Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Multiple Sclerosis and Related Disorders 51 (2021) 102917

Contents lists available at ScienceDirect

Multiple Sclerosis and Related Disorders

journal homepage: www.elsevier.com/locate/msard

Original article

COVID-19 and emerging spinal cord complications: A systematic review

Ritwick Mondal [a], Shramana Deb [b], Gourav Shome [c], Upasana Ganguly [a], Durjoy Lahiri [a,d,*], Julián Benito-León [e,f,g,**]

[a] Institute of Post Graduate Medical Education and Research, SSKM Hospital, Kolkata, India
[b] S.N. Pradhan Centre for Neuroscience, University of Calcutta, Kolkata, India
[c] Department of Microbiology, University of Calcutta, Kolkata, India
[d] R.G. Kar Medical College and Hospital, Kolkata, India
[e] Department of Neurology, University Hospital "12 de Octubre", Madrid, Spain
[f] Centro de Investigación Biomédica en Red sobre Enfermedades Neurodegenerativas (CIBERNED), Madrid, Spain
[g] Department of Medicine, Complutense University, Madrid, Spain

ARTICLE INFO

Keywords:
Sars-cov-2
Covid-19
Coronavirus
Demyelinating disorders
Multiple sclerosis
Encephalomyelitis

ABSTRACT

Background: : Spinal cord complications associated with coronavirus infectious disease of 2019 (COVID-19) are being widely reported. The purpose of this systematic review was to summarize so far available pieces of evidence documenting *de novo* novel severe acute respiratory syndrome coronavirus (SARS-CoV-2) mediated spinal cord demyelinating diseases. Indeed, the spinal demyelinating disorders that have been reported in those patients who have suffered from COVID-19 rather than on the people already living with diagnosed or undiagnosed primary demyelinating disorders.
Methods: : We used the existing PRISMA consensus statement. Data were collected from PubMed, NIH Litcovid, EMBASE and Cochrane library databases, as well as Pre-print servers (medRxiv, bioRxiv, and pre-preints.org), until September 10, 2020, using pre-specified searching strategies.
Results: : The 21 selected articles were all case reports and included 11 (52%) men and 10 (48%) women. The mean age was of 46.7 ± 18.0. The neurological manifestations included weakness, sensory deficit, autonomic dysfunction and ataxia. In most cases, elevated cerebrospinal fluid protein as well as lymphocytic pleocytosis were found. SARS-CoV-2 was detected in five (24%) patients, meanwhile in 13 (62%) patients, the testing was negative. Testing was not performed in two cases and, in one, data were unavailable. Nearly half of the cases ($N = 9$) were associated with isolated long extensive transverse myelitis (LETM), whereas a combination of both LETM and patchy involvement was found in two. Only five patients had isolated short segment involvement and two patchy involvement. Furthermore, concomitant demyelination of both brain and spine was reported in six patients. Concerning the prognosis, most of the patients improved and the mortality rate was low ($N = 2$, <10%).
Conclusion: : Spinal cord demyelination should be added to the plethora of immune mediated neurologic complications associated with COVID-19.

1. Introduction

The novel severe acute respiratory syndrome coronavirus (SARS-CoV-2) has now prevailed across the world since WHO declared it as a pandemic on March 11, 2020. Initially, SARS-CoV-2 was primarily considered as a respiratory pathogen. However, with time it has behaved as a virus with the potential to cause multi-system involvement. Apart from pulmonary, renal, gastrointestinal, and hematological complications, neurological manifestations have also been reported frequently (Roy et al., 2021). It is currently known that several central and peripheral nervous system disorders may appear following SARS-CoV-2 infection (Roy et al., 2021, Yavarpour-Bali and Ghasemi-Kasman, 2020). Neurological features may occasionally precede the typical constitutional or respiratory symptoms of the coronavirus infectious disease of 2019 (COVID-19) (Lahiri and Ardila, 2020). Among the severe central nervous system (CNS) manifestations, stroke is one of the most frequently reported (Roy et al., 2021, Yavarpour-Bali and Ghasemi-Kasman, 2020, Lahiri and Ardila, 2020, Asadi-Pooya, 2020),

* Corresponding author: Durjoy Lahiri, Bangur Institute of Neurosciences, IPGME&R, Kolkata, India.
** Corresponding author: Julián Benito-León, Department of Neurology, University Hospital "12 de Octubre", Madrid, Spain.
E-mail addresses: dlahiri1988@gmail.com (D. Lahiri), jbenitol67@gmail.com (J. Benito-León).

https://doi.org/10.1016/j.msard.2021.102917
Received 7 October 2020; Received in revised form 18 January 2021; Accepted 17 March 2021
Available online 21 March 2021

meanwhile demyelinating disorders and seizures are now being increasingly documented as well (Roy et al., 2021, Yavarpour-Bali and Ghasemi-Kasman, 2020, Lahiri and Ardila, 2020, Asadi-Pooya, 2020, Ellul et al., 2020, Nepal et al., 2020). COVID-19 related peripheral nervous system (PNS) involvement has mostly been seen in the form of Guillain-Barré syndrome (GBS) and myositis (Roy et al., 2021, Yavarpour-Bali and Ghasemi-Kasman, 2020, Lahiri and Ardila, 2020, Asadi--Pooya, 2020, Nepal et al., 2020). Further, spinal cord complications associated with COVID-19 are being widely reported (Sánchez-Raya and Sampol, 2020).

The inter-relationship between demyelinating disorders and COVID-19 has two dimensions. On the one hand, SARS-CoV-2 infection may lead to brain and spinal cord demyelination. On the other hand, patients with known primary demyelinating disorders may experience an exacerbation of pre-existing neurological features (Roy et al., 2021). The purpose of this systematic review was to summarize so far available pieces of evidence documenting de novo SARS-CoV-2 mediated spinal cord demyelinating diseases. Indeed, the spinal demyelinating disorders that have been reported in those patients who have suffered from COVID-19 rather than on the people already living with diagnosed or undiagnosed primary demyelinating disorders.

2. Methods

2.1. Design

This systematic review was conducted by following the *Preferred Reporting for Systematic Review and Meta-Analysis* (PRISMA) consensus statement (CRD42020201843) [https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42020201843]. Studies relevant to cases of COVID-19 with suspected or confirmed spinal cord demyelinating diseases were included.

2.2. Search strategy

In this systemic review, data were collected from PubMed, NIH Litcovid, EMBASE and Cochrane library databases, until September 10, 2020, using pre-specified searching strategies. The search strategy consisted of a variation of keywords of relevant medical subject headings (MeSH) and keywords, including “SARS-CoV-2”, “COVID-19”, “coronavirus”, “demyelinating disorders”, “multiple sclerosis” and “encephalomyelitis”. Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV), Middle East Respiratory Syndrome Coronavirus (MERS-CoV) and various other human coronaviruses were also included in our search strategy to capture related articles. We also hand-searched additional COVID-19 specific articles using the reference list of the selected studies, relevant journal websites, and renowned pre-print servers (medRxiv, bioRxiv, and pre-preints.org) from 2019 to the current date for literature inclusion. To decrease publication bias, we invigilated the references of all studies potentially missed in the electrical search. Content experts also searched the gray literature of any relevant articles.

