POST-COVID PRESENTATIONS IN NEUROMUSCULAR DISEASES

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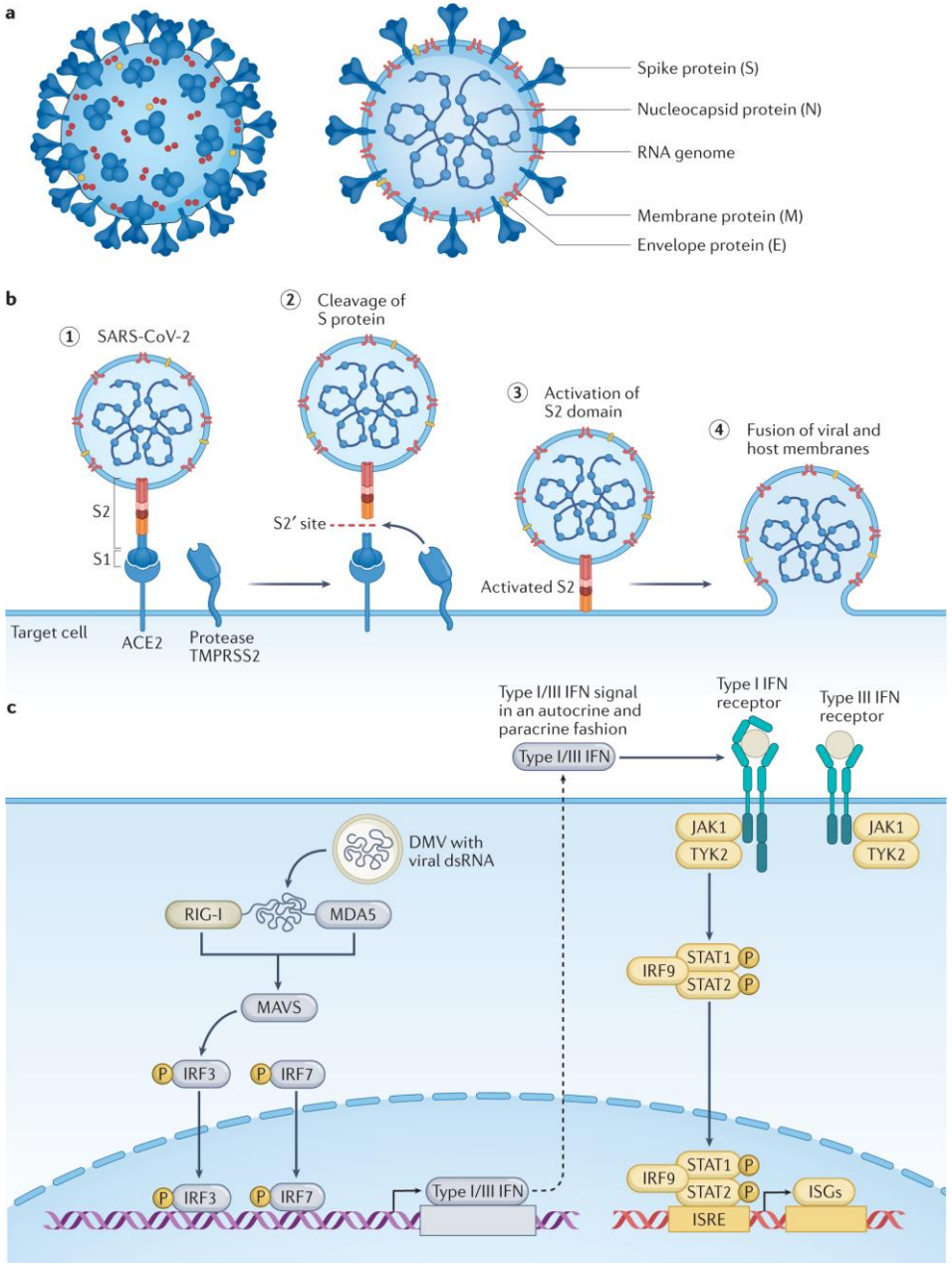
SARS-CoV-2

- Coronaviruses (CoV) are large, enveloped, positive-sense RNA viruses divided into 3 genera
  - alphacoronavirus,
  - betacoronavirus,
  - gammacoronavirus.
- Currently, there are 7 CoV that can infect humans, including human coronavirus (HCoV)–229E, HCoV-NL63, HCoV-HKU1, HCoV-OC43, MERS-CoV, SARS-CoV-1, and SARS-CoV-2.
- Betacoronaviruses SARS-CoV-2, SARS-CoV-1, and MERS-CoV are associated with severe disease in humans.

Pathogenesis of SARS-CoV-2



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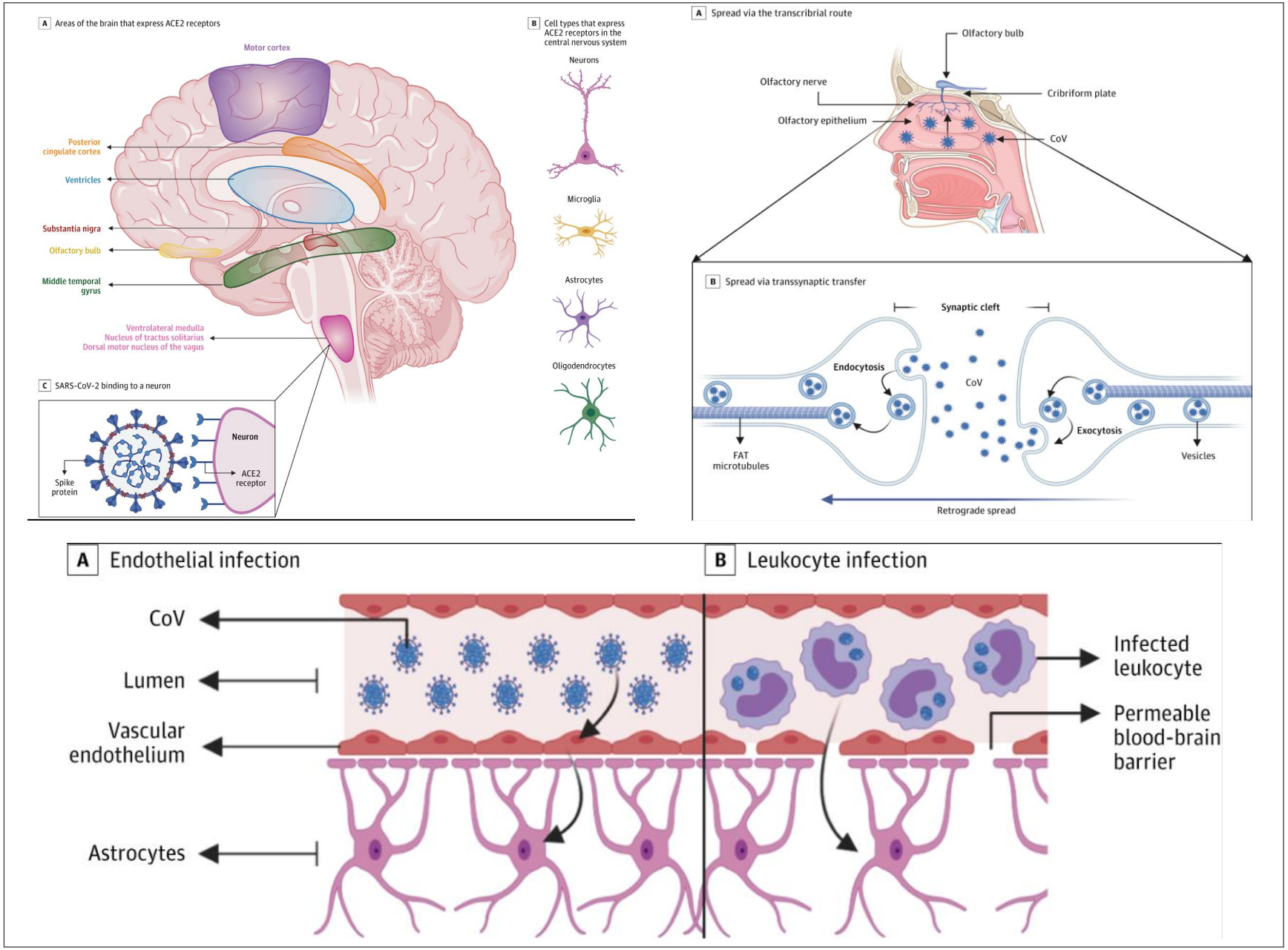
Mechanism of neuroinvasion



