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.

Correspondence

Clinical characteristics and outcomes of multiple sclerosis patients with COVID-19 in Toronto, Canada

ARTICLE INFO

ABSTRACT

Objective: To report clinical characteristics and outcomes of people with multiple sclerosis (PwMS) who developed COVID-19 infection in Toronto, Canada.
Methods: Descriptive, retrospective, single-center study that included all known PwMS at the St. Michael's Hospital MS Clinic who had PCR-confirmed COVID-19 infection between March 2020 and May 2021.
Results: Of 7000 PwMS in our clinic, 80 (1.1%) tested positive for SARS-CoV-2. Fifty-four (67.5%) were on disease-modifying therapy (DMT) without over-representation of any single treatment. Seventy-one patients (88.8%) had mild symptoms, but nine (11.3%) were hospitalized and one 70-year-old male patient not on treatment died. Of those hospitalized, one-third were treated with ocrelizumab.
Conclusion: In Toronto, PwMS did not appear to have higher prevalence of COVID-19 infection compared to the general population, but disease severity may be affected by DMT use. Our findings add to the accumulating global data regarding COVID-19 infection in PwMS.

1. Introduction

The management of people with multiple sclerosis (PwMS) has been challenging during the COVID-19 pandemic as they may theoretically have a greater risk of developing severe COVID-19-related outcomes due to chronic immunosuppression. Accumulating evidence globally suggests that this is not the case for most PwMS (Loupre et al., 2020; Sormani et al., 2021; Simpson-Yap et al., 2021). However, older age, higher disability, vascular comorbidities, and anti-CD20 therapy have been identified as risk factors associated with developing severe COVID-19 and COVID-19-related complications (Loupre et al., 2020; Sormani et al., 2021; Simpson-Yap et al., 2021). Due to the substantial regional variability of COVID-19 prevalence, there is a continued need to evaluate COVID-19 cases in PwMS in different regions globally. Toronto has been one of the most affected areas in Canada during COVID-19 and has the largest MS clinic nationally. Accordingly, our objective was to evaluate clinical characteristics and outcomes of PwMS at the St. Michael's Hospital (SMH) MS Clinic in Toronto, Canada who developed COVID-19.

2. Methods

All patients in the MS clinic with self-reported COVID-19 infection between March 2020 and May 2021 were included in the study. COVID-19 infection was confirmed by polymerase chain reaction (PCR) on nasopharyngeal swab. Verbal and written reminders were sent on a weekly basis during this period to all neurologists and clinic team members to prompt them to report their pwMS with confirmed COVID-19 to the study team. Clinical characteristics, MS treatment, and COVID-19 disease course and outcomes (no hospitalization, hospitalization, ventilation, intensive care unit (ICU) admission, and death) were

subsequently obtained using the SMH Clinic Registry data and retrospective chart review. Descriptive data are presented.

The study was approved by the Research Ethics Board of St. Michael's Hospital.

3. Results

Among 7000 PwMS in the St. Michael's Hospital MS clinic, 80 (1.1%) tested positive for SARS-CoV-2 between March 2020 and May 2021. Out of these, 57 (71.3%) resided in the Greater Toronto Area (GTA). Patients had a mean age of 38.2 years, 75.0% were women, and the median EDSS score was 1.5 (range 0–6.5). Most patients (86.3%) had relapsing-remitting MS (RRMS). Fifty-four patients (67.5%) were treated with a disease-modifying therapy (DMT) and eight patients (10.0%) received corticosteroids within one month of infection (Table 1). Only four patients (5.0%) had received one dose of a Health Canada approved COVID-19 vaccine, and no patients were fully vaccinated at the time of COVID-19 infection. One patient was on teriflunomide and vaccinated eight days prior to COVID-19 diagnosis, one patient was on dimethyl fumarate and vaccinated seven days prior to diagnosis, one patient had secondary progressive MS and was not on a DMT, and vaccinated 23 days prior to diagnosis, and one patient had completed a course of cladribine tablets three months earlier and was vaccinated 20 days prior to COVID-19 diagnosis. Among all PwMS in our clinic, nine (11.3%) were hospitalized, and 13.0% of identified cases who were on DMT were hospitalized. Characteristics of hospitalized patients are displayed in Table 2. The most common DMT among hospitalized patients was ocrelizumab (*n* = 3). Four patients (one on interferon-beta, one on teriflunomide, and two on ocrelizumab) required high-flow oxygen or non-invasive ventilation without ICU admission, while four patients (one on glatiramer acetate, one on dimethyl fumarate, one on ocrelizumab, and

Table 1

Clinical and demographic characteristics of patients with MS who developed COVID-19.