2.3. Study selection criteria

All peer-reviewed, pre-print (not-peer-reviewed) including cohort, case-control studies, and case reports, which met the pre-specified inclusion and exclusion criteria, were included in this study.

2.4. Inclusion criteria

Studies meeting the following inclusion criteria were included: (i) Studies regarding COVID-19 positive patients with suspected or confirmed spinal cord demyelinating diseases; (ii) COVID-19 studies revealing possible association with multiple sclerosis (MS) or related neuroimmune disorders with confirmed or suspected spinal involvement; and (iii) Studies published in English. Simultaneously, parallel search was conducted to have a comparative as well as a retrospective outlook into the distribution of cases with similar neurological manifestations in previous outbreaks, i.e., Severe Acute Respiratory Syndrome (SARS-CoV), Middle East Respiratory Syndrome Coronavirus (MERS-CoV) and various other human coronaviruses.

2.5. Exclusion criteria

We excluded studies if COVID-19 had not been confirmed and those written in languages other than English. We also excluded review papers, viewpoints, commentaries, and studies where information related to neurological manifestations or spinal demyelination was not reported.

2.6. Data extraction

Before the screening process, a team of two reviewers (GS and SD) participated in the calibration and screening exercises. The first reviewer (GS) subsequently screened independently the titles and abstracts of all identified citations, meanwhile the second reviewer (SD) verified those citations and screened papers by the first reviewer (GS). Another reviewer (UG) then retrieved and screened independently the full texts of all citations deemed eligible by the reviewer (SD) and analyzed those data. The other two reviewers (RM and DL) independently verified these extracted full texts for eligibility towards analysis and designed the overall study structure. JBL resolved disagreements whenever necessary and took final decisions regarding the study. Throughout the screening and data extraction process, the reviewers used piloted forms. In addition to the relevant clinical data, the reviewers also extracted data on the following features: study characteristics (i.e., study identifier, study design, setting, and timeframe); outcomes (qualitative and/or quantitative); clinical factors (definition and measurement methods); and study limitations. The Newcastle-Ottawa scale was used to assess the selection procedure, the comparability, and the outcomes of each reviewed study.

2.7. Statistical analysis

Both qualitative and quantitative data were expressed in percentages. Unit discordance among the variables was resolved by converting the variables to a standard unit of measurement. A p value < 0.05 was considered as statistically significant, but it could not be calculated due to insufficient data. A meta-analysis was planned to analyze the association of the demographic findings, symptoms, biochemical parameters, and outcomes, but was later omitted due to lack of sufficient data.

3. Results

Around 750 articles were initially identified from the databases and 253 from different pre-prints servers. Finally, 712 articles were selected after removing the duplicates. Of these selected articles, 600 were excluded after screening titles and abstracts, leaving 112 articles for full-text review for possible inclusion in this study. Of these, 60 articles were excluded based on the inclusion and exclusion criteria for the study sample and few other articles were excluded for study types (e.g., review papers, correspondence, viewpoints, or commentaries). Fifty-two articles were finally selected for this study. Of these 52, 21 articles were included in the analysis (Abdelhady et al., 2020, AlKetbi et al., 2020, Chakraborty et al., 2020, Chow et al., 2020, Domingues et al., 2020, Kaur et al., 2020, Lisnic et al., Maideniuc and Memon, 2021, McCuddy et al., 2020, Munz et al., 2020, Novi et al., 2020, Otluoglu et al., 2020, Sarma and Bilello, 2020, Sotoca and Rodríguez-Álvarez, 2020, Utukuri et al., 2020, Valiuddin et al., 2020, Zachariadis et al., 2020, Zanin et al., 2020, Zhao et al., 2021, Zhou et al., 2020, Zoghi et al., 2020), and the remaining 31 were synthesized narratively (See, Fig. 1 and Table 1).

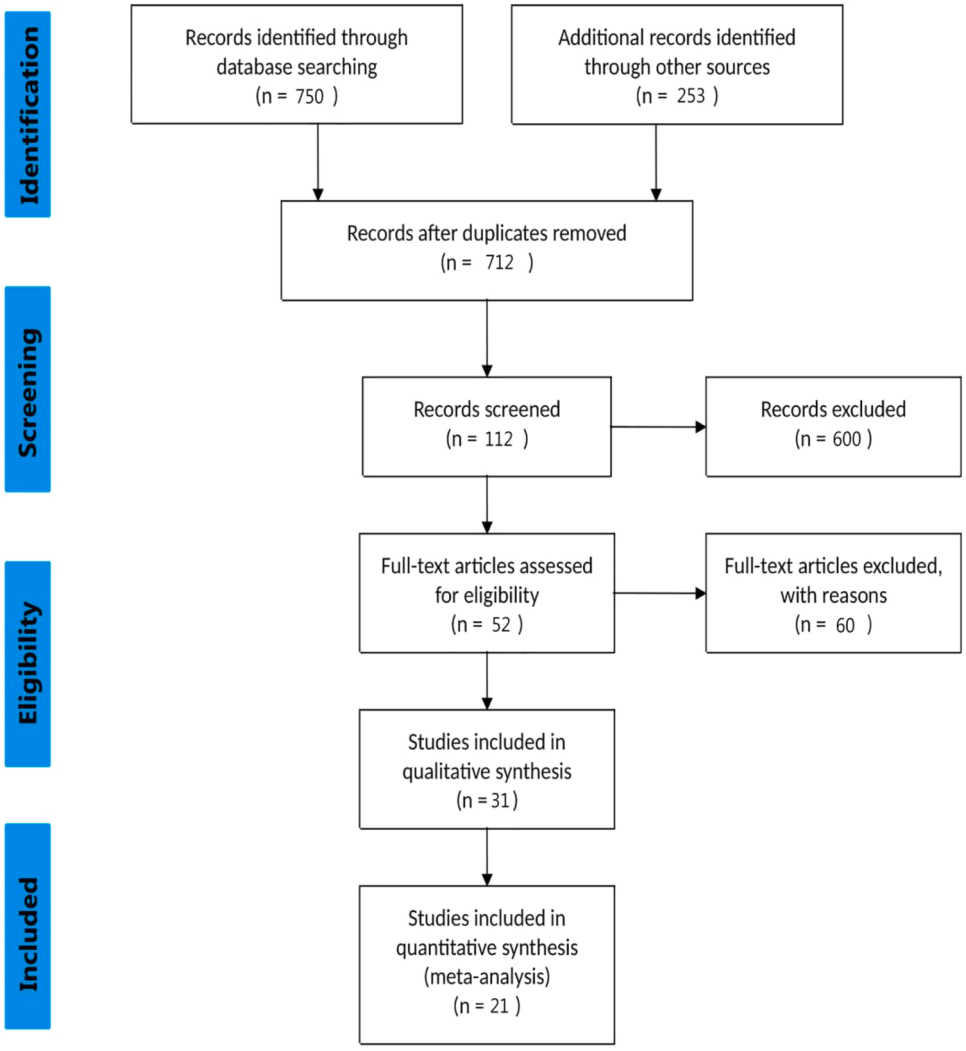

Fig. 1. : flowchart showing the algorithm used to identify the studies included in this review. Flow diagram template was adopted from PRISMA.

