involved 62,354 patients covering both inpatients during infection and those at home after recovery. All studies identified depression and anxiety as being relevant to COVID-19 infection, both during and after infection. Additionally, one study reported

suicidality during infection, two studies reported post-traumatic stress disorder after infection, one study suggested obsessive-compulsive disorder after infection, one study suggested insomnia after infection, one study suggested a higher incidence of psychosis, and two studies suggested a higher incidence of dementia diagnosis as being relevant to having been diagnosed with COVID-19.

Table 3: Studies reporting psychiatric effects related to COVID-19 infection.

Study	Type	Country	Setting	Number, age	Condition/scale	Results	Conclusions
Epstein et al.[11]	Case report	Israel	Isolation, hospital ward	N=1; Males: n=1 Age=34	Anxiety, insomnia	Suicide attempted on day 7	Regular screening needed for depression, anxiety and suicidality
Mazza et al.[12]	Cross-sectional	Italy	Home (post hospital discharge)	N=402; Males:n=265, Females: n=137; Mean age=58	IES-R, PCL-5, ZZSDS, OCI, BDI-13, STAI-Y, MOS-SS, WHIIRS	A significant proportion of patients self-rated in the psycho-pathological range: 28% for PTSD, 31% for depression, 42% for anxiety, 20% for OC symptoms, and 40% for insomnia.	Regular assessment of psychopathology of COVID-19 survivor needed to diagnose and treat emergent psychiatric conditions
Yuan et al.[13]	Cross-sectional	China	Home (post hospital discharge)	N=96; Males: n=47, Females:n=49; 18-45 years: n=44, >46 years: n=52	PTSD-SS, ZSDS, ZSAS	44% reported depressive symptoms. No significant correlation of depression with sex, age, comorbidity, severity of initial infection, and duration of initial illness. There were changes in immune system function.	Appropriate psychological interventions are necessary for COVID-19 survivors
Taquet et al.[14]	Cross-sectional	USA	Various, during the first 14 to 90 days after diagnosis	N=62,354; Males: n=27,525, Females: n=34,564, Other: n=265; Mean age=49.3	Incidence of psychiatric diagnosis, including dementia	Incidence of any psychiatric diagnosis= 18.1%; Incidence of a first diagnosis of dementia= 1.6%	There is psychiatric morbidity to be anticipated in survivors of COVID-19 and for which services need to plan.

Discussion

The literature published on the neurological symptoms observed in patients with COVID-19 is vast. Through our review, we aimed to summarise all available literature, as well as include more recent studies that older reviews may not have included. Our review specifically served to identify and examine the frequency and severity of these symptoms through combining

this existing literature. In total, 307 neurological studies covering 60,097 patients, were included in this systematic review, which has shown that COVID-19 is associated with a large variety of neurological symptoms. The most frequently reported symptoms included ageusia, hyposmia/anosmia, dizziness, headache, and loss of consciousness. These symptoms are not specific to SARS-CoV-2 infection and are of low severity, however they may suggest

neurotropism. They also associate with high resolution rates (all >80%). The most common severe neurological complication of COVID-19 was acute cerebrovascular events. This result is in keeping with other systematic reviews [18,19].

Direct neurological damage including ischemic strokes, meningitis/encephalitis, or Guillain-Barre syndrome are relatively common extra-pulmonary neurological presentations according to our review. These results should be the springboard for further research efforts aiming to distinguish whether these neurological entities are a consequence of direct brain injury/infection or an interaction with other vascular comorbidities of patients suffering severe/critical COVID-19 disease.

A significant proportion of COVID-19 patients were asymptomatic due to the course of SARS-CoV-2 infection. In addition, patients may not present with respiratory symptoms or fever but still have initial neurological manifestations. Thus, when patients present with neurological symptoms, despite the absence of respiratory symptoms, clinicians should maintain a high level of clinical suspicion for the possibility of underlying COVID-19 asymptomatic infection.