Patient characteristic	Total $N = 80$
Age, mean (range)	38.2 (19–74)
Female, n (%)	60 (75.0)
Disease classification, n (%)	
Relapsing–remitting multiple sclerosis	69 (86.3)
Primary-progressive multiple sclerosis	2 (2.5)
Secondary-progressive multiple sclerosis	3 (3.8)
Clinically isolated syndrome	5 (6.3)
Radiologically isolated syndrome	1 (1.3)
EDSS, median (range)	1.5 (0–6.5)
Disease duration in years, median (range)	7 (0–39)
DMT treatment at the time of infection, n (%)	54 (67.5)
Corticosteroids within one month prior to infection, n (%)	8 (10.0)
Comorbidity[†], n (%)	23 (28.8)
Hospital admission, n (%)	9 (11.3)
Intensive care unit admission and death, n (%)	1 (1.3)

EDSS: Expanded Disability Status Scale; DMT: disease-modifying therapy.

[†] Comorbidities included cardiovascular disease, cerebrovascular disease, cancer, chronic lung disease, diabetes, hypertension, morbid obesity, and other autoimmune diseases.

Table 2

Characteristics of hospitalized and non-hospitalized PwMS with COVID-19.

	Hospitalized patients ($n = 9$)	Non-hospitalized patients ($n = 71$)
DMT treatment at the time of infection, n (%)		
No DMT	2 (22.2)	24 (33.8)
Glatiramer acetate	1 (11.1)	10 (14.1)
Interferon-beta	1 (11.1)	3 (4.2)
Teriflunomide	1 (11.1)	5 (7.0)
Dimethyl fumarate	1 (11.1)	7 (9.9)
Fingolimod	0	4 (5.6)
Cladribine	0	9 (12.7)
Natalizumab	0	2 (2.8)
Alemtuzumab	0	1 (1.4)
Ocrelizumab	3 (33.3)	6 (8.5)
Corticosteroids within one month prior to infection, n (%)	1 (11.1)	7 (9.9)
Comorbidity[†], n (%)	4 (44.4)	19 (26.8)
Ventilation support for COVID-19 infection, n (%)		
Nasal cannula oxygenation	3 (33.3)	n/a
Non-invasive ventilation	1 (11.1)	n/a
Mechanical ventilation	1 (11.1)	n/a
COVID-19 specific treatment, n (%)		
Glucocorticoids	4 (44.4)	0 (0.0)
Antibiotics	3 (33.3)	2 (2.8)
IVIG	1 (11.1)	0 (0.0)

IVIG: Intravenous immune globulin.

[†] Comorbidities included cardiovascular disease, cerebrovascular disease, cancer, chronic lung disease, diabetes, hypertension, morbid obesity, and other autoimmune diseases.

one not on a DMT) did not require oxygen. One patient, a 70-year-old male with relapsing-remitting MS (EDSS 1.0) and hypertension not on a DMT, was admitted to the ICU, intubated due to respiratory failure, and subsequently died. Among those hospitalized, four patients had a comorbidity (two with hypertension, one with asthma, and one with inflammatory bowel disease) and one patient received corticosteroids within one month of infection. All of the hospitalized patients had normal white blood cell counts and absolute lymphocyte counts based on available laboratory assessments within the last six months prior to COVID-19 infection.

Five patients developed subjective worsening after COVID-19 infection with fatigue and brain fog, as well as worsening of pre-existing MS symptoms, which were felt to represent post-viral syndromes and/or pseudorelapses as MRIs performed at this time did not reveal new or enhancing lesions. However, one patient with RRMS on dimethyl fumarate who was not hospitalized developed brain fog after their COVID-19 infection and was found to have 11 new lesions on their subsequent brain MRI.

4. Discussion

Between March 2020 and May 2021, 168,339 individuals in the Greater Toronto Area (GTA) were diagnosed with COVID-19 (COVID-19: Case Counts – City of Toronto), or about 2.5% of the population. Among the 7000 PwMS at the St. Michael's Hospital MS clinic, 0.8% had COVID-19 while residing in the GTA, suggesting PwMS were not disproportionately affected. However, 11.3% of identified cases were hospitalized, and 13.0% of identified cases who were on DMT were hospitalized, which are higher proportions than the 4.3% observed in the general population in the GTA (COVID-19: Epidemiological Summary of Cases – City of Toronto). These findings suggest that although PwMS at our center may not have had a higher risk of COVID-19 acquisition, which is typically mediated by occupational risk, those infected may have had a higher risk of COVID-19-related hospitalization, possibly related to specific DMT use (Sundaram et al., 2021).

