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COVID-19 in MS and NMOSD: A multicentric online national survey in Chile

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1. Introduction

A myriad of publications addressing COVID-19 and its impact on acute and chronic neurological disorders have been published in the last few months. Special interest has arisen in chronic demyelinating disorders, such as Multiple Sclerosis (MS) and Neuromyelitis Optica Spectrum Disorders (NMOSD), mainly due to immunotherapy and increased risk of infections (Brownlee et al., 2020). In MS, a multicentric study led by the Italian program for COVID-19 infection in multiple sclerosis, including 238 symptomatic patients (57 had positive RT-PCR) from 38 centers, seems to reassure that most patients (96%) developed a mild disease. Unfortunately, 5 patients died, all of them with EDSS $\geq$ 6.5[2]. An observational study including 8 patients from North America, also highlights the importance of EDSS in the risk of fatal outcome (Bowen et al., 2020). A more recent multicentric study, including 347 patients from the Covisep French registry, showed that 21% of the patients at least required hospitalization, while 12 patients (3.5%) died. Multivariate analyses determined that EDSS, age and obesity were independent risk factors for hospitalization or more severe COVID-19, while no association between disease-modifying therapy exposure and COVID-19 severity was observed (Louapre et al., 2020). In NMOSD fewer articles have been published, also suggesting a similar rate of infection compared to the general population (Sahraian et al., 2020).

On May 16th, our group published a first report addressing the impact of COVID-19 using an online survey completed by 280 patients, highlighting the relevance of early communication for infection prevention measures, and social impact of telemedicine and remote-working. Main results included a high percentage of patients under disease-modifying therapy (95%), a high percentage of patients reporting at least one comorbidity (60%), 75% stated to be remote working/studying since early March, and 8% declared to be unemployed. Three patients were confirmed with COVID-19, with no fatal outcomes (Ciampi et al., 2020). Unfortunately, over 100 days after the first patient was confirmed in Chile, things have dramatically changed. The number of cases and deaths due to COVID-19 has exponentially increased, with over 300,000 patients diagnosed (1.6% of the total population) and over 6500 deaths (2.2%) (MINSAL, 2020). Therefore, a second online questionnaire was distributed among MS and NMOSD treating neurologists throughout the country in order to assess a national representation of the impact of COVID-19 in their patients' lives, and to improve and update the recommendations given to patients and caregivers, in the event of a confirmed infection. Patients under regular clinical care had already given written informed consent approved by the local Ethics Committee. Also, before survey completion, patients were asked to agree on an online informed consent. A total of 409 surveys from 9 centers have been completed, 71% women, mean age 41 years, 98% with MS, and 88% receiving immunotherapy. Most prevalent self-reported comorbidities were being overweight/obese (17%), current smoking (14%), insulin resistance/type 2 diabetes (9%), thyroid disorders (8%) and hypertension (8%). Remote working-studying remains high (74%), but unemployment has risen to 10%. Compared to our previous study, a similar proportion of patients (16%) reported having any symptom suggestive of COVID-19 (Table 1). Eighteen patients have been diagnosed with COVID-19 (14 RRMS, 4 NMOSD), 12 women (67%), median age of 32.5 years (range 17–61), median disease duration of 7 years (range 0.3–12) and median EDSS of 1.0 (0–6.0). No progressive MS patient has yet been infected. All patients had at least one comorbidity, and all were receiving immunotherapy. No changes in disease-modifying therapy were suggested in 11 patients, while 6 patients required transient suspension, and one patient required stress dose steroids. Five patients (28%, 3/5 men) required hospitalization, while one patient (NMOSD, male, EDSS 6.0, with hypertension and type 2 diabetes), required invasive mechanical ventilation, and had a fatal outcome due to critical illness polyneuromyopathy and secondary bacterial infection (Table 2).

The sustained worsening of the COVID-19 pandemic in our country warrants an urgent need in maintaining fluid communication with our patients. Although this is a small study in a country with an estimated prevalence of 13.4 per 100,000 habitants (Fernández, 2008), we achieved a representative 16% of the estimated total MS population of 2546 patients. We noticed a possible impact of comorbidities, age, male gender and higher EDSS in the outcome of COVID-19 severe acute respiratory syndrome, with no clear relationship with any specific disease-modifying therapy. Nonetheless, the small sample size of this case

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Table 1
Characteristics of surveyed patients $N = 409$.