Table 1
Included Articles.

Authors name	Article name	Number of cases
Abdelhady et al. (Abdelhady et al., 2020) (Qatar)	Acute flaccid myelitis in COVID-19	1
AlKetbi et al. (AlKetbi et al., 2020) (UAE)	Acute myelitis as a neurological as a neurological complication of COVID-19: A case report and MRI findings	1
Chakraborty et al. (Chakraborty et al., 2020) (India)	COVID-19 associated acute transverse myelitis: rare entity	1
Chow et al. (Chow et al., 2020) (Australia)	Acute transverse myelitis in COVID-19 infection	1
Domingues et al. (Domingues et al., 2020) (Brazil)	First case of SARS-CoV-2 sequencing in CSF of a patient with suspected demyelinating disease	1
Kaur et al. (Kaur et al., 2020) (USA)	Transverse myelitis in a child with COVID-19	1
Lisnic et al. (Lisnic et al., 02 August 2020) (Moldova)	Acute transverse myelitis in a HIV positive patient with COVID-19	1
Maideniuc and Memon (Maideniuc and Memon, 2021) (USA)	Acute necrotizing myelitis and acute motor axonal neuropathy in COVID-19 patient	1
Mc Cuddy et al. (McCuddy et al., 2020) (USA)	Acute demyelinating encephalomyelitis (ADEM) in COVID-19 infection: A case series	1
Munz et al. (Munz et al., 2020) (Germany)	Acute transverse myelitis after COVID-19 Pneumonia	1
Novi et al. (Novi et al., 2020) (Italy)	Acute disseminated encephalomyelitis after SARS-CoV-2 infection	1
Otluoglu et al. (Otluoglu et al., 2020) (Turkey)	Encephalomyelitis associated with COVID-19 infection: case report	1
Sarma et al. (Sarma and Bilello, 2020) (USA)	A case report of acute transverse myelitis following novel Coronavirus	1
Sotoca et al. (Sotoca and Rodríguez-Álvarez, 2020) (Spain)	COVID-19 associated acute necrotizing myelitis	1
Utukuri et al. (Utukuri et al., 2020) (USA)	Possible acute disseminated encephalomyelitis related to severe acute respiratory syndrome coronavirus 2 infection	1
Valiuddin et al. (Valiuddin et al., 2020) (USA)	Acute transverse myelitis associated SARS-CoV-2: A case report	1
Zachariadis et al. (Zachariadis et al., 2020) (Switzerland)	Transverse myelitis related to COVID-19 infection	1
Zanin et al. (Zanin et al., 2020) (Italy)	SARS-CoV-2 can induce brain and spine demyelinating lesions	1
Zhao et al. (Zhao et al., 2021) (China)	Acute myelitis after SARS-CoV-2 infection: a case report	1
Zhou et al. (Zhou et al., 2020) (USA)	Myelin oligodendrocyte glycoprotein antibody- associated optic neuritis and myelitis in COVID-19	1
Zoghi et al. (Zoghi et al., 2020) (Iran)	A case of possible atypical demyelinating event of the central nervous system following COVID-19	1

Table 2
Demographic and clinical features.

Authors	Sex, age (yrs)	Comorbidities	Neurological signs/ symptoms	CSF characteristics SARS-Cov2 detection	CSF characteristics Abnormal parameters	Clinical diagnosis	Clinical features of COVID-19	Latency (days)	Treatment	Outcome
Abdelhady et al. (Abdelhady et al., 2020)	M, 52	Type 2 diabetes mellitus and G6PD deficiency	Lower abdominal pain, inability to pass urine, and flaccid paralysis	Negative	Increased WBC and proteins	Acute flaccid myelitis	Fever	Not mentioned	Steroids and acyclovir	Death
AlKetbi et al. (AlKetbi et al., 2020)	M, 32	Not mentioned	Flaccid paralysis	Not mentioned	Not mentioned	Acute myelitis	Fever with flu-like symptoms	1	Methylprednisolone, acyclovir, and andenoxaparin	In treatment
Chakraborty et al. (Chakraborty et al., 2020)	F, 59	Obesity	Acute, progressive, ascending flaccid paraplegia, urinary retention, and constipation. No sensation below Th10 level	Negative	Increased protein and adenosine deaminase	Acute transverse myelitis	Fever	Not mentioned	Methylprednisolone, antipyretics, and supportive care	Death
Chow et al. (Chow et al., 2020)	M, 60	Arterial hypertension and hypercholesterolemia	Paraparesis with constipation, urinary retention, hyperreflexia, reduced proprioception of lower limbs, and patchy paresthesia to the level of umbilicus	Negative	Increased WBC and proteins	Acute transverse myelitis	Fever, dysgeusia, anosmia and cough	2	Methylprednisolone	Discharged
Domingues et al. (Domingues et al., 2020)	F, 42	Similar clinical picture 3 years ago with spontaneous full recovery.	Paresthesia of upper left limb progressing to left hemithorax and hemiface	Positive	Normal	Clinically isolated syndrome	Mild respiratory symptoms	Not mentioned	Not mentioned	Discharged with full recovery
Kaur et al. (Kaur et al., 2020)	F, 3	Not mentioned	Flaccid quadriparesis and neurogenic respiratory failure requiring intubation. Complete quadriplegia after 12 h.	Negative	Increased RBC, WBC mainly neutrophilic and protein	LETM	None	21	Methylprednisolone, IVIG, plasma exchange and rituximab	Discharged
Lisnic et al. (Lisnic et al.,)	M, 27	HIV infection for 1 year, on anti-retroviral therapy	Spastic tetraparesis,Th7 superficial and C7 deep sensory level disturbance	Negative	Normal	Acute transverse myelitis	Mild fever	Not mentioned	Methylprednisolone and plasma exchange	Still in treatment
Maideniuc and Memon (Maideniuc and Memon, 2021)	F, 61	Arterial Hypertension, hyperlipidemia, hypothyroidism, and history of nasopharyngeal and uterine cancer	Tingling sensation in fingers and toes. Lost sensation from chest down and progressive spastic paraparesis. Bowel and bladder retention. Sensory level at C3.	Negative	Increased RBC, protein, and glucose	Acute necrotizing myelitis with acute motor axonal neuropathy	Runny nose and chills	4	Methylprednisolone and plasma exchange	Discharged with rehabilitation facility
Mc Cuddy et al. (McCuddy et al., 2020)	F,40 (patient 1)	Type 2 diabetes mellitus, arterial hypertension, obesity and 30 weeks pregnant	Paraplegia and significant, symmetric weakness in the upper extremity.	Negative	Increased protein and glucose	ADEM	Cough, chest pain, fever and shortness of breath	Not mentioned	Dexamethasone, HCQ, Zinc, and convalescent plasma therapy	Improving.
Munz et al. (Munz et al., 2020)	M, 60	Arterial hypertension, mild fatty liver and ureterolithiasis	Bladder dysfunction, progressive spastic paraparesis, and hypesthesia below Th9 level	Negative	Abnormal lymphocytic pleocytosis and increased protein	Acute transverse myelitis	Respiratory features	2	Acyclovir, ceftriaxone, and methylprednisolone	Dischargedwith steroid taper scheme
Novi et al. (Novi et al., 2020)	F, 64	Vitiligo, arterial hypertension, and monoclonal gammopathy	Irritability, headache, bilateral pupillary defect, visual loss, right abdominal sensory level deficit, and left sided lower limb hyperreflexia with Babinski sign	Positive	Lymphocytic pleocytosis, increased protein and positive OCB	Suspected ADEM	Flu-like symptoms, anosmia and ageusia	25	Methylprednisolone, oral prednisolone, and IVIG	Discharged with oral prednisolone tapering
Otluoglu et al. (Otluoglu et al., 2020)	M, 48	None	Progressive headache.	Positive	Increased glucose	Viral encephalitis and myelitis	Persistent cough, fatigue, myalgia, and anosmia	Not mentioned	HCQ, favipiravir, acyclovir, methylprednisolone, levetiracetam, piperacillin and tazobactam	Still under treatment with stable condition