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Effect of viral infection on nervous system

Three main categories,

1. Neuromuscular complications which are a direct consequence of viral infection
2. Neuromuscular disorders which result from autoimmunity triggered by viral infection
3. Neuromuscular degenerative disorders which are associated with viral infections due to unclear mechanisms, or as part of a multifactorial etiology

TABLE 1 | Viruses directly causing neuromuscular deficits.

Virus	Neurologic complication/disorder	Observations	Mechanisms
Coronaviridae			
Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2)	Parsonage-Turner Syndrome (PTS)	The association is uncertain or very rare. Isolated case reports have a temporal relationship to SARS-CoV-2 infection (3, 4).	No mechanisms have been proposed.
	Mononeuritis Multiplex (MNM)	Series of 11 patients with COVID-19 who required mechanical ventilation and ICU care (2).	The aetiology is unclear but authors proposed possibility of parainfectious vasculitis.
	Rhabdomyolysis	Multiple case reports of patients of rhabdomyolysis with SARS-CoV-2. Milder muscle involvement with myalgias and milder creatine kinase elevations appear to be very common (5).	Suggested mechanisms include direct invasion of myocytes by the virus, or immune mediated injury.
Herpesviridae			
Herpes simplex virus-1 or 2	Bell palsy	Lower motor neurone-type unilateral facial weakness.	Bell palsy remains of unclear aetiology but numerous lines of evidence suggest a role for HSV-1/2 and VZV in the infection of lower cranial nerves (see also VZV below) (6).
Herpes simplex virus-2 (HSV-2)	Lumbosacral plexitis (Elsberg syndrome)	Acute lumbosacral radiculitis which may also include lower spinal cord myelitis (7).	HSV-2 primary infection or reactivation.
Cytomegalovirus (CMV)	Mononeuritis Multiplex (MNM)	CMV reactivation in the context of AIDS due to HIV infection has been associated with MNM (8).	Autoimmunity is the proposed mechanism.
Varicella-Zoster Virus (VZV)	Post herpetic neuralgia	VZV reactivation (commonly known as shingles) can result in PHN in 10% of patients (9).	VZV remains dormant within dorsal root ganglia. Immune response to VZV reactivation is proposed to damage peripheral and central nervous systems leading to PHN.
	Lower Cranial Neuropathy (Ramsay Hunt syndrome)	Reports of cranial neuropathy associated with VZV reactivation (10).	Mechanism is unknown.
Orthomyxoviridae			
Influenza A and B virus	Influenza-associated myositis (IAM)	Influenza B is thought to be the major cause of viral myositis, mainly affecting calf muscles in males aged 5–9 with moderate CK elevations (11).	Postulated mechanisms include direct infection of myoctes or post-infectious immune mediated injury.
Human Immunodeficiency Virus (HIV)	Distal Symmetric Polyneuropathy (DSP)	A frequent complication of HIV presenting with numbness, tightness, burning pain, paraesthesiae, and allodynia (12).	The mechanisms are broadly suggested to be due to direct neurotoxicity of HIV, and as toxic consequences of antiretroviral therapy.
Hepeviridae			
Hepatitis E virus (HEV)	Parsonage Turner syndrome	Case reports suggest an association of acute HEV infection with PTS, which commonly has bilateral presentation (13).	Mechanism is unknown.
Picornaviridae			
Coxsackievirus	Myositis	A review of prior viral myositis and rhabdomyolysis cases showed coxsackieviruses as the second most common association (14) with broad age of onset from infancy to late adulthood.	
Echovirus	Myositis	Echovirus has been reported in cases predominnantly with young adult onset (14).	Direct viral invasion is suspected based on virus cultured from muscle specimen in one report (15).

Category 1

Direct consequence of viral infection

Jacob S, Kapadia R, Soule T, Luo H, Schellenberg KL, Douville RN and Pfeffer G (2022) Neuromuscular Complications of SARS-CoV-2 and Other Viral Infections. Front. Neurol. 13:914411. doi: 10.3389/fneur.2022.914411

TABLE 2 | Viruses that have been linked to neuromuscular autoimmune disorders.