PwMS who developed COVID-19 were treated with a wide range of DMTs, without clear predominance of one particular DMT. In fact, a large proportion of those who developed COVID-19 were not on a DMT. Among pwMS who were hospitalized with COVID-19, ocrelizumab was the most common DMT (used in one-third of hospitalized cases). Although our sample size is small and therefore it is difficult to draw definitive conclusions, this observation may reflect the association between anti-CD20 agents and severe COVID-19 outcomes that has been observed in some, but not all, registries around the world (Arrambide et al., 2021; Louapre et al., 2020; Reder et al., 2021; Sen et al., 2021; Sormani et al., 2021).

A significant limitation of this study is that we likely underestimated the total number of COVID-19 cases in PwMS in our clinic as we relied on cases of COVID-19 infection to be self-reported by patients or identified during routine clinical care by the care team based on laboratory tests. In addition, in the early stages of the pandemic, COVID-19 testing was not as widely available, therefore early cases were likely not captured. Moreover, patients who contracted COVID-19 after their annual clinic visit were also likely missed. All of these factors likely resulted in selection bias and clinical characteristics of those not captured may differ. Despite this limitation, since most PwMS in our clinic are seen at least annually and were likely evaluated at least once during the study period, it is expected that most COVID-19 cases, and in particular, hospitalized cases were identified and captured.

5. Conclusion

People with MS in Toronto did not appear to have an increased risk of COVID-19 acquisition, and if infected, symptoms were mild in the majority of cases. However, 11.3% of identified cases in pwMS were hospitalized, and 13.0% of cases in pwMS treated with DMTs were hospitalized, raising the possibility that specific DMT use may affect COVID-19 disease severity. Specifically, of those treated with DMTs, one-third were being treated with ocrelizumab, further supporting the association between anti-CD20 agents and COVID-19 disease severity. Our findings add to accumulating global data regarding COVID-19 risk in PwMS and highlight the regional variability of COVID-19 prevalence, as well as the importance of contextualizing risk at a regional level to optimize the management of patients with MS. Future studies evaluating COVID-19 vaccine effectiveness in PwMS on various DMTs will be important to better inform clinical care and management during the current pandemic, as well as for future viral pathogens.

Ethical considerations

Funding source

CRediT authorship contribution statement

Jacqueline M. Solomon: Funding acquisition, Formal analysis, Visualization, Writing – original draft, Writing – review & editing. **Ashley Jones:** Funding acquisition, Formal analysis, Visualization, Writing – original draft, Writing – review & editing. **Marika Hohol:** Funding acquisition, Formal analysis, Visualization, Writing – original draft, Writing – review & editing. **Kristen M. Krysko:** Funding acquisition, Formal analysis, Visualization, Writing – original draft, Writing – review & editing. **Alexandra Muccilli:** Funding acquisition, Formal analysis, Visualization, Writing – original draft, Writing – review & editing. **Alexandra Roll:** Funding acquisition, Formal analysis, Visualization, Writing – original draft, Writing – review & editing. **Dalia Rotstein:** Funding acquisition, Formal analysis, Visualization, Writing – original draft, Writing – review & editing. **Raphael Schneider:** Funding acquisition, Formal analysis, Visualization, Writing – original draft, Writing – review & editing. **Daniel Selchen:** Funding acquisition, Formal analysis, Visualization, Writing – original draft, Writing – review & editing. **Reza Vosoughi:** Funding acquisition, Formal analysis, Visualization, Writing – original draft, Writing – review & editing. **Stefan D. Baral:** . **Jiwon Oh:** Funding acquisition, Formal analysis, Visualization, Writing – original draft, Writing – review & editing.

Declaration of Competing Interest

J.M.S. declares no potential conflicts of interest.

A.J. declares no potential conflicts of interest.

M.H. reports personal fees for consulting or speaking from Biogen-Idec, Alexion Pharma, EMD Serono, Roche, BMS, Novartis, and Sanofi-Genzyme.

K.M.K. has received personal fees for consulting or speaking from Normative Inc., Biogen-Idec, EMD-Serono, Roche, and Novartis.

D.R. has received research support from the MS Society of Canada, CMSC, and Roche Canada. She has acted as a speaker or consultant for Alexion, Biogen, EMD Serono, Novartis, Roche, and Sanofi Aventis.

R.S. reports personal fees for consulting or speaking from Biogen-Idec, EMD Serono, and BMS.

R.V. has received educational support from Biogen Idec, and EMD Serono. He has received honoraria as chair of the LAUNCH program (EMD Serono), for participation in advisory committees from Biogen Idec, EMD Serono, Genzyme, Novartis, Alexion, and Roche, and BMS, and as speaker from Biogen Idec, and Genzyme. He has received grants from CIHR and MHRC for Canadian CCSVI trial, and remuneration as consultant from Biogen Idec, EMD Serono, Teva, Genzyme, Novartis, and Roche, and BMS.