Demographic	Disease-related		
Sex N(%) female: male	290 (71):118(29)	Diagnosis	N (%)
Age mean + SD (range)	41.2 + 11.4(17–81)	MS	400(98)
Health Insurance N(%) public:private:other	77(19)/325(79)/7(2)	NMOSD	5(1)
Current pregnancy N(%)	3(1)	Other	4(1)
Current treatment	N (%)	Self-reported comorbidities	N (%)
Any DMT	360(88)	Overweight/obese	70(17)
Interferon beta	47(11)	Current smoking	57(14)
Glatiramer acetate	16(4)	Insulin resistance/type 2 diabetes	36(9)
Teriflunomide	20(5)	Thyroid disorder	32(8)
Dimethyl fumarate	17(4)	Hypertension	32(8)
Fingolimod	118(29)	Other autoimmune disease	36(9)
Cladribine	17(4)	Dyslipidemia	25(6)
Natalizumab	12(3)	Asthma/COPD	20(5)
Ocrelizumab	77(19)	Mood disorder	5(1)
Rituximab	16(4)	Cancer	4(1)
Alemtuzumab	17(4)	Cardiac disease	3(1)
Azathioprine	1(0)	Epilepsy	3(1)
Mycophenolate	2(1)	Another comorbidity	12(3)
No immunotherapy	49(12)	No comorbidity	159(39)
Social Information	N (%)	COVID-19	N (%)
Medical leave due to MS	12(3)	Any symptom suggestive of COVID-19	65(16)
Medical leave du to other diagnosis	16(4)	Headache	35(54)
Unemployed	41(10)	Sore throat	33(52)
Homesteader/Home keeper	42(10)	Cough	28(44)
Full-time student	11(3)	Malaise	26(40)
Part-time student	1(0)	Diarrhea	21(33)
Retired due to MS	33(8)	Fever	12(19)
Retired due to age	8(2)	Dyspnea	11(17)
Full-time job	200(49)	Anosmia	6(9)
Part-time job	45(11)	Nasal congestion	2(3)
Remote working/studying	303(74)	Eye infection	1(2)
In-office working/studying	45(11)	Measures taken after symptom onset	
Mixed remote and in-office	61(15)	Stayed at home	42(65)
		Visited Emergency Room	6(9)
		Consulted treating neurologist	8(13)
		Consulted another doctor	9(14)
		COVID-19 test	14(22)
		Required hospitalization	5(8)

DMT disease-modifying therapy, MS multiple sclerosis, NMOSD Neuromyelitis Optica Spectrum Disorders, COPD chronic obstructive pulmonary disease.

series is a major limitation for further conclusions. Results from large multicentric databases such as the Italian (Sormani, 2020) and French (Louapre et al., 2020) registries will better elucidate the real influence of these variables on COVID-19 outcomes.

The results from this survey has also impacted our clinical practice and we have changed the way our MS program works. We have implemented telemedicine consultations in over 80% of our routine or emergent visits, infusions have been postponed and rescheduled to an outpatient clinic infusion center, physical therapy, neurocognitive rehabilitation and psychological support access have decreased and efforts are being made in order to maintain the standard clinical care for our MS-NMOSD community.

Maintaining the connection between the different MS groups at national and international levels will be essential to delineate future directions regarding the changes that COVID-19 is generating in the care of our patients.

Declaration of Competing Interest

EC received the ECTRIMS Clinical Fellowship (2013–2014), ECTRIMS travel grant awards, and academic travel support from Novartis, Genzyme, Merck, Biogen and Roche, has been a member of advisory boards at Genzyme, Biogen, Merck and Novartis, has received sub-investigator fees from the ISS "Social Cognition in MS" project at Teva. RUSM received academic travel support from Novartis, Genzyme, Merck, Biogen andRoche, has been a member of advisory boards at Genzyme, Biogen, Merck and Novartis. BS received academic travel support from Novartis, Teva, Merck and Biogen RF received academic travel support from Genzyme, Biogen, Merck, Novartis, Roche, Teva and speaker compensations from Teva and Biogen. PG nothing to disclose CN received academic travel support from Biogen, Genzyme, Novartis and Merck JMT nothing to disclose RT received academic travel support from Biogen, Roche, Teva, Sanofi, Novaris and Merck JP received academic travel support from Biogen, Novartis, Genzyme, Merck and Roche FS nothing to disclose MJC nothing to disclose CC received academic travel support from Novartis, Genzyme, Merck, Biogen and Roche, has been a member of advisory boards at Genzyme, Biogen, Merck and Novartis, has received PI fees from the ISS "Social Cognition in MS" project at Teva.