Virus	Neurological disorders	Observations	Proposed mechanisms
Coronaviridae			
Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2)	Guillain-Barré Syndrome (GBS)	Several case reports and series suggest a possible association (16). Larger epidemiologic studies have not confirmed the association. Atypical phenotypes such as facial diplegia may be more common.	GBS presentations have been described as para-infectious and post-infectious phenomena. The mechanism remains unclear but may be similar to mechanisms for GBS associated with other viral infections.
	Myasthenia Gravis (MG)	Multiple case reports of patients developing acetylcholine receptor (AChR) or muscle-specific kinase (MuSK) antibodies with generalized presentation, following SARS-CoV-2 infection (17).	Pathogenesis mechanisms of AChR-MG and MuSK-MG are distinct. May involve a break down in self-tolerance mechanisms.
Orthomyxoviridae			
Influenza A Virus	Guillain-Barré Syndrome (GBS)	A study showed that 26/150 (17%) GBS patients had a positive serology for Influenza A (18).	Molecular mimicry mechanism is a likely model in post-infectious GBS, however data that supports this hypothesis is sparse (19).
Influenza B Virus	Guillain-Barré Syndrome (GBS)	A study showed that 24/150 (16%) GBS patients had a positive serology for influenza B (18). 7 patients with preceding influenza B infection had a pure motor GBS without sensory deficits.	Molecular mimicry mechanism is a likely model in postinfectious GBS, however data that supports this hypothesis is sparse (19).
Flaviviridae			
West Nile Virus (WNV)	Myasthenia Gravis	Several months post WNV infection, MG was reported by 6 patients in one series (20).	Postulated to be from autoimmunity resulting in reduced self tolerance in initiating MG.
Zika Virus (ZIKV)	Guillain-Barré Syndrome (GBS)	A study in 2016 conducted during the Colombian outbreak of ZIKV showed 17/42 people (40%) tested for ZIKV were positive (21).	Parainfectious clinical presentation suggests a possible differing mechanism for ZIKV, still speculated to be from molecular mimicry or other immune dysregulation.
	Myasthenia Gravis (MG)	MG was presented in 2 case reports upon 8–10 weeks of ZIKV infection (22).	Unknown mechanisms, suspected environmental and genetic factors.
Hepatitis C virus (HCV)	Cryoglobulinaemic vasculitic neuropathy	Clinical presentation may include pure sensory polyneuropathy, sensorimotor polyneuropathy, or mononeuropathy multiplex. There appears to be female predilection (23).	Cold-insoluble immune complexes deposit on the vascular endothelium causing end-organ damage, including peripheral nerves (24).
Phenuiviridae			
Toscana Virus (TOSV)	Guillain-Barré Syndrome (GBS) - like syndrome	Report of a patient that was infected with TOSV which preceded GBS-like axonal polyneuropathy (25). Additionally, another study with 13 participants suggested a relationship to TOSV (26).	TOSV could be facilitating GBS immunological cascade. T-cell involvement and molecular mimicry mechanisms between axolemmal and microbial surface molecules could be considered.
Picornaviridae			
Enterovirus D68 (EV-D68)	Guillain-Barré Syndrome (GBS)	8 adult and 4 child cases of GBS, and variants of GBS such as AMAN, were reported in Wales (27).	Adult cases were all male. Geographic clustering of cases. This suggested combination of host genetic and environmental factors.
Hepatitis A Virus (HAV)	Guillain-Barré Syndrome (GBS)	A study showed that 7/150 (5%) GBS patients had a positive serology for hepatitis A (18). There was also a detailed study focused on a child with HAV infection that developed GBS (28).	Mechanisms unknown, may be a relationship to liver inflammation in addition to autoimmunity.
Enteroviruses			
Polymyositis	Autoimmune myositis	In adult study of 13 patients with myositis, 11 had idiopathic polymyositis (29). Study shows possible evidence of enteroviral infection being associated with autoimmune myositis.	Mechanisms unclear due to limited study.
Dermatomyositis	Autoimmune myositis	In adult study of 13 patients with myositis, 2 had dermatomyositis (29). Study shows possible evidence of enteroviral infection being associated with autoimmune myositis.	Mechanisms unclear due to limited study.
Hepeviridae			
Hepatitis E Virus (HEV)	Guillain-Barré Syndrome (GBS)	HEV RNA has been detected in cerebrospinal fluid (CSF) from some patients with HEV-associated GBS (30).	Two mechanisms have been proposed which include either direct viral damage or by molecular mimicry. HEV can infect neural cells in mouse models.

Category 2

Autoimmunity triggered by viral infection

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TABLE 3 | Viruses possibly associated with chronic neuromuscular degenerative conditions.

Virus	Neurologic disorder	Observations	Proposed mechanisms
Picornaviridae			
Enteroviruses (EVs)	Amyotrophic Lateral Sclerosis (ALS)	EV genomic material was detected in spinal cord/brain of 60–88% of ALS patients compared 0–14% in controls (37). RT-PCR analysis of cerebrospinal fluid detected EV in 14.5% of 242 ALS patients and 7.6% present in 354 controls.	EV infection may lead to disease pathogenesis via seeding of protein misfolding and TDP-43 cytoplasmic aggregation.
Coxsackievirus B3 (CVB3)	Amyotrophic Lateral Sclerosis (ALS)	TDP-43 transactivation occurs during *in vitro* CVB3 infection (38). SODI-G58R mice infected with CVB3 have shortened lifespan with early onset and accelerated ALS-like motor dysfunction (39).	Cytoplasmic translocation and aggregation of TDP-43 is a hallmark for ALS, and CVB3 infection may contribute to this effect (40).
Echovirus-7 (echo-7)	Amyotrophic Lateral Sclerosis (ALS)	There were positive results from a neutralization test for echo-7 in over half (55%) of the ALS patients tested (41).	Exact mechanism is unclear. Echo-7 was explored because of the known ability of EVs to infect spinal and cortical motor neurons.
Retroviridae			
Human Immunodeficiency Virus (HIV)	Motor neuron disorder variations	Reports of HIV-positive patients having brachial amyotrophic diplegia (42).	Mechanism is unknown.
	ALS-like syndrome	HIV infection can be associated with ALS-like syndromes (43).	HIV is known to trigger the expression of HERV-K, which is associated with ALS neuropathology (44).
	Nemaline myopathy (NM)	In a study of 76 cases, HIV-NM cases showed similar presentation of features as those with sporadic late onset nemaline myopathy (SLONM) (45).	Formation of rods may be triggered by altered genome integrity, immunological triggers or direct impact of viral particles.
	Ocular myopathy	Reported patients with chronic progressive external ophthalmoplegia (CPEO) associated with long duration of HIV infection and antiretrovirals (46).	Prolonged HIV infection, or mitochondrial toxicity from therapy, or a combination of both may have resulted in these presentations.
	Sporadic Inclusion Body Myositis (sIBM)	Several reported cases of HIV-affected patients that developed IBM (47). An earlier onset age and higher CK level may be present compared to typical sIBM.	HIV-infected CD8+ T-cells may clonally expand within muscle tissues and cross-react with muscle surface antigens. Premature ageing and complications of antiretroviral therapy may be related.
Human T-lymphotropic Virus (HTLV-1/2)	ALS-like syndrome	In a study from 1995, 50% of sporadic ALS (sALS) patients showed immunoblot seroreactivity against HTLV-1/2 antigens (48). However, it is now recognized that HTLV can trigger ALS-like syndromes in some patients, and that the majority of patients with ALS are HTLV-1 seronegative (49).	HTLV has been associated with alterations in PTH regulation and motor neuron dysfunction. HTLV is also a known trigger of HERV-K expression, and thus may be associated with ALS-like neuropathology.
	Sporadic Inclusion Body Myositis (sIBM)	Reports of two patient that developed sIBM and tests and findings, such as anti-HTLV-1 antibodies in plasma and CSF suggest HTLV-1 was indeed present (50).	HTLV-1 infects mononuclear infiltrating cells that trigger IBM (51). It is also likely that retroviral infection and some sort inflammatory response also play a role.
Human Endogenous Retrovirus-K (HERV-K / ERVK)	Amyotrophic Lateral Sclerosis (ALS)	HERV-K *gag*, *pol*, and *env* gene transcripts are elevated in ALS brain tissues (52). Expression of HERV-K viral proteins is present in ALS pyramidal neurons and spinal cord oligodendrocytes (53).	HERV-K *env* protein can cause retraction and beading of neurites in human neurons. In transgenic mice, progressive motor dysfunction develops.