(*continued on next page*)

Table 2 (*continued*)

Authors	Sex, age (yrs)	Comorbidities	Neurological signs/ symptoms	CSF characteristics SARS-Cov2 detection	CSF characteristics Abnormal parameters	Clinical diagnosis	Clinical features of COVID-19	Latency (days)	Treatment	Outcome
Sarma et al. (Sarma and Bilello, 2020)	F, 28	Hypothyroidism	Persisting lumbosacral back pain without radiation. Paresthesia in lower limbs with total loss of sensation upwards until tip of tongue, urinary retention, decreased sensation below Th5 level and Lhermitte's sign	Not mentioned	Increased WBC and protein	Transverse myelitis	Cough, low grade fever, low back pain, myalgia, rhinorrhea, nausea and vomiting	Not mentioned	Prednisolone and plasma exchange	Discharged with steroid tapering
Sotoca et al. (Sotoca and Rodríguez-Álvarez, 2020)	F, 69	Not mentioned	Irradiated cervical pain, imbalance, motor weakness, numbness in left hand, right facial and left hand hypesthesia, left hand weakness and hyperreflexia	Negative	Lymphocytic pleocytosis	Acute necrotizing myelitis	Fever and dry cough	1	Methylprednisolone and plasma exchange	Discharged with oral prednisolone
Utukuri et al. (Utukuri et al., 2020)	M, 44	Not mentioned	Paraparesis and urinary retention	Positive	Increased WBC, mainly lymphocytes	ADEM	Lethargy	Not mentioned	Methylprednisolone and IVIG	Dischargedwith rehabilitation facility
Valiuddin et al. (Valiuddin et al., 2020)	F, 61	Not mentioned	Progressing paraparesis with bilateral extensor plantar responses, constipation, difficulty in voiding and upper limb weakness	Negative	Increased protein	Acute transverse myelitis	Generalized weakness, rhinorrhea and chills	4	Methylprednisolone and plasma exchange	Still in treatment with rehabilitation facility
Zachariadis et al. (Zachariadis et al., 2020)	M, 63	Obesity	Paraplegia with total anesthesia below Th10 and sphincter dysfunction	Negative	Increased WBC and protein	Transverse myelitis	Rhinorrhea, odynophagia, myalgia and fever	5	IVIG and corticosteroids	Transferred to neurorehabilitation center
Zanin et al. (Zanin et al., 2020)	F, 54	Anterior communicating artery aneurysm 20 years ago, treated surgically	Found unconscious at home	Negative	Normal	Spinal demyelinating lesion	Anosmia and ageusia.	Not mentioned	Dexamethasone, antiepileptic, antiretroviral drugs, and HCQ	Discharged but with rehabilitation facility
Zhao et al. (Zhao et al., 2021)	M, 66	Not mentioned	Paraparesis with urinary and bowel incontinence and sensory level at Th10. Decreased tendon reflexes of both lower limbs	Not done	Not done	Acute myelitis	Fever and fatigue	6	Lopinavir/Ritonavir, ganciclovir, dexamethasone, moxifloxacin, meropenem, glutathione and mecobalamin	Transferred to rehabilitation center
Zhou et al. (Zhou et al., 2020)	M,26	Not mentioned	Numbness in lower limbs, neck discomfort, and sequential vision loss	Negative	Increased WBC	MOG-Ab associated optic neuritis with myelitis	Dry cough	Not mentioned	Methylprednisolone followed by prednisolone taper	Complete resolution
Zoghi et al. (Zoghi et al., 2020)	M, 21	Not mentioned	Tetraparesis with absent Babinski's sign and impaired sensation below Th8 level	IgG positive	Increased protein and WBC	LETM	Fever, cough, sore throat, loss of appetite, vomiting, malaise	17	Plasma exchange, vancomycin, meropenem and acyclovir	Discharged but with lower limbs paresis

ADEM = Acute disseminated encephalomyelitis; CSF = Cerebrospinal fluid; *F* = Female; G6PD = Glucose-6-phosphate dehydrogenase; HCQ = Hydroxychloroquine; HIV = Human immune deficiency virus; IgG = Immunoglobulin; IVIG =Intravenous immunoglobulin; LETM = Long extensive transverse myelitis; *M* = Male; MOG-Ab = Myelin oligodendrocyte glycoprotein antibody; OCB = Oligoclonal bands; RBC = Red Blood Cells. WBC = White Blood Cells.

Table 3
Neuroimaging features and autoimmune profiling.