The resolution rates of neurological symptoms also varied. Patients presenting with loss of consciousness and ageusia reported the highest resolution rates (93% and 92% respectively), with ageusia resolution rates being 100% in one study [20]. On the other hand, patients who experienced spinal cord syndromes, such as acute myelitis, had the lowest resolution rates of their symptoms (33%). This finding is supported by the established poor overall outcomes associated with acute myelitis, with only approximately one-third of patients experiencing a favourable outcome [21].

A statistically significant relationship was noted between Asian ethnicity and peripheral neuropathy. The relationship between ethnicity and peripheral neuropathy in the context of COVID-19 has yet to be explored. However, peripheral neuropathy as a complication of diabetes has been found to be more prevalent among Caucasian patients [22] and less common in those with Indo-Asian and African- Caribbean origins [23]. Moreover, a statistically significant relationship was noted between Asian ethnicity and neuro-syndromic symptoms. Nonetheless, it is important to note that both of these relationships may have been influenced by the fact that the majority of the participants in the studies included were Asian and that a number of papers did not disclose the ethnicity of their participants.

Additionally, flu-like symptoms were statistically more prevalent in females, possibly because males have been found to have a higher risk of severe illness with COVID-19 [24]. Hyposmia and haemoptysis were statistically more prevalent in males. This is in contrast to several previous studies that found hyposmia to be more common in females with COVID-19 infection [25-28]. However, our patient cohort was predominantly male (62%), which may have contributed to the differing results. Regarding haemoptysis, it is a very uncommon presentation that was only present in 10 patients.

ITU admission was found to have a statistically significant relationship with male sex, but not with age. A meta-analysis of patients with COVID-19 also demonstrated a relationship between sex and ITU admission, with male patients having almost three times the probability of requiring ITU admission compared to females [29]. Surprisingly, our study did not determine any relationship between age and ITU admission. In contrast, another meta-analysis found that patients greater than 70 years old have a higher risk of needing intensive care [30]. Furthermore, there was a statistically significant relationship between ITU admission and the symptoms of hyposmia/anosmia, headache, acute CVA, seizure, meningitis, and encephalopathies.

Treatment varied, with several different therapies and drug routes being used depending on the neurological manifestation and severity of the presentation. The most frequent treatments used were intravenous immunoglobulins (IVIG), followed by antibiotics such as azithromycin, antivirals, and hydroxychloroquine, with patients receiving treatment for a mean duration of 6 days. A systematic review assessing treatment strategies for COVID-19 similarly found antivirals, antimalarials, and antibiotics to be the mainstay of treatment [31]. The frequency of IVIG can be attributed to its use in treating many different neurological conditions, most notably Guillain-Barre Syndrome, which was the fourth most common neurological complication reported in this review. Finally, it is important to consider that the COVID-19 pandemic is rapidly evolving and that treatment options are continually being trialled and developed.

Even though we established an abundance of studies for neurological symptoms, there appears to be a lack of studies regarding the psychiatric effects during and after COVID-19 infection. Nonetheless, all the studies we were able to identify reporting psychiatric effects have found depression and anxiety to be relevant, both during and after infection with COVID-19. In severe cases, there may even be a risk of patients attempting suicide. Compared to people who had flu or other respiratory tract infections, COVID-19 survivors were more likely to receive a diagnosis of anxiety or depression over the same period [17]. It was found that involving psychiatric care for these patients was effective in reducing their symptoms of anxiety and depression. Without proper psychiatric intervention, there is a risk that these psychiatric symptoms could increase the risk of suicidal ideation. Overall, it is recommended that psychiatric and/or psychological support should be available in hospitals to patients admitted to medical wards due to COVID-19, as well as in the community following recovery. This process may involve both the use of pharmacological and/or psychological interventions. Given the fact that COVID-19 survivors were at higher risk of receiving a diagnosis of dementia at 6-months follow-up, access to memory clinics should also be available to this group of patients. More studies examining the short-term and long-term psychiatric effects during and after COVID-19 infection are required in the future to obtain a better understanding of the symptoms, as well as to develop effective management strategies.

Supplementary Materials

Supplementary table 1 lists demographic information of the studies included in the review reporting neurological symptoms in the context of COVID-19 infection and/or recovery.

Supplementary Material 1: List of studies for neurological symptoms of COVID-19 included in the systematic review.