Category 3

Unclear mechanism vs multifactorial

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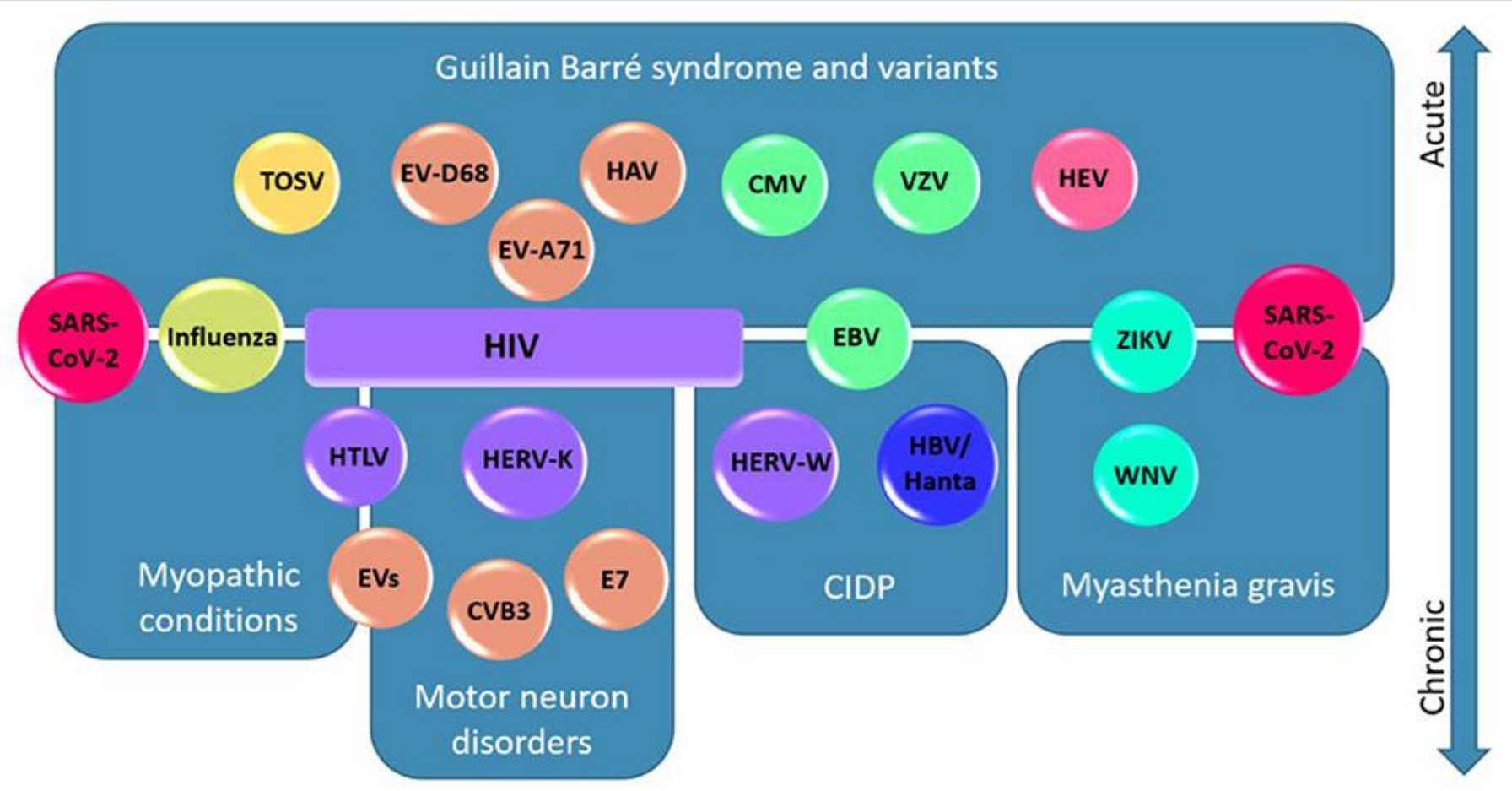
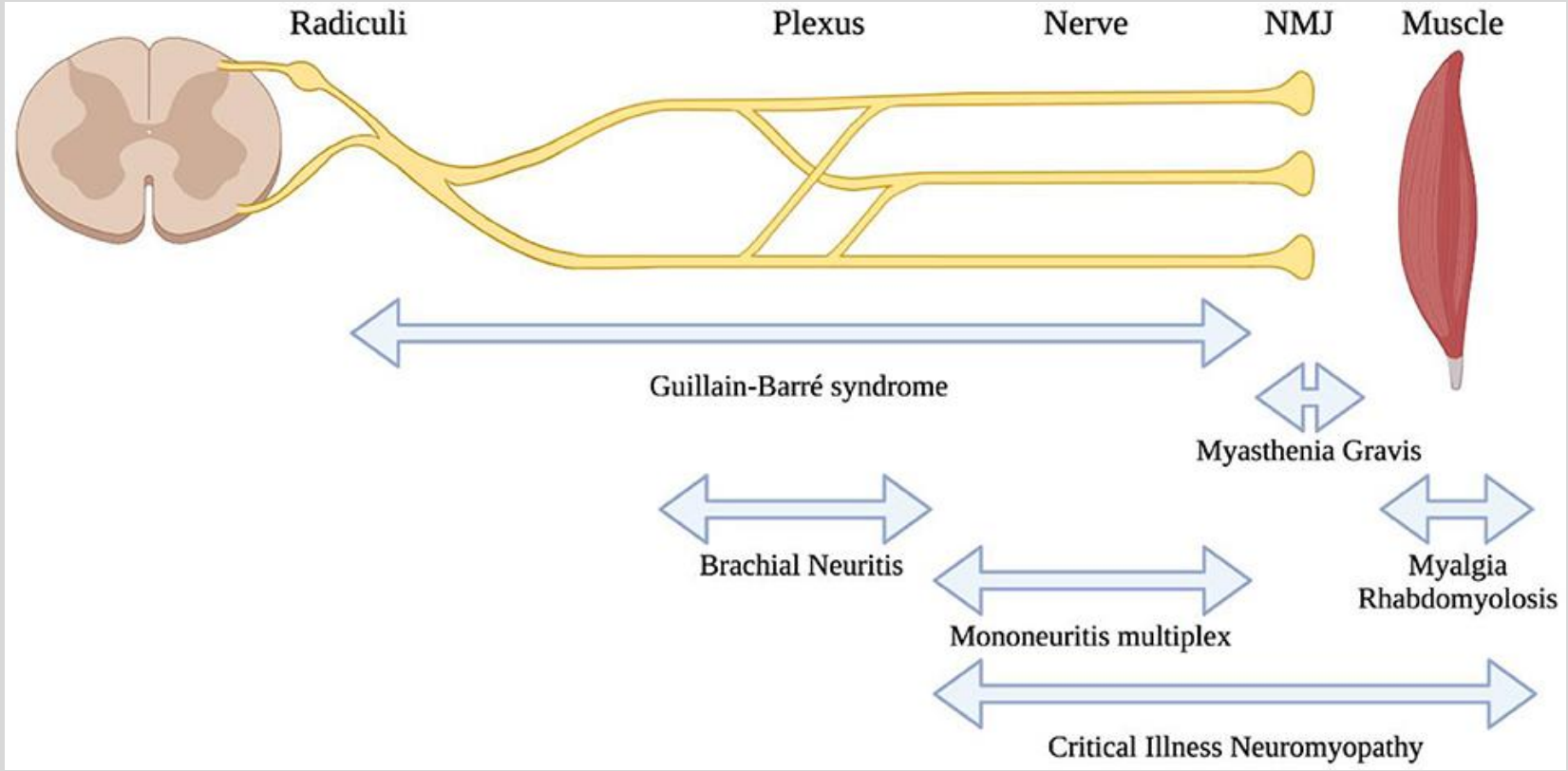
SARS-CoV-2 in NMD spectrum