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Table 2
Characteristics of patients with confirmed or suspected COVID-19 and MS or NMOSD.

Patient	RT-PCR	Sex	Age (years)	Diagnosis	Disease Duration (years)	EDSS	Comorbidities	DMT	DMT modification or interruption	Hospitalization	IMV	COVID-19 symptoms and Follow-up	Outcome
1	positive	male	30	RRMS	6	1	insulin resistance, hypothyroidism	ocrelizumab	no change - last infusion 10 days before symptoms onset	yes	no	bilateral pneumonia, readmission due to Adenovirus pneumonia	full recovery
2	positive	female	23	RRMS	8	1	insulin resistance	dimethyl fumarate	suspended for 35 days until clinical recovery	yes	no	bilateral pneumonia	full recovery
3	positive	female	24	RRMS	9	1	migraine, depression, insulin resistance	fingolimod	suspended for 21 days until clinical recovery	yes	no	myalgias and fever	full recovery
4	positive	male	61	NMOSD-AQP4	0.3	6	hypertension, type 2 diabetes	prednisone	steroid stress dose	yes	yes	bilateral pneumonia, tracheostomy	fatal
5	positive	female	54	NMOSD-AQP4	12	3	insulin resistance, pernicious anemia, osteoarthritis	mycophenolate	no change	no	no	anosmia	full recovery
6	positive	female	29	RRMS	7	1	hypothyroidism	fingolimod	suspended for 5 days until clinical recovery	no	no	myalgias and fever	full recovery
7	not performed - close contact with positive PCR, positive IgM	female	23	RRMS	2.5	1	obesity	dimethyl fumarate	no change	no	no	myalgias and fever	full recovery
8	positive	male	55	RRMS	7	1	depression	teriflunomide	suspended for 7 days until clinical recovery	no	no	myalgias and fever, recovering at home	full recovery
9	positive	female	57	RRMS	7	4	anxiety, type 2 diabetes	fingolimod	no change	no	no	sore throat, headache, mild dyspnea	full recovery
10	positive	male	17	RRMS	2	0	asthma	fingolimod	no change	no	no	asymptomatic	full recovery
11	not performed - close contact with positive PCR	female	28	NMOSD	3	2.5	obesity	mycophenolate	no change	no	no	anosmia, fever and diarrhea	full recovery
12	not performed - close contact with positive PCR, positive IgG	female	44	RRMS	6	3	depression, cutaneous amyloidosis	natalizumab	last dose 4 months prior infection - waiting for switching to cladribine	no	no	anosmia, diarrhea, fever	full recovery
13	positive	male	40	NMOSD-MOG	0.6	2.5	depression	azathioprine	suspension for 1 month	yes	no	myalgia, fever and sore throat, dyspnea, suspected bacterial sobreinfection, received tocilizumab	full recovery
14	positive	female	52	RRMS	8	1	depression, obesity, hypertension, insulin resistance	teriflunomide	no change	no	no	dry cough	full recovery
15	positive	female	31	RRMS	3	2	hypothyroidism	fingolimod	no change	no	no	asymptomatic	full recovery
16	positive, IgG positive	female	34	RRMS	7	1	secondary thyroiditis	alemtuzumab	no change - last dose October 2018	no	no	myalgia, headache, anosmia	recovering at home
17	positive	male	36	RRMS	4	2	migraine, depression	interferon beta 1a IM	no change	no	no	myalgia, rhinorrhea, anosmia	recovering at home
18	not performed, negative IgG	female	31	RRMS	14	1	migraine	alemtuzumab 4 doses, ocrelizumab	no change - last infusion 2 months before symptom onset	no	no	fever, myalgia, headache, anosmia	recovering at home

RT-PCR: real-time polymerase chain reaction; RRMS relapsing-remitting multiple sclerosis; NMOSD Neuromyelitis Optica Spectrum Disorder; AQP4 aquaporin 4; MOG myelin oligodendrocyte glycoprotein; EDSS expanded disability status scale, DMT disease modifying therapy, IMV invasive mechanical ventilation.

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