Authors	Spinal Involvement			Level of involvement	Brain involvement	Autoimmune profiling
	LETM	Patchy	Short			
Abdelhady et al. (Abdelhady et al., 2020)	+	–	–	Hyperintense signal in ventral horns of gray matter in upper and mid thoracic spinal cord on T2WI	Normal	ANCA and ANA were negative
AlKetbi et al. (AlKetbi et al., 2020)	–	+	–	Extensive diffuse hyperintense signal involving predominantly the gray matter of the cervical, dorsal, and lumbar regions of the spinal cordon T2WI	Not done	Anti-LA, ANCA, RF, anti-cardiolipin, and anti –beta gp were negative
Chakraborty et al. (Chakraborty et al., 2020)	–	–	+	Dorsal spine hyperintensity at T_6 – T_7 on T2WI	Not done	Not done
Chow et al. (Chow et al., 2020)	+	–	–	T2 signal increased centrally in spinal cord from T_7.T_{10}	Normal	Anti-myelin associated gp IgM, anti-MOG and anti-NMO IgG were negative
Domingues et al. (Domingues et al., 2020)	–	–	+	Hyperintense signal in cervical spine on T2WI and STIR, indicating small left lateral ventral lesion with mass effect (0.4 cm) (with Gd contrast)	Normal	Anti SSA and anti SSB were negative
Kaur et al. (Kaur et al., 2020)	+	–	–	Swelling of cervical spinal cord, involving most of the transverse aspect of spinal cord, from lower medulla to mid thoracic level	Normal	Negative rheumatoid assessment. Anti-AQP-4 and anti-MOG were negative
Lisnic et al. (Lisnic et al.,)	+	–	–	Extensive C_4-T_5 lesion in posterior column on T2WI and right lateral column with Gd contrast	Normal	ANA, ANCA, anti-AQP-4 and anti-MOG were negative
Maideniuc and Memon (Maideniuc and Memon, 2021)	+	–	–	Hyperintense signal at C_3–C_4 level on T1WI	Normal	Lupus antibody was positive. Anti-MOG and anti-AQP-4 were negative
McCuddy et al. (McCuddy et al., 2020)	–	–	–	Normal	Multiple T2WI hyperintense lesions with restricted diffusion, involving corpus callosum, bilateral cerebral white matter, right pons and in the bilateral ventral medulla	Autoimmune profiling of cerebrospinal fluid was negative
Munz et al. (Munz et al., 2020)	–	–	+	Patchy hyperintense signal at T_9-T_{10} and T_3-T_5	Normal	Anti-neuronal, anti-MOG and anti-AQP4 were negative
Novi et al. (Novi et al., 2020)	–	–	+	Hyperintense spindle like single lesion al T_8 level on T2WI	Multiple T1WI post Gd enhancing lesions in brain. Follow-up MRI showed reduction in number of lesions	Anti-AQ4 and anti-MOG were negative
Otluoglu et al. (Otluoglu et al., 2020)	–	–	+	Confined hyperintense lesion at upper cervical spine	Hyperintense lesions both in the posterior medial cortical surface of the temporal lobe	Not done
Sarma et al. (Sarma and Bilello, 2020)	+	–	–	Elongated signal changes involving medulla and throughout the spinal cord to conus medullaris	Not done	ANA was negative
Sotoca et al. (Sotoca and Rodríguez-Álvarez, 2020)	+	–	–	Hyperintense signal lesion extending from medulla oblongata to C_7	Normal	Neuronal surface antibody was ruled out
Utukuri et al. (Utukuri et al., 2020)	+	+	–	Hyperintense signal lesions throughout cervical and thoracic spinal cord and conus medullaris	Hyperintense lesions within left posterior parietal lobe and periventricular region on FLAIR	Cardiolipin antibody immunoglobulin M was mildly elevated
Valiuddin et al. (Valiuddin et al., 2020)	–	+	–	Extensive ill-defined patchy hyperintense signal throughout the central aspect of spinal cord on STIR	Not done	Anti-GFAP, mGLUR, NMDA-R and anti-MOG were negative
Zachariadis et al.[24]	–	–	–	Normal	Normal	ANCA, ANA, anti-MOG, anti-SSB, anti-SSA, RF, GFAP, and Beta 2 glycoprotein 1 were negative
Zanin et al. (Zanin et al., 2020)	+	+	–	Hyperintense intra-medullary signal lesions on T2WI at bulb-medullary junction, and from C_3 to Th_6	T2W1 hyperintense lesions in periventricular white matter without restriction of diffusion nor contrast enhancement	Not done
Zhou et al. (Zhao et al., 2021)	+	–	–	Spinal signal enhancement at lower cervical and upper thoracic segment with mild central cord thickening	Bilateral optic nerve thickening up to the perichiasmal segments on T1WI	AQP4 was negative. Anti-MOG IgG was elevated
Zoghi et al. (Zhou et al., 2020)	+	–	–	LETM of upper cervical with intramedullary lesion	Corticospinal tract lesions in internal capsule extending to cerebral peduncles and pons on T2-FLAIR. Heterogeneous marble patterned hyperintensity in splenium of corpus callosum without diffusion weighted restrictions or contrast enhancement.	Anti-NMDAR, anti-MOG, anti-AQP4, anti-phospholipid, HLA B5, and ACE were negative

ACE = angiotensin converting enzyme; ANA = antinuclear antibody; ANCA = antineutrophil cytoplasmic antibodies; Anti-SSA = anti-Sjögren's syndrome-related antigen A; Anti-SSB = anti-Sjögren's syndrome-related antigen B; AQP-4 = aquaporin-4; FLAIR = fluid-attenuated inversion recovery; Gd = gadolinium; GFAP = glial fibrillary acidic protein; HLA = human leukocyte antigen; LA = lupus antigen; m-GLUR = metabotropic glutamate receptors; LETM = long extensive transverse myelitis; NMDA-R = N-methyl-D-aspartate receptor; NMO = neuromyelitis optica; RF = rheumatoid factor; STIR = short T1 inversion recovery; T2WI = T2-weighted image.

The 21 selected articles were all case reports and included 11 (52%) men and 10 (48%) women. The mean age was 46.7 ± 18.0. Fever (*N* = 11, 52%), cough (*N* = 6, 29%), myalgia (*N* = 6, 29%), vomiting (*N* = 2, 10%) and nausea (*N* = 1, 5%) were among the most frequent COVID-19 related features (See Table 2). The neurological manifestations included weakness (*N* = 14, 66.7%), sensory deficit (*N* = 14, 66.7%) autonomic dysfunction (*N* = 8, 3.1%), and ataxia (*N* = 1, 4.8%) (See Table 2).

Biochemical analysis of cerebrospinal fluid (CSF) revealed that glucose was within the normal range in most of the cases (*N* = 12, 57.1%), whereas one case was found with elevated glucose, another one with glucose below the normal range and the value of the remaining seven cases were not mentioned (See Table 2). The mean range of glucose (mg/dl) in CSF was 64.5 ± 16.4. In only three cases, both blood and CSF glucose were mentioned (blood glucose = 135 mg/dl, CSF glucose = 73 mg/dl, ratio = 0.5 (Valiuddin et al., 2020); and blood glucose = 110 mg/dl, CSF glucose = 34 mg/dl, ratio = 0.30 (Zhao et al., 2021)). In the report by Otluoglu et al. (Otluoglu et al., 2020), the CSF glucose was 5 mmol/L (90 mg/dl), while the corresponding value of blood glucose was 105 mmol/L (1890 mg/dl), which seems to be erroneous. Apart from this, CSF protein was found to be increased in most of the cases (*N* = 12, 57.1%), whereas in six cases (*N* = 6, 28.6%), it was below the normal range and the value was not mentioned in the remaining three cases (See Table 2). Median value of CSF protein (mg/dl) was 59 (IQR 36–79.1). Certain cell count parameters, such as white blood count (*N* = 10, 47.6%) and red blood count (*N* = 2, 10%) were found to be elevated (See Table 2). In addition, lymphocytic pleocytosis (*N* = 4, 19.0%) was also reported (See Table 2). SARS-CoV-2 was detected in the CSF in five (24%) patients, by means of qualitative real-time reverse-transcriptase–polymerase-chain-reaction assay (RT-PCR) in four and IgG positivity in one (See Table 2). SARS-CoV-2 detection was negative in 13 (62%) patients, whereas SARS-CoV-2 testing was not performed in two cases and data was unavailable in one case (See Table 2). Autoimmune profiling was negative in most cases, except two cases with positive oligoclonal bands and lupus antigen, respectively (See Tables 2 and 3).