SARS-CoV-2 INOLVEMENT



SARS-CoV-2
Direct Neuromuscular Complications

- Anosmia and dysgeusia- olfactory sensory neurons are the route of entry to CNS although they do not express ACE2 receptor.
- Myalgia- with elevated CK
- Critical illness neuromyopathy, or downstream neuromuscular effects due to other end-organ injury or deconditioning.

SARS-CoV-2
Autoimmune Neuromuscular Complications

- Guillain-Barre-Syndrome
- Mononeuritis multiplex
- Brachial neuritis
- Myasthenia gravis

COVID-19 In Patients With Pre-existing Neuromuscular Diseases

- Pre-existing NMD pose an added risk for various reasons such as,
  a. Respiratory muscle weakness
  b. Increase exposure due to care takers entering home
  c. Immunosuppression
  d. Cardiac involvement (in certain NMD)
  e. Reduced mobility and limited transport options reduce access to health services

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COVID-19 IN MYASTHENIA GRAVIS

COVID-19 IN MYASTHENIA GRAVIS

- 377 Myasthenia patients
- Age range: median 68 years
- Comorbidities: obesity, COPD, cardiovascular disease, diabetes, dysphagia
- Immunosuppressants: 59% (prednisone, AZA, mycophenolate) and 8% on IVIG.
- High hospitalization- 28% increased risk for hospitalization
- ICU admission- 51% higher
- Ventilator use, mortality rate- no significant difference

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COVID-19 IN MG

	No. (%)	Crude RR (95% CI)	*p*-value	Adjusted RR* in reference to None (95% CI)	*p*-value	Adjusted RR* in reference to MG (95% CI)	*p*-value
Hospitalization							
None	57,613 (14.0)	1.00 (Reference)		1.00 (Reference)		0.78 (0.69–0.89)	<0.001
MG	145 (38.5)	2.74 (2.41–3.11)	<0.001	1.28 (1.13–1.46)	<0.001	1.00 (Reference)	
RA	1,903 (25.8)	1.84 (1.77–1.92)	<0.001	1.01 (0.97–1.04)	0.78	0.78 (0.69–0.89)	<0.001
SLE	315 (23.8)	1.70 (1.54–1.87)	<0.001	1.20 (1.10–1.31)	<0.001	0.94 (0.80–1.09)	0.41
MS	358 (23.6)	1.68 (1.53–1.84)	<0.001	1.39 (1.27–1.51)	<0.001	1.08 (0.93–1.26)	0.31
ICU							
None	13,561 (3.3)	1.00 (Reference)		1.00 (Reference)		0.66 (0.51–0.86)	0.002
MG	48 (12.7)	3.85 (2.96–5.02)	<0.001	1.51 (1.16–1.96)	0.002	1.00 (Reference)	
RA	503 (6.8)	2.07 (1.90–2.25)	<0.001	1.00 (0.92–1.09)	0.92	0.67 (0.51–0.88)	0.004
SLE	79 (6.0)	1.81 (1.46–2.24)	<0.001	1.18 (0.96–1.46)	0.11	0.79 (0.56–1.10)	0.16
MS	92 (6.1)	1.83 (1.50–2.24)	<0.001	1.43 (1.18–1.74)	<0.001	0.95 (0.69–1.32)	0.77
Ventilator							
None	4,892 (1.2)	1.00 (Reference)		1.00 (Reference)		0.87 (0.52–1.46)	0.59
MG	14 (3.7)	3.12 (1.86–5.21)	<0.001	1.15 (0.69–1.93)	0.60	1.00 (Reference)	
RA	161 (2.2)	1.84 (1.57–2.14)	<0.001	0.92 (0.78–1.07)	0.27	0.80 (0.47–1.36)	0.41
SLE	32 (2.4)	2.03 (1.44–2.86)	<0.001	1.30 (0.92–1.83)	0.13	1.13 (0.61–2.10)	0.70
MS	33 (2.2)	1.82 (1.30–2.56)	0.001	1.30 (0.94–1.81)	0.12	1.13 (0.62–2.09)	0.69
Death							
None	12,211 (3.0)	1.00 (Reference)		1.00 (Reference)		0.92 (0.69–1.23)	0.59
MG	40 (10.6)	3.57 (2.66–4.78)	<0.001	1.08 (0.81–1.44)	0.59	1.00 (Reference)	
RA	518 (7.0)	2.37 (2.17–2.57)	<0.001	1.02 (0.94–1.10)	0.67	0.94 (0.70–1.26)	0.69
SLE	75 (5.7)	1.91 (1.53–2.38)	<0.001	1.60 (1.30–1.97)	<0.001	1.48 (1.04–2.10)	0.020
MS	79 (5.2)	1.75 (1.41–2.17)	<0.001	1.54 (1.26–1.88)	<0.001	1.42 (1.01–2.01)	0.036

RR, risk ratio; MG, myasthenia gravis; RA, rheumatoid arthritis; SLE, systemic lupus erythematosus; MS, multiple sclerosis.
**The COVID-19 outcomes were compared across disease groups and risk ratios (RRs) were estimated using modified multivariable Poisson regression models adjusting for age, sex, race/ethnicity, region, COVID-19 test month, and comorbidities, such as chronic pulmonary disease, cardiovascular disease, cerebrovascular disease, peripheral vascular disease, diabetes, liver disease, renal disease, obesity, and smoking.*