S.D.B. declares no potential conflicts of interest.

J.O. reports grants from MS Society of Canada, Barford and Love MS Fund of St. Michael's Hospital Foundation, National MS Society, Brain Canada, Biogen-Idec, Roche, and EMD-Serono; and personal fees for consulting or speaking from Biogen-Idec, EMD-Serono, Roche, Sanofi-Genzyme, Novartis, and BMS.

References

Arrambide, G., Llaneza-Gonzalez, M.A., Costa-Frossard Franca, L., et al., 2021. SARS-CoV-2 Infection in multiple sclerosis: results of the Spanish neurology society registry. Neurol. Neuroimmunol. Neuroinflamm. 8 (5) https://doi.org/10.1212/NXI.0000000000001024.

COVID-19: Case Counts, City of Toronto, Available online: https://www.toronto.ca/home/covid-19/covid-19-latest-city-of-toronto-news/covid-19-pandemic-data/covid-19-weekday-status-of-cases-data/ (accessed 20 June 2021).

COVID-19: Epidemiological Summary of Cases, City of Toronto, Available online: https://www.toronto.ca/home/covid-19/covid-19-latest-city-of-toronto-news/covid-19-pandemic-data/covid-19-epidemiological-summary-of-cases-data/ (accessed 20 August 2021).

Louapre, C., Collongues, N., Stankoff, B., et al., 2020. Clinical characteristics and outcomes in patients with coronavirus disease 2019 and multiple sclerosis. JAMA Neurol. 77 (9), 1079–1088. https://doi.org/10.1001/jamaneurol.2020.2581.

Reder, A.T., Centonze, D., Naylor, M.L., et al., 2021. COVID-19 in patients with multiple sclerosis: associations with disease-modifying therapies. CNS Drugs 35 (3), 317–330. https://doi.org/10.1007/s40263-021-00804-1.

Sen, S., Karabudak, R., Schiavetti, I., et al., 2021. The outcome of a national MS-COVID-19 study: what the Turkish MS cohort reveals? Mult. Scler. Relat. Disord. 52, 102968 https://doi.org/10.1016/j.msard.2021.102968.

Simpson-Yap, S., De Brouwer, E., Kalincik, T. et al., 2021. Associations of DMT therapies with COVID-19 severity in multiple sclerosis. medRxiv, 10.1101/2021.02.08.21251316.

Sormani, M.P., De Rossi, N., Schiavetti, I., et al., 2021. Disease-modifying therapies and coronavirus disease 2019 severity in multiple sclerosis. Ann. Neurol. 89 (4), 780–789. https://doi.org/10.1002/ana.26028.

Sundaram, M.E., Calzavara, A., Mishra, S., et al., 2021. Individual and social determinants of SARS-CoV-2 testing and positivity in Ontario, Canada: a population-wide study. CMAJ 193 (20), E723–E734. https://doi.org/10.1503/cmaj.202608.

Jacqueline M. Solomon[a,b], Ashley Jones[a], Marika Hohol[a], Kristen M. Krysko[a], Alexandra Muccilli[a], Alexandra Roll[a], Dalia Rotstein[a], Raphael Schneider[a,c], Daniel Selchen[a], Reza Vosoughi[a], Stefan D. Baral[d], Jiwon Oh[a,*]

[a] *Division of Neurology, Department of Medicine, St. Michael's Hospital, University of Toronto, 36 Queen St E, Toronto, Ontario M5B 1W8, Canada*
[b] *Division of Neurology, Department of Medicine, Hamilton Health Sciences, McMaster University, 237 Barton St E, Hamilton, Ontario L8L 2X2, Canada*
[c] *Keenan Research Centre for Biomedical Science, St. Michael's Hospital, 209 Victoria St, Toronto, Ontario M5B 1T8, Canada*
[d] *Department of Epidemiology, Johns Hopkins School of Public Health, 615 N Wolfe St, Baltimore, MD 21205, USA*

[*] Corresponding author.
E-mail addresses: solomonja@hhsc.ca (J.M. Solomon), ashley.jones@unityhealth.to (A. Jones), marika.Hohol@unityhealth.to (M. Hohol), kristen.krysko@mail.utoronto.ca (K.M. Krysko), alexandra.muccilli@unityhealth.to (A. Muccilli), alexandra.roll@unityhealth.to (A. Roll), dalia.rotstein@unityhealth.to (D. Rotstein), raphael.schneider@unityhealth.to (R. Schneider), daniel.selchen@unityhealth.to (D. Selchen), reza.vosoughi@unityhealth.to (R. Vosoughi), sbaral@jhu.edu (S.D. Baral), ohjiw@smh.ca (J. Oh).