Neuroimaging findings were reported in all except one patient. Among the neuroimaging modalities, MRI of the spine was done in 20 patients, whereas MRI of the brain in 16. Computed tomography (CT) scan of the spine and brain were done in one and four patients, respectively. We found that nearly half of the cases (*N* = 9, 45%) were associated with isolated long extensive transverse myelitis (LETM), whereas a combination of both LETM and patchy involvement was found in two (See Table 3). Only five patients had isolated short segment involvement and two patchy involvement (See Table 3). Furthermore, concomitant demyelination of both brain (including the brainstem) and spine was reported in six patients (Table 3).

Treatment was mainly carried out with corticosteroids (*N* = 18, 86%), including intravenous methylprednisolone (*N* = 14, 67%), intravenous dexamethasone (*N* = 2, 10%), and oral prednisolone (*N* = 1, 5%). Intravenous immunoglobulin was administered to five (24%) patients, meanwhile plasma exchange sessions to eight (38%). Antiviral drugs, such as acyclovir, lopinavir/ritonavir, ganciclovir and favipiravir, were administered to seven patients (33.3%), being acyclovir the most common drug of choice (*N* = 5, 24%). Hydroxychloroquine was administered to three (14.3%) patients. Two patients also received antiepileptic drugs. Most of the patients recovered although they were still under treatment at the time of discharge. Specifically, approximately one-third of the discharged patients were transferred to a rehabilitation center (*N* = 6, 28.6%) for further improvement. Only two (10%) patients died during the period of study.

4. Discussion

During this ongoing pandemic, clinicians and researchers worldwide have observed several immunological manifestations of SARS-CoV-2, affecting different organ systems. In the case of neurological manifestations of COVID-19, immunological mechanisms are known to play an important role in giving rise to diverse clinical presentations affecting both CNS and PNS (Roy et al., 2021). Contrary to how SARS-CoV-2 affects PNS (mostly in the form of GBS spectrum) (Abu-Rumeileh et al., 2020, Ghosh et al., 2020, Zhao et al., 2020, Finsterer et al., 2020, Gutiérrez-Ortiz et al., 2020), data regarding spinal cord involvement are scarce.

Spinal cord demyelination in COVID-19 might be an underrecognized neurological complication. Thus, in the present systematic review, we have only found 21 patients with SARS-CoV-2 mediated spinal cord complications. Eight (38.1%) of these patients had parainfectious acute myelitis and three (14.3%) post-infectious acute myelitis. Weakness, sensory deficit, autonomic dysfunction, including sphincter dysfunction and ataxia were the most frequent neurological manifestations. Most cases showed elevated cerebrospinal fluid protein as well as lymphocytic pleocytosis. With respect to neuroimaging data, almost half of the patients presented with LETM, followed by short segment and patchy involvement. LETM is usually observed in neuromyelitis optica spectrum disorder, infectious myelitis, lupus-related demyelination, and, occasionally, in MS. In India, tuberculosis is a known cause of LETM (Sahu et al., 2014). From a clinician's perspective, the above observations extend the differential diagnosis of LETM to include COVID-19 related spinal cord demyelination. Concerning the prognosis, most of the patients could be discharged and the mortality rate was low (<10%).

Pathogenetic mechanisms for the development of spinal cord demyelinating diseases following SARS-CoV-2 infection may be either mediated by direct neurotropism or by aberrant immune mediated injury, the latter being the most likely.

There are several pieces of evidence to support an aberrant immune mediated injury. SARS-CoV-2 infection is known to cause a cytokine storm (Mehta et al., 2020). The pro-inflammatory state, induced by cytokine storm, mainly sustained by IL-6, IL-1,and TNF-alpha, may be the responsible for the activation of glial cells, which may also trigger the onset of demyelination (Schett et al., 2020). In line with this, different strains of coronaviruses, such as HCoV-OC43 and MERS-CoV, have been found to initiate several immunopathogenic responses, which further cause the progression of demyelinating events in the CNS (Khateb et al., 2020). Furthermore, the S gene of the coronavirus mouse hepatitis virus is related to certain molecular aspects of demyelination, which indicates the potential role of viral envelope S glycoproteins in immune mediated demyelination (Sarma et al., 2000). Kim and Perlman (2005) demonstrated that an experimental strain of coronavirus JHM, even in the absence of T and B cells, developed an autoimmune demyelinating disorder in a mouse model, which suggests that the formation of anti-JHM antibodies is sufficient to cause the demyelination. In addition, last but not the least, dramatic response to intravenous immunoglobulin or plasma exchange sessions in several cases of SARS-CoV-2 mediated spinal cord demyelinating diseases points towards an underlying immune driven process.

Direct neurotropism as a pathogenic process of demyelination did not lie far behind. The presence of HCoV RNA in the CNS of patients with demyelinating disorders, suggests a possible association between coronaviruses and demyelination (Arbour et al., 2000). In a previous study, nucleic acids of HCoV-229E have been detected in the CNS tissue in four out of eleven MS patients, which suggests neurotropism of this species of coronavirus (Stewart et al., 1992). Moreover, coronavirus-like particles have been found from autopsies of two MS patients (Burks et al., 1980). Using *in situ* hybridization technique with cloned coronavirus cDNA probes, Murray et al. (Murray et al., 1992) detected coronavirus RNA in the demyelinating plaques in 12 of their 22 MS patients. In addition, significant amounts of coronavirus antigen and RNA were observed in active demyelinating plaques from two patients with rapidly progressive MS (Murray et al., 1992). Further, a 15-year-old boy, who presented with acute demyelinating encephalomyelitis (ADEM), tested positive for

HCoV-OC43 in CSF using RT-PCR (Yeh et al., 2004). In a series of four patients affected with neurological complications due to MERS-CoV, one of them met some criteria for diagnosis of the ADEM (Arabi et al., 2015). Interestingly, in four of the cases included in our systematic review, SARS-CoV-2 RNA could be detected in CSF.

There are some implicit limitations in the present review. Given the notable asymmetry between the total number of affected cases and reported cases of SARS-CoV-2 mediated spinal cord demyelinating diseases, it can be assumed that cases are currently under-reported. The current systematic review is based on a small number of cases, even after an extensive search of available literature, both peer-reviewed, and preprint. Also, several of the available reports do not describe the timeline of events in an organized manner making interpretation difficult. Laboratory features have also not been mentioned in detail in a few of the cases. In addition, there is a considerable heterogeneity in the available data that may be considered a hindrance in advanced analysis. Despite these shortcomings, the present organized review will act as a preliminary guide for clinicians while dealing with SARS-CoV-2 mediated spinal cord demyelinating diseases.

Authors' contributions

Dr. Mondal in: 1) the conception, organization of the research project; 2) the statistical analyses; and 3) the writing of the manuscript first draft and the review and critique of the manuscript.

Dr. Deb in: 1) the conception, organization of the research project; 2) the statistical analyses; and 3) the writing of the manuscript first draft and the review and critique of the manuscript.