	Year published	Type of study	Country of publication	Sample size	% Female	% Male
Al Mazrouei et al	2020	Case Report	UAE	1	0	100
Al-Olama et al	2020	Case Report	UAE	1	0	100
AlKetbi, R. et al	2020	Case Report	UAE	1	0	100
Capelli, M. et al	2020	Case Series	Italy	27	63	37
Cotelli, M. et al	2020	Case Report	Italy	1	100	0
Daher, V. B. et al	2020	Case Report	Brazil	1	0	100
Dalakas, M. C.	2020	Case Series	..	11
De Freitas F. et al	2020	Case Study	Brazil	1	0	100
Deliwala, S. et al	2020	Case Report	USA	1	100	0
Dugue, R. et al	2020	Case Report	..	1	0	100
Espinosa, P. S. et al	2020	Case Report	..	1	0	100
Fadakar, N. et al	2020	Case Report	Iran	1	0	100
Fan, S. et al	2020	Case Series	China	86	32	63
Farhadian, S. et al	2020	Case Report	USA	1	100	0
Farley, M. and Zuberi, J.	2020	Case Report	..	1	0	100
Farzi, M. A. et al	2020	Case Report	Iran	1	0	100
Gilani, S. et al	2020	Case Series	Iran	8	75	25
Goldberg, M. F. et al	2020	Case Report	USA	64	0	100
Haddad, S. et al	2020	Case Report	USA	41	0	100
Haddadi, K. et al	2020	Case Report	Iran	1	100	0
Hamidi, A. et al	2020	Case Report	Iran	1	0	100
Hanafi, R. et al	2020	Case Report	..	1	0	100
Hepburn, M. et al	2020	Case Series	USA	2	0	100
Hernández-Fernández, F. et al	2020	Case Series	Spain	23	22	78
Klironomos, S. et al	2020	Cohort Study	Sweden	185	25	75
Koleva, T. et al	2020	Retrospective Study	Bulgaria	133
Kremer, S. et al	2020	Retrospective Study	France	64	33	67
Lascano, A. M. et al	2020	Case Series	Switzerland	..	100	0
Mahboob, S. et al	2020	Case Report	USA	1	100	0
Mao, L. et al	2020	Case Series	China	214	59	41
Najjar, S. et al	2020	Case Series		3	100	0
Ottaviani, D. et al	2020	Case Report	Italy	1	100	0
Paniz-Mondolfi, A. et al	2020	Case Report		1	0	100
Parsons, T. et al	2020	Case Report	USA	1	100	0
Paybast, S. et al	2020	Case Report	Iran	2	50	50
Pinna, P. et al	2020	Case Series	USA	50	42	58
Poncet-Megemont, L. et al	2020	Cohort Study	France	139	33	67
Reichard, R. R. et al	2020	Case Report	USA	1	0	100
Rogg, J. et al	2020	Case Report		1	1	100

Romero Cantero, V. et al	2020	Case Series		2	0	100
Romero-Sánchez, C. et al	2020	Observational Study	Spain	841	44	56
Collantes, M. E. V.	2020	Systematic Review	Philippines	6,335
Chang, D. et al.	2020		China	13	23	77
Chen, T. et al.	2020	Retrospective Study	China	203	47	53
Chung, M. et al.	2020	Retrospective study	China	21	38	62
Du, RH et al.	2020	Prospective study	China	179
Gupta, N. et a.	2020	Retrospective study	India	21
Kim et al.	2020	Cohort study	Korea	28	46	54
Lei, Z. et al.	2020	Cross sectional study	China	20	50	50
Li, X et al.	2020	Retrospective study	China	548	49	51
Liu, Y. et al.	2020	Retrospective	China	12	33	67
Pan, F. et al.	2020	Retrospective	China	21	71	29
Shen, L. et al.	2020	Retrospective	China	119	53	47
Shi, H. et al.	2020	Retrospective study	China	81	48	52
Song, F. et al.	2020	Retrospective study	China	51	51	49
Vu, D. et al.	2020	Case report		1	0	100
Wang, R. et al.	2020	Retrospective study	China	125	43	57
Wang Z. et al.	2020	Retrospective study	China	2	50	50
Pongpirul, WA. et al.	2020		Thailand	11	45	55
Wu, J. et al.	2020	Retrospective study	China	80	47	53
Xu, X. et al.	2020	Case series	China	90	57	43
Yang, X. et al.	2020	Retrospective study	China	52	33	67
Zheng, F. et al.	2020	Retrospective study	China	161	50	50
Correia, A. O.	2020	Systematic Review	Brazil	409
Moriguchi et al.	2020	Case Report	Japan	1	..	100
Poyiadji et al.	2020	Case Report	USA	1	100	
De Sanctis, P.	2020	Systematic Review	Italy	18	44	56
Toscano, G. et al	2020	Case series	Italy	5	20	80
Virani et al.	2020	Case report	USA	1	0	100
Zhao H. et al.	2020	Case report	China	1	100	0
Sedaghat and Karimi	2020	Case report	Iran	1	0	100
Alberti et al.	2020	Case report	Italy	1	100	0
Camdessanche et al.	2020	Case report	France	1	0	100
Padroni et al.	2020	Case report	Italy	1	100	0
El Otmani et al.	2020	Case report	Morocco	1	100	0