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COVID-19 IN MG

	Crude RR (95% CI)	*p*-value	Adjusted RR* (95% CI)	*p*-valu
Age				
18–64	1.00 (Reference)		1.00 (Reference)	
65–74	5.50 (1.57–19.27)	0.008	4.95 (0.78–31.62)	0.09
75+	11.56 (3.58–37.32)	<0.001	9.57 (1.56–58.76)	0.015
Sex				
Female	1.00 (Reference)		1.00 (Reference)	
Male	1.39 (0.77–2.52)	0.28	1.35 (0.74–2.46)	0.32
Race/Ethnicity				
White	1.00 (Reference)		1.00 (Reference)	
Black	0.42 (0.10–1.67)	0.22	1.66 (0.22–12.67)	0.62
Hispanic	0.73 (0.19–2.83)	0.64	1.95 (0.54–7.03)	0.31
Other/unknown	0.38 (0.05–2.65)	0.33	0.43 (0.05–3.97)	0.46
Comorbidities				
Chronic pulmonary disease	1.66 (0.90–3.05)	0.10	1.27 (0.64–2.51)	0.49
Cardiovascular disease	5.38 (1.95–14.81)	0.001	2.62 (0.99–6.96)	0.05
Cerebrovascular disease	1.40 (0.77–2.56)	0.27	1.04 (0.54–2.04)	0.90
Peripheral vascular disease	2.46 (1.38–4.39)	0.002	1.53 (0.72–3.25)	0.27
Diabetes	1.09 (0.60–1.96)	0.78	0.85 (0.49–1.48)	0.57
Liver disease	0.63 (0.25–1.54)	0.31	0.65 (0.24–1.76)	0.40
Renal disease	1.48 (0.82–2.68)	0.20	0.70 (0.38–1.28)	0.24
Dysphagia	2.09 (1.16–3.79)	0.015	1.84 (1.06–3.21)	0.031
Dyspnea	1.11 (0.55–2.24)	0.300	0.71 (0.33–1.49)	0.36
Recent MG treatment				
Pyridostigmine	1.28 (0.71–2.31)	0.41	0.96 (0.47–1.98)	0.91
Chronic immunosuppressants	1.59 (0.84–3.04)	0.16	1.27 (0.61–2.63)	0.52
IVIG	0.94 (0.31–2.87)	0.91	0.79 (0.15–4.03)	0.77

RR, risk ratio; MG, myasthenia gravis; IVIG, intravenous immune globulin.
**Adjusted RR (aRR) were reported from modified Poisson regression including age, sex, race/ethnicity, region, COVID-19 test month, and comorbidities, such as chronic pulmonar disease, cardiovascular disease, cerebrovascular disease, peripheral vascular disease, diabetes, liver disease, renal disease, dysphagia, and dyspnea.*

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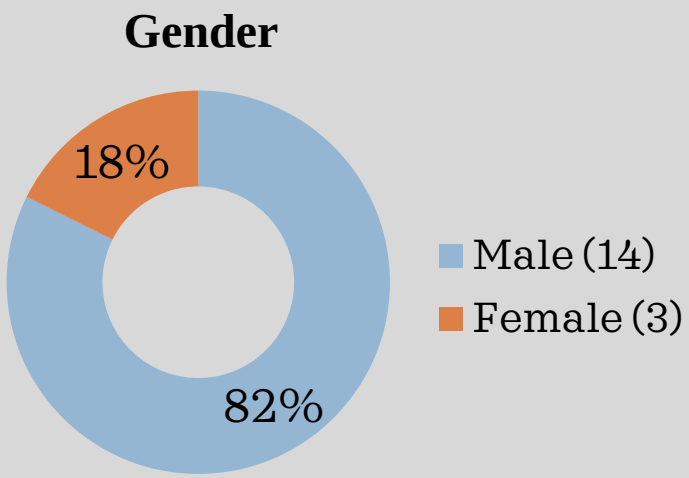
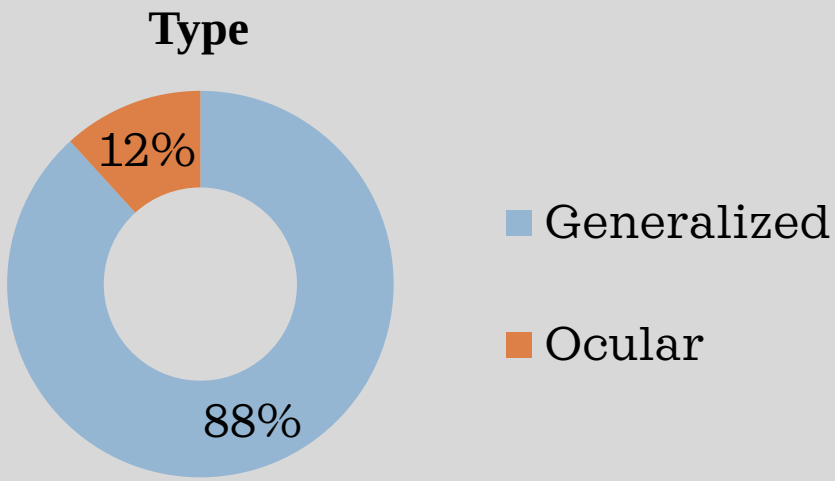
COVID-19 IN MYASYHENIA GRAVIS (HMH)

Patient characteristics





Age range: 31-84yrs

AchR + : 12

Immunosuppressive Therapy

- 9 patients were on >2 immunosuppressive therapy
- Most common Mycophenolate mofetil or Azathioprine with prednisone
- 6/17 patients were on IVIG infusions
- 4/17 were receiving Plasmapheresis

Classification & scoring

MGFA Classification:

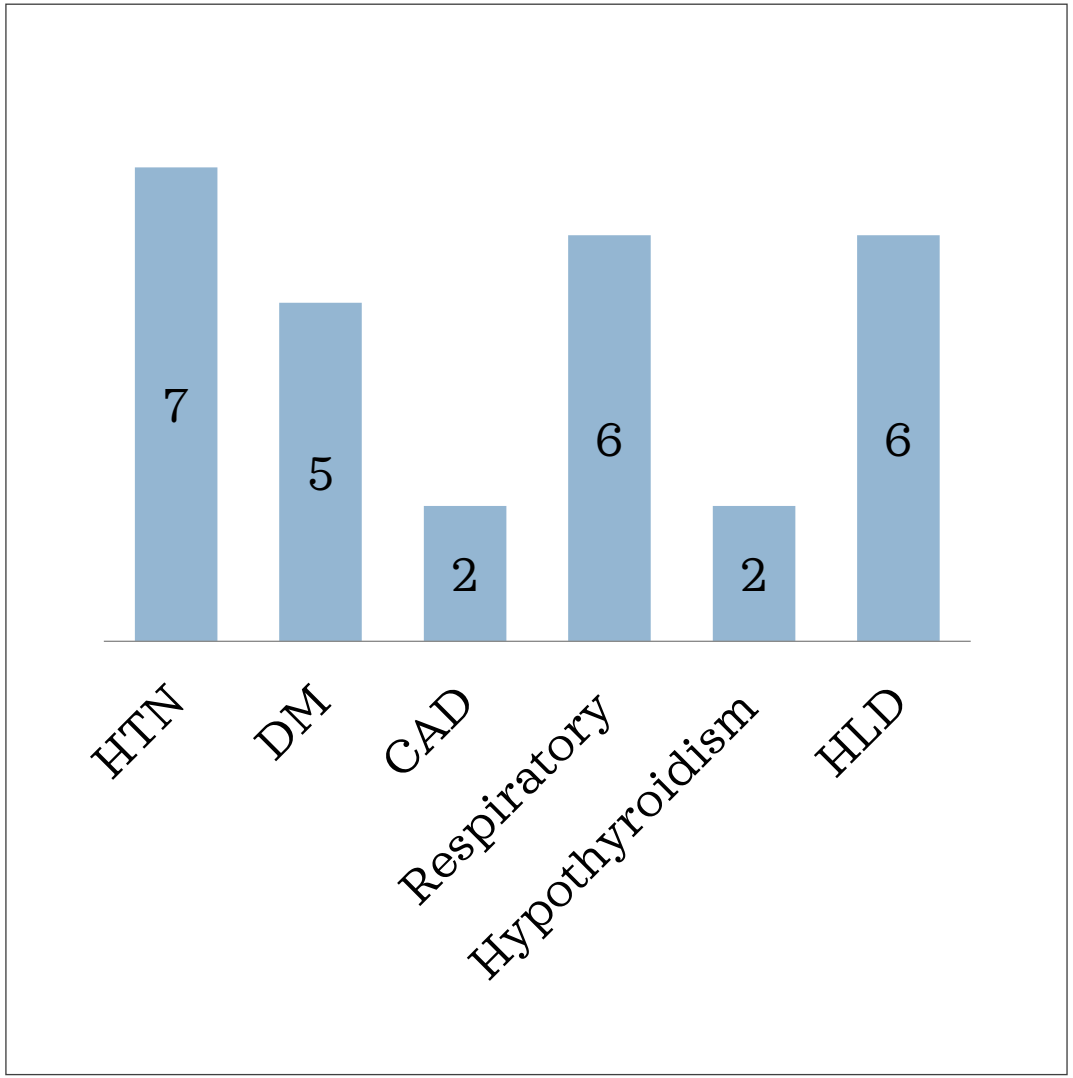
MGFA Classes	Description
Class I	Any ocular muscle weakness. All other muscle strength is normal.
Class II	**Mild** weakness affecting other than ocular muscles
Class IIa	Predominantly affecting limb, axial muscles, or both.
Class IIb	Predominantly affecting oropharyngeal, respiratory muscles, or both.
Class III	**Moderate** weakness affecting other than ocular muscle
Class IIIa	Predominantly affecting limb, axial muscles, or both.
Class IIIb	Predominantly affecting oropharyngeal, respiratory muscles, or both.
Class IV	**Severe** weakness affecting other than ocular muscles
Class Iva	Predominantly affecting limb, axial muscles, or both.
Class IVb	Predominantly affecting oropharyngeal, respiratory muscles, or both.

Immunosuppressive Therapy & baseline MGFA hospitalized patients

Patients	Immunotherapy	MGFA
Patient 1	Mycophenolate, prednisone and IVIG	MGFA2a
Patient 2	Azathioprine, prednisone	MGFA2b
Patient 3	Azathioprine, prednisone, PLEX	Asymptomatic
Patient 4	Mycophenolate, prednisone, IVIG	MGFA2a
Patient 5	Prednisone	Asymptomatic
Patient 6	Mycophenolate, IVIG	MGFA2a
Patient 7	Prednisone, PLEX	MGFA2a
Patient 8	Azathioprine, IVIG	MGFA2a
Patient 9	Prednisone, Rituximab	MGFA1
Patient 10	Azathioprine, Eculizumab	MGFA2a
Patient 11	Azathioprine, IVIG	MGFA2a
Patient 12	Mycophenolate, PLEX	N/A

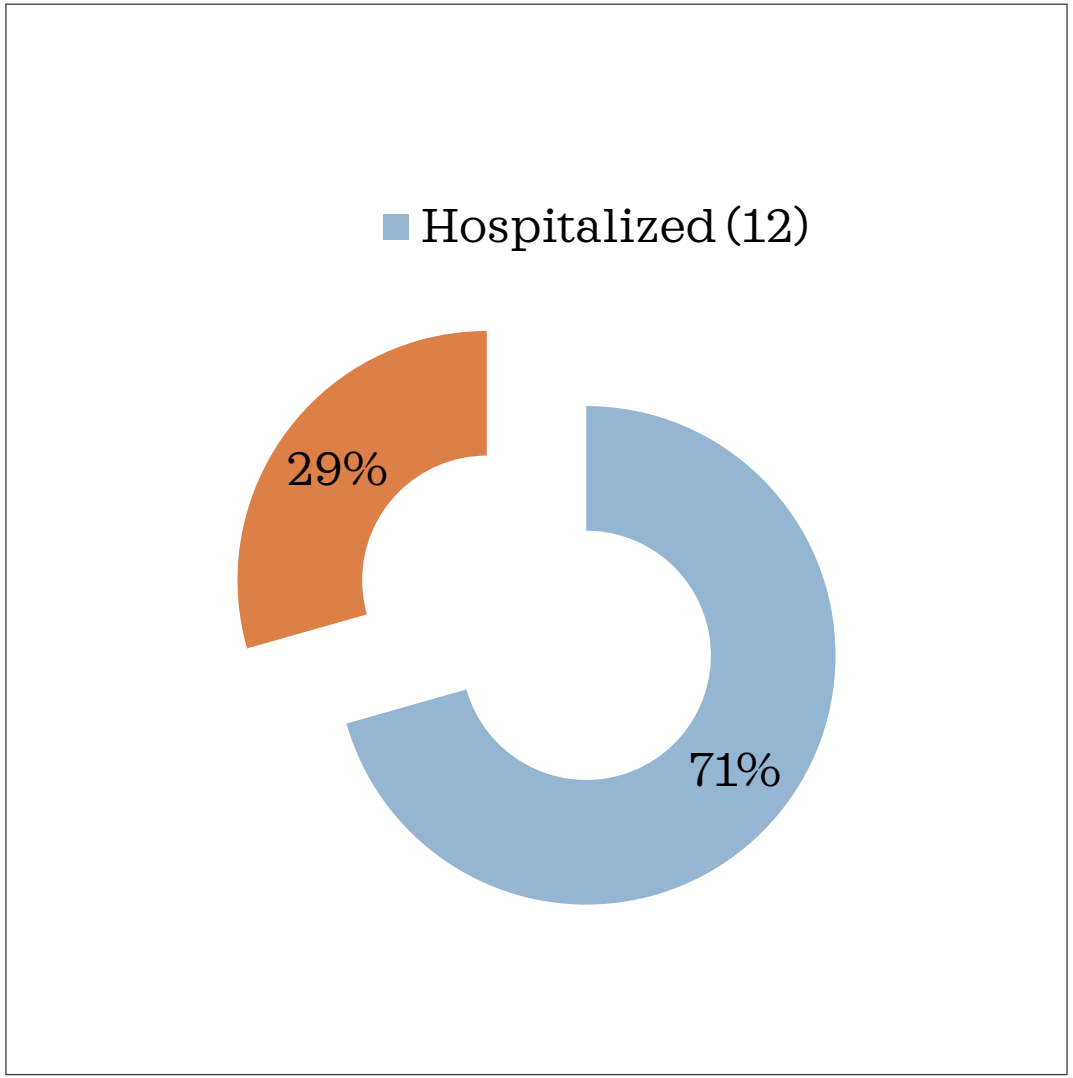
Immunosuppressive Therapy & baseline MGFA non-hospitalized patients