Dr. Shome in: 1) the conception, organization of the research project; 2) the statistical analyses; and 3) the writing of the manuscript first draft and the review and critique of the manuscript.

Dr. Ganguly in: 1) the conception, organization of the research project; 2) the statistical analyses; and 3) the writing of the manuscript first draft and the review and critique of the manuscript.

Dr. Lahiri in: 1) the conception, organization of the research project; 2) the statistical analyses; and 3) the writing of the manuscript first draft and the review and critique of the manuscript.

Dr. Benito-León collaborated in: 1) the conception, organization and execution of the research project; 2) the writing of the manuscript first draft and the review and critique of the manuscript.

Declaration of Competing Interest

We wish to confirm that there are no known conflicts of interest associated with this publication and there has been no significant financial support for this work that could have influenced its outcome. We confirm that the manuscript has been read and approved by all named authors and that there are no other persons who satisfied the criteria for authorship but are not listed. We further confirm that the order of authors listed in the manuscript has been approved by all of us.

We confirm that we have given due consideration to the protection of intellectual property associated with this work and that there are no impediments to publication, including the timing of publication, with respect to intellectual property. In so doing we confirm that we have followed the regulations of our institutions concerning intellectual property.

We further confirm that any aspect of the work covered in this manuscript that has involved either experimental animals or human patients has been conducted with the ethical approval of all relevant bodies and that such approvals are acknowledged within the manuscript.

Acknowledgement

We are sincerely thankful to Rohan Sarkhel (Department of Computer Science and Engineering, Maulana Abul Kalam Azad University, West Bengal, India) for his assistance in the literature search and preparing the illustrations for this paper. Dr. Benito-León is supported by the National Institutes of Health, Bethesda, MD, USA (NINDS #R01 NS39422), European Commission (grant ICT-2011–287739, NeuroTREMOR), the Ministry of Economy and Competitiveness (grant RTC-2015–3967–1, NetMD—platform for the tracking of movement disorder), and the Spanish Health Research Agency (grant FIS PI12/01602 and grant FIS PI16/00451).

References

Abdelhady, M., Elsotouhy, A., Vattoth, S., 2020. Acute Flaccid Myelitis in COVID-19. BJR Case Rep 6. https://doi.org/10.1259/bjrcr.20200098, 20200098.

Abu-Rumeileh, S., Abdelhak, A., Foschi, M., Tumani, H., Otto, M., 2020 Aug 25. Guillain-Barré syndrome spectrum associated with COVID-19: an up-to-date systematic review of 73 cases. J Neurol 1–38. https://doi.org/10.1007/s00415-020-10124-x. Epub ahead of print. PMID: 32840686; PMCID: PMC7445716.

AlKetbi, R., AlNuaimi, D., AlMulla, M., et al., 2020. Acute myelitis as a neurological complication of Covid-19: a case report and MRI findings. Radiol Case Rep 15 (9), 1591–1595. https://doi.org/10.1016/j.radcr.2020.06.001.

Arabi, Y.M., Harthi, A., Hussein, J., et al., 2015. Severe neurologic syndrome associated with Middle East respiratory syndrome corona virus (MERS-CoV). Infection 43 (4), 495–501. https://doi.org/10.1007/s15010-015-0720-y.

Arbour, N., Day, R., Newcombe, J., Talbot, P.J., 2000. Neuroinvasion by human respiratory coronaviruses. J Virol 74 (19), 8913–8921. https://doi.org/10.1128/jvi.74.19.8913-8921.2000.

Asadi-Pooya, A.A., 2020. Seizures associated with coronavirus infections. Seizure 79, 49–52. https://doi.org/10.1016/j.seizure.2020.05.005.

Burks, J.S., DeVald, B.L., Jankovsky, L.D., Gerdes, J.C., 1980. Two coronaviruses isolated from central nervous system tissue of two multiple sclerosis patients. Science 209 (4459), 933–934. https://doi.org/10.1126/science.7403860.

Chakraborty, U., Chandra, A., Ray, A.K., Biswas, P., 2020. COVID-19-associated acute transverse myelitis: a rare entity. BMJ Case Rep 13 (8), e238668. https://doi.org/10.1136/bcr-2020-238668.

Chow, C.C.N., Magnussen, J., Ip, J., Su, Y., 2020. Acute transverse myelitis in COVID-19 infection. BMJ Case Rep 13 (8), e236720. https://doi.org/10.1136/bcr-2020-236720.

Domingues, R.B., Mendes-Correa, M.C., de Moura Leite, F.B.V., et al., 2020. First case of SARS-COV-2 sequencing in cerebrospinal fluid of a patient with suspected demyelinating disease. J Neurol 267, 3154–3156. https://doi.org/10.1007/s00415-020-09996-w.

Ellul, M.A., Benjamin, L., Singh, B., Lant, S., Michael, B.D., Easton, A., Kneen, R., Defres, S., Sejvar, J., Solomon, T., 2020 Sep. Neurological associations of COVID-19. Lancet Neurol 19 (9), 767–783. https://doi.org/10.1016/S1474-4422(20)30221-0.

Finsterer, J., Scorza, F.A., Ghosh, R., 2020. COVID-19 polyradiculitis in 24 patients without SARS-CoV-2 in the cerebro-spinal fluid. J. Med. Virol. https://doi.org/10.1002/jmv.26121, 4 Jun. 2020, doi:10.1002/jmv.26121.

Ghosh, R., Roy, D., Sengupta, S., Benito-León, J., 2020. Autonomic dysfunction heralding acute motor axonal neuropathy in COVID-19. J Neurovirol 26 (6), 964–966. https://doi.org/10.1007/s13365-020-00908-2.

Gutiérrez-Ortiz, C., Méndez-Guerrero, A., Rodrigo-Rey, S., et al., 2020. Miller Fisher syndrome and Polineuritis Cranialis in COVID-19. Neurology. https://doi.org/10.1212/WNL.0000000000009619.

Kaur, H., Mason, J.A., Bajracharya, M., et al., 2020. Transverse Myelitis in a Child With COVID-19. Pediatr Neurol 112, 5–6. https://doi.org/10.1016/j.pediatrneurol.2020.07.017.

Khateb, M., Bosak, N., Muqary, M., 2020. Coronaviruses and Central Nervous System Manifestations. Front Neurol. 11, 715. https://doi.org/10.3389/fneur.2020.00715. Published 2020 Jun 23.

Kim, T.S., Perlman, S., 2005. Virus-specific antibody, in the absence of T cells, mediates demyelination in mice infected with a neurotropic coronavirus. Am J Pathol 166, 801–809. https://doi.org/10.1016/S0002-9440(10)62301-2.

Lahiri, D., Ardila, A., 2020. COVID-19 Pandemic: a Neurological Perspective. Cureus 12 (4), e7889. https://doi.org/10.7759/cureus.7889.

Lisnic V., Nemtan V., Hacina E., et al. Acute transverse myelitis in a HIV-positive patient with COVID-19, 02 August 2020, PREPRINT (Version 1) available at *Research Square* [https://doi.org/10.21203/rs.3.rs-50901/v1+].