Coen et al.	2020	Case report	Switzerland	1	0	100
Galan et al.	2020	Case report	Spain	1	0	100
Marta-Enguita et al.	2020	Case report	Spain	1	100	0
Scheidl et al.	2020	Case report	Germany	1	100	0
Juliao Caamano et al.	2020	Case report	Spain	1	0	100
Di Carlo, D. T.	2020	Systematic Review	Italy	12,157	49.4	50.6
Beltran-Corbellini A et al.	2020	Case-control study	Spain	79
Chen et al.	2020	Descriptive study	China	99	32	68
Duanmu Y et al.	2020	Cross-sectional study	USA	100	44	56
Feng et al.	2020	Retrospective study	China
Giacomelli A et al.	2020	Cross-sectional	Italy	59	32	68
Helms et al.	2020		France	58
Jain R. et al.	2020	Retrospective study	USA	454	39	61
Lechien et al.	2020		France-Italy	417	63	37
Li K et al.	2020	Retrospective study	China	83	47	53
Mahammedi et al.	2020	Retrospective study	Italy	108	36	64
Qin et al.	2020	Retrospective study	China	1,875	50	50
Radmanesh et al.	2020	Retrospective Case Series	USA	242	38	62
Tian et al.	2020	Retrospective study	China	262	52	48
Wan et al.	2020	Case series	China	135	47	53
Wang et al	2020	Case series	China	138	46	54
Xu et al.	2020	Retrospective case series	China	62	44	56
Dinakaran, D.	2020	Systematic Review		399
Yin et al.	2020	Case report	China	1	0	100
Ye et al.	2020	Case report	China	1	0	100
Alkeridy et al.	2020	Case report	Saudi Arabia	1	0	100
Duong et al.	2020	Case report		1	100	0
Avula et al.	2020	Case series		4	75	25
Ellul, M. A. et al	2020	Systematic Review	UK
Bernard-Valnet et al	2020	Case series	Switzerland	2	100	0
Pilotto et al	2020	Case report	Italy	1	0	100
Sohal et al	2020	Case report	USA	1	0	100
Vollono et al	2020	Case report	Italy	1	100	0
Wong et al	2020	Case report	UK	1	0	100
Benussi et al	2020	Case series	Italy	15		
Chacon-Aguilar et al	2020	Case report	Spain	1	0	100
Filatov A. et al	2020	Case report	USA	1	0	100
Garazzino S. et al	2020	Case series	Italy	5