Patients	Immunotherapy	MGFA
Patient 1	Azathioprine	MGFA2a
Patient 2	Azathioprine, prednisone	Asymptomatic
Patient 3	Azathioprine, IVIG	MGFA2b
Patient 4	None	MGFA1
Patient 5	Azathioprine, PLEX	MGFA2a



Comorbid conditions

- 2/17 had no comorbid conditions
- 10 of them 2 or more of these listed conditions



Exacerbation

- Among the hospitalized, 8 patients had exacerbation of myasthenia symptoms
- Received IVIG or Plasmapheresis

Exacerbation: MGFA before and after

Patients	Immunotherapy	MGFA	New MGFA
Patient 1	*Mycophenolate, prednisone and IVIG*	MGFA2a	Death
Patient 2	*Azathioprine, prednisone*	MGFA2b	MGFA3b
Patient 3	*Azathioprine, prednisone, PLEX*	Asymptomatic	Death
Patient 4	Mycophenolate, prednisone, IVIG	MGFA2a	MGFA2a
Patient 5	*Prednisone*	Asymptomatic	Death
Patient 6	Mycophenolate, IVIG	MGFA2a	MGFA2a
Patient 7	*Prednisone, PLEX*	MGFA2a	MGFA2b
Patient 8	*Azathioprine, IVIG*	MGFA2a	MGFA3a
Patient 9	*Prednisone, Rituximab*	MGFA1	Death
Patient 10	*Azathioprine, Eculizumab*	MGFA2a	MGFA3a
Patient 11	*Azathioprine, IVIG*	MGFA2a	MGFA4b
Patient 12	Mycophenolate, PLEX	N/A	N/A

Length of stay in hospitalized patients

Patients	Immunotherapy	MGFA- before	Length of stay
Patient 1	Mycophenolate, prednisone and IVIG	MGFA2a	37 days
Patient 2	Azathioprine, prednisone	MGFA2b	18 days
Patient 3	Azathioprine, prednisone, PLEX	Asymptomatic	43 days
Patient 4	Mycophenolate, prednisone, IVIG	MGFA2a	20 days
Patient 5	Prednisone	Asymptomatic	n/a
Patient 6	Mycophenolate, IVIG	MGFA2a	n/a
Patient 7	Prednisone, PLEX	MGFA2a	7 days
Patient 8	Azathioprine, IVIG	MGFA2a	21 days
Patient 9	Prednisone, Rituximab	MGFA1	12 days
Patient 10	Azathioprine, Eculizumab	MGFA2a	10 days
Patient 11	Azathioprine, IVIG	MGFA2a	n/a
Patient 12	Mycophenolate, PLEX	N/A	n/a

Cause of death in MG patients

Patient	MG type	MGFA	Comorbidities	BMI	Treatment	Cause of death
Patient 1	Generalized	MGFA2a	CAD, COPD, A.fib	26.2	Mycophenolate, prednisone, IVIG	Pneumonia, ARDS
Patient 3	Generalized	Asymptomatic	HTN, HLD	39.6	Azathioprine, prednisone, PLEX	Pneumonia, ARDS, renal failure
Patient 5	Ocular	Asymptomatic	None	30.6	Prednisone	Pneumonia, ARDS, renal failure
Patient 9	Generalized	MGFA1	OSA, A.fib	27.6	Prednisone, Rituximab	Pneumonia, septic shock

Results

1. This study was done prior to vaccination.
2. 70% of MG patients were hospitalized and among them 66% had exacerbations.
3. Overall mortality among all patients was 23%.

Conclusion

Immunosuppression was not protective.

Outcomes were variable possibly related to other underlying comorbidities as well.

Immunosuppressive agents used to treat MG is different than cytokine suppressive agents used for COVID19.

Larger and longer studies are required to understand the COVID19 related outcomes in MG population.

POST-COVID19 MYASTHENIA GRAVIS

- About 4 patients who have developed MG like symptoms (3 seropositive and 1 seronegative)
- All of them had COVID-19 about 3-6 months prior to symptom onset
- They all are responding to standard MG therapies
- Still collecting data on post-COVID-19 MG patients

COVID-19 NEUROPATHY (OUR COHORT AT METHODIST)

COVID Neuropathy

- Review of the electrodiagnostic studies on COVID-19 patients.
- About ~30 patients
- Majority of them are inpatients (admitted to ICU) with <10 being outpatients

COVID Neuropathy

1. Brachial plexopathy

2. Predominantly motor demyelinating polyneuropathy (like multifocal motor neuropathy) with sparing or lesser degree of involvement of sensory nerves

3. Critical illness polyneuropathy (in ICU patients with prolonged stay)

4. Small fiber neuropathy

COVID-19 Neuropathy

1. Brachial plexopathy

2. Predominantly motor demyelinating polyneuropathy (like multifocal motor neuropathy)

- Treatment early on within 4 weeks of symptom onset we noticed improvement in the weakness.
- None of the patients recovered all the way back to baseline yet.

COVID-19 IN ALS

POST COVID-19 ALS

- 4 patients developed ALS symptoms after COVID-19 infection
- In literature there are association with motor neuron disease/ ALS with picornaviridae (Coxsackie/ entero/echovirius) & retroviridae (HIV/ HTLV) family

Possible mechanisms:

- TDP43 accumulation
- Activation of glial cells and eventually inflammation

COVID-19 IN MUSCULAR DYSTROPHIES

COVID-19 IN MUSCULAR DYSTROPHIES

- Duchenne/Becker's muscular dystrophy patients
- 116 COVID-19 (+) patients, DMD (6 patients) and BMD (1 patient) were positive
- 2 were symptomatic and required hospitalization
- Age range: 8-17 yrs
- Incidence was 6%
- Risk factors: Cardiomyopathy, obesity
- All symptomatic patients recovered without any significant sequelae
- Prior use of NIV might have helped
- Small cohort

CONCLUDING REMARKS

- We are now entering post pandemic era (endemic era in future), which means we will be seeing long term effects.
- Are we going to see more neurodegenerative diseases/ autoimmune neuromuscular diseases?
- We need prospective studies to understand the long term effects of COVID-19 and neuromuscular diseases.

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THANK YOU