Maideniuc, C., Memon, A.B., 2021. Acute necrotizing myelitis and acute motor axonal neuropathy in a COVID-19 patient. J Neurol 268, 739. https://doi.org/10.1007/s00415-020-10145-6.

McCuddy, M., Kelkar, P., Zhao, Y., Wicklund, David, 2020.07.15. Acute Demyelinating Encephalomyelitis (ADEM) in COVID-19 infection: a Case Series. medRxiv, 20126730. https://doi.org/10.1101/2020.07.15.20126730.

Mehta, P., McAuley, D.F., Brown, M., Sanchez, E., Tattersall, R.S., Manson, J.J., 2020. COVID-19: consider cytokine storm syndromes and immunosuppression. Lancet. 395 (10229), 1033–1034.

Munz, M., Wessendorf, S., Koretsis, G., et al., 2020. Acute transverse myelitis after COVID-19 pneumonia. J Neurol 267 (8), 2196–2197. https://doi.org/10.1007/s00415-020-09934-w.

Murray, R.S., Brown, B., Brian, D., Cabirac, G.F., 1992. Detection of coronavirus RNA and antigen in multiple sclerosis brain. Ann Neurol 31 (5), 525–533. https://doi.org/10.1002/ana.410310511.

Nepal, G., Rehrig, J.H., Shrestha, G.S., et al., 2020. Neurological manifestations of COVID-19: a systematic review. Crit Care 24, 421. https://doi.org/10.1186/s13054-020-03121-z.

Novi, G., Rossi, T., Pedemonte, E., et al., 2020. Acute disseminated encephalomyelitis after SARS-CoV-2 infection. Neurol Neuroimmunol Neuroinflamm 7 (5), e797. https://doi.org/10.1212/NXI.0000000000000797.

Otluoglu, G.D., Yener, U., Demir, M.K., Yilmaz, B., 2020. Encephalomyelitis associated with Covid-19 infection: case report [published online ahead of print, 2020 Jul 7]. Br J Neurosurg 1–3. https://doi.org/10.1080/02688697.2020.1787342.

Roy, D., Ghosh, R., Dubey, S., Dubey, M.J., Benito-León, J., Kanti Ray, B, 2021. Neurological and Neuropsychiatric Impacts of COVID-19 Pandemic. Can J Neurol Sci 48 (1), 9–24. https://doi.org/10.1017/cjn.2020.173.

Sánchez-Raya, J., Sampol, J., 2020. Spinal cord injury and COVID-19: some thoughts after the first wave. Spinal Cord 58, 841–843. https://doi.org/10.1038/s41393-020-0524-5.

Sahu, S.K., Giri, S., Gupta, N., 2014. Longitudinal extensive transverse myelitis due to tuberculosis: a report of four cases. J Postgrad Med. 60 (4), 409–412. https://doi.org/10.4103/0022-3859.143977.

Sarma, D., Bilello, L.A., 2020. A Case Report of Acute Transverse Myelitis Following Novel Coronavirus Infection. Clin Pract Cases Emerg Med 4 (3), 321–323. https://doi.org/10.5811/cpcem.2020.5.47937.

Sarma, J.D., Fu, L., Tsai, J.C., Weiss, S.R., Lavi, E., 2000. Demyelination determinants map to the spike glycoprotein gene of coronavirus mouse hepatitis virus. J Virol 74, 9206–9213. https://doi.org/10.1128/JVI.74.19.9206-9213.2000.

Schett, G., Sticherling, M., Neurath, M.F., 2020 May. COVID-19: risk for cytokine targeting in chronic inflammatory diseases? Nat Rev Immunol 20 (5), 271–272. https://doi.org/10.1038/s41577-020-0312-7.

Sotoca, J., Rodríguez-Álvarez, Y., 2020. COVID-19-associated acute necrotizing myelitis. Neurol Neuroimmunol Neuroinflamm 7 (5), e803. https://doi.org/10.1212/NXI.0000000000000803.

Stewart, J.N., Mounir, S., Talbot, P.J., 1992. Human coronavirus gene expression in the brains of multiple sclerosis patients. Virology 191 (1), 502–505. https://doi.org/10.1016/0042-6822(92)90220-j.

Utukuri, P.S., Bautista, A., Lignelli, A., Moonis, G., 2020. Possible Acute Disseminated Encephalomyelitis Related to Severe Acute Respiratory Syndrome Coronavirus 2 Infection. AJNR Am J Neuroradiol 41 (9), E82–E83. https://doi.org/10.3174/ajnr.A6714.

Valiuddin, H., Skwirsk, B., Paz-Arabo, P., 2020. Acute transverse myelitis associated with SARS-CoV-2: a Case-Report. Brain BehavImmun Health 5, 100091. https://doi.org/10.1016/j.bbih.2020.100091.

Yavarpour-Bali, H., Ghasemi-Kasman, M, 2020 Sep 15. Update on neurological manifestations of COVID-19. Life Sci 257, 118063. https://doi.org/10.1016/j.lfs.2020.118063.

Yeh, E.A., Collins, A., Cohen, M.E., Duffner, P.K., Faden, H., 2004. Detection of coronavirus in the central nervous system of a child with acute disseminated encephalomyelitis. Pediatrics 113 (1 Pt 1), e73–e76. https://doi.org/10.1542/peds.113.1.e73.

Zachariadis, A., Tulbu, A., Strambo, D., Dumoulin, A., Di Virgilio, G., 2020. Transverse myelitis related to COVID-19 infection. J Neurol 267, 3459–3461. https://doi.org/10.1007/s00415-020-09997-9.

Zanin, L., Saraceno, G., Panciani, P.P., et al., 2020. SARS-CoV-2 can induce brain and spine demyelinating lesions. Acta Neurochir (Wien) 162 (7), 1491–1494. https://doi.org/10.1007/s00701-020-04374-x.

Zhao, H., Shen, D., Zhou, H., Liu, J., Chen, S., 2020. Guillain-Barré syndrome associated with SARS-CoV-2 infection: causality or coincidence? Lancet Neurol 19 (5), 383–384. https://doi.org/10.1016/S1474-4422(20)30109-5.

Zhao, K., Huang, J., Dai, D., Feng, Y., Liu, L., Nie, S., 2021. Acute Myelitis After SARS-CoV-2 infection: a Case Report. https://doi.org/10.1101/2020.03.16.20035105.

Zhou, S., Jones-Lopez, E.C., Soneji, D.J., Azevedo, C.J., Patel, V.R., 2020. Myelin Oligodendrocyte Glycoprotein Antibody-Associated Optic Neuritis and Myelitis in COVID-19. J Neuroophthalmol 40 (3), 398–402. https://doi.org/10.1097/WNO.0000000000001049.

Zoghi, A., Ramezani, M., Roozbeh, M., Darazam, I.A., Sahraian, M.A., 2020. A case of possible atypical demyelinating event of the central nervous system following COVID-19 [published online ahead of print, 2020 Jun 24]. Mult Scler Relat Disord 44, 102324. https://doi.org/10.1016/j.msard.2020.102324.