Neerland et al	2020	Case report	Norway	1	100	0
Zhou et al	2020	Case report	China	1
Zhao K. et al	2020	Case report	China	1	0	100
Zanin et al	2020	Case report	Italy	1	100	0
Zhang T. et al	2020	Case report	USA	1	100	0
Abdelnour L. et al	2020	Case report	UK	1	0	100
Dinkin et al	2020	Case report	USA	1	0	100
Gutierrez-Ortiz C.	2020	Case report	Spain	1	0	100
Pellitero S.	2020	Case report	Spain	1	100	0
Jin M	2020	Case report	China	1	0	100
Suwanwongse	2020	Case report	USA	1	0	100
Benezit	2020	Case series	France	63
Haehner	2020	Case series	Germany	22
Hornuss D.	2020	Case series	Germany	18
Klopfenstein	2020	Case series	France	114
Moien	2020	Case series	Iran	59
Vaira LA.	2020	Case series		72
Al Saeigh	2020	Case report	USA	2	50	50
Beyrouiti	2020	Case series	UK	6	17	83
Gonzalez-Pinto T.	2020	Case report	Spain	1	100	0
Klok FA	2020	Case series	Netherlands	184	24	76
Li, Y. et al.	2020	Retrospective study	China	221	41	59
Lodigiani	2020	Case series	Italy	388	32	68
Lushina, N.	2020	Case series	USA	1	0	100
Morassi, M	2020	Case series	Italy	6	17	83
Moshayedi P.	2020	Case report	USA	1	0	100
Oxley	2020	Case series	USA	5	0	100
Zhang Y.	2020	Case series	China	3	33	67
Zhai	2020	Case report	China	1	0	100
Sharifi-Razavi, A	2020	Case report	Iran	1	0	100
Garg, Ravindra Kumar.	2020	Systematic Review	..	56
Huang et al.	2020	Case Report	USA	1	100	0
Benameur et al.	2020	Case series	USA	3	33	67
McAbee et al.	2020	Case report	USA	1	0	100
Chaumont et al.	2020	Case report	Guadeloupe	1	0	100
Hayashi M et al.	2020	Case report	Japan	1	0	100
Afshar et al.	2020	Case report	Iran	1	100	0
Dixon et al.	2020	Case report	UK	1	100	0
Elkady et al.	2020	Case report	Egypt	1	100	0
Dogan et al.	2020	Case series	Turkey	6	17	83
Brun et al.	2020	Case report	France	1	100	0
Byrnes et al.	2020	Case report	USA	1	0	100
Novi et al.	2020	Case report	Italy	1	100	0
Nepal P. et al.	2020	Case report	USA	1	0	100
Balestrino R. et al	2020	Case report	Italy	1	0	100
Zayet S. et al.	2020	Case series	France	2	0	100

Somani et al.	2020	Case series	USA	1	100	0
Balloy et al.	2020	Case report	France	1	0	100
Anzalone et al.	2020	Case series	Italy	4	50	50
Sachs JR et al.	2020	Case study	USA	1	0	100
Kaya et al.	2020	Case report	Turkey	1	0	100
Franceschi et al.	2020	Case series	USA	2	50	50
Kishfy et al.	2020	Case series	USA	2	50	50
Packwood et al.	2020	Case report	USA	1	0	100
Matos et al.	2020	Case report	Portugal	1	0	100
Ghannam, M. et al	2020	Systematic Review	USA	82	18	82
Wei H. et al	2020	Case study	China	1	0	100
Zhou B. et al.	2020	Case report	China	1	100	0
Valderrama EV. Et al.	2020	Case report		1	0	100
Viguiet A. et al.	2020	Case report		1	0	100
Hughes et al.	2020	Case report		1	0	100
Gupta, I.	2020	Systematic Review		1034	55	45
Gane et al.	2020	Case report	UK	1	0	100
Eliezer et al.	2020	Case report	France	1	100	0
Spinato et al.	2020		Italy	202	52	48
Munhoz, R. P.	2020	Systematic Review	
Huang, C. et al.	2020		China	41	29	71
Lu, L. et al.	2020	Retrospective study	China	304	40	60
Neishaboori, A. M.	2020	Systematic Review		1,643	41	59
Chen, T. et al.	2020	Retrospective study	China	274	38	62
Nepal, G.	2020	Systematic Review	
Karimi, N. et al.	2020	Case report	Iran	1	100	0
Qiu, H. et al.	2020	Cohort study	China	36
Zhou, F. et al.	2020	Cohort study	China	191
Guan, WJ. et al.	2020		China	1,099	49	51
Fu, B. et al.	2020	Case series	China	2	0	100
Wan, Y. et al.	2020	Case report	China	1	100	0
Yan, CH. et al.	2020	Retrospective study	USA	169
Payus, A. O.	2020	Systematic Review	
Xinhua et al.	2020	Case report	China	1	0	100
Pinzon, R. T.	2020	Systematic Review	Indonesia	7,559
Qian, GQ. et al.	2020	Case series	China	88
Hu et al.	2020	Case series	China	24
Wu, J. et al.	2020	Cross-sectional	China	80
Liu, K. et al.	2020	Cross-sectional	China	137

Guan, WJ. Et al.	2020	Cohort study	China	1,590
Zhang, X. et al.	2020	Cohort study	China	645
Han Y, et al.	2020	Cohort study	China	25
Wang, L. et al.	2020	Cohort study	China	339
Cai, Q. et al.	2020	Cohort study	China	298
Cao, J. et al.	2020	Cohort study	China	102
Yang, W. et al.	2020	Cohort study	China	149
Korea Centers for Disease Control and Prevention	2020	Case series	South Korea	28
Zhao, W. et al.	2020	Cohort study	China	101
Xu, YH. et al.	2020	Cohort study		50
Li, X. et al.	2020	Cohort study	China	131
Wang, X. et al.	2020	Cohort study	China	1,012
Rogers, J. P.	2020	Systematic Review	UK	3,559
Chen, G. et al.	2020	Cohort study	China	21	19	81
Zhang, B. et al.	2020	Cohort study	China	82	38	62
Qi, D. et al.	2020	Retrospective study	China	267	44	56
Huang, Y. et al.	2020	Cohort study	China	36	31	69
Leung et al.	2020		China	50	54	46
Seyed Hamidreza Bagheri et al	2020	Cross-sectional study	Iran	10,069	81.68	18.32
Á. Beltrán-Corbellini et al	2020	Case control study	UK	79	39.2	60.8
R. Bernard-Valnet et al	2020	Case report	UK	2	100%	0
Tao Chen et al	2020	Retrospective case series	UK	274	38	62
Lisa Duong et al	2020	Case report	USA	1	100	0
Asia Filatov et al	2020	Case report	USA	1	0	100
Consuelo Gutiérrez-Ortiz et al	2020	Case series	Germany	2	0	100
Julie Helms et al	2020	Case series	USA	58
Jerome R Lechien et al	2020	Case series	Germany	417	63.1	36.9
Yanan Li et al	2020	Case series	UK	219	59.4	40.6
Lu Lu et al	2020	Case series	USA	304	40.1	59.9
Ling Mao et al	2020	Case series	USA	214	59.3	40.7
Shima T Moein et al	2020	Case-control study	USA	60	33.3	66.6
Takeshi Moriguchi Takeda et al	2020	Case report	Netherlands	1	0	100
Marina Padroni et al	2020	Case report	Germany	1	100	0
Neo Poyiadji et al	2020	Case report	USA	1	100	0
Z. Sedaghata and N. Karimib	2020	Case report	USA	1	0	100
A. Sharifi-Razavi et al	2020	Case report	Netherlands	1	0	100
Gianpaolo Toscano et al	2020	Case series	USA	5	20	80
Catello Vollono et al	2020	Case report	UK	1	100	0
Carol H. Yan et al	2020	Cross-sectional	USA	59	49.2	49.2

Mingxiang Ye et al	2020	Case report	USA	1	0	100
Rong Yin et al	2020	Case report	USA	1	0	100
Tianshu Zhang et al	2020	Case report	USA	1	100	0
Hua Zhao et al	2020	Case report	UK	1	100	0
Kang Zhao et al	2020	Case report	..	1	0	100
Giacomo Spinato et al	2020	Case series	USA	202	51	49
François Bénézit et al	2020	Case series	UK	259
Sancho-Saldaña et al	2020	Case Report	UK	1	100	0

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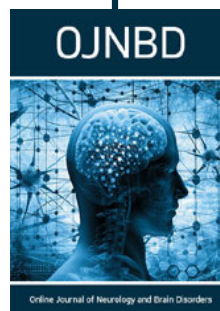
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