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Pandemic forward: Lessons learned and expert perspectives on multiple sclerosis care in the COVID-19 era

1. Introduction

Coronavirus disease 2019 (COVID-19), caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), is a serious global health threat that has impacted healthcare delivery and accessibility across the globe. Individuals with chronic neuroimmunological diseases such as multiple sclerosis (MS) are of particular interest as they may be more vulnerable to infections due to treatment involving immunomodulatory disease modifying therapies (DMTs). Given the uncertainties and rapidly evolving circumstances associated with the pandemic, we aim to provide expert perspectives on pragmatic approaches to patient-centered MS care, which in recent years has shifted towards early intervention to substantively alter disease course and prevent irreversible progression. We will emphasize the need for flexible and evidence-based shared decision-making to provide holistic care for people with MS (PwMS) throughout the pandemic and beyond.

2. The multifaceted impact of the pandemic on MS care

The pandemic has changed the day-to-day management of MS (Mateen et al., 2020). Stay-at-home orders and social distancing measures have limited in-person interactions with MS care teams and reduced access to health facilities for diagnosis and monitoring. Pandemic-related restrictions and patient concerns of potential infection outside of the home have led to gaps in clinical care, resulting in potential delayed disease evaluation, diagnosis, and monitoring as well as care for non-MS comorbidities (Vogel et al., 2020). Access to critical rehabilitative care such as physical, occupational, and speech therapy has also been disrupted, impacting the holistic approach to patient support. These changes to interactions with the MS care team have resulted in swift adaptations to patient care, including an increased reliance on telehealth and other services (Sullivan et al., 2020).

Along with its clinical impacts, the COVID-19 pandemic has adversely affected the physical, emotional, and mental wellbeing of many PwMS (Motl et al., 2020). For instance, pandemic-related fears and stay-at-home orders may have reduced activity levels for many PwMS, which could negatively impact their physical condition and quality of life, and increase their risk of developing non-MS comorbidities (Synnott, 2020). Social distancing measures have limited in-person engagements with their social support networks, thereby potentially impacting their mental health (Bhaskar et al., 2020). Mental wellbeing may be further compromised by financial concerns stemming from self-quarantining or job loss, and heightened fears about contracting COVID-19 (Vogel et al., 2020). It is therefore important to ensure that PwMS receive the physical and psychosocial care needed to see them safely through the pandemic (Figure 1). Fortunately, telehealth services

may be leveraged to fill the gap (Sullivan et al., 2020) and could be an effective tool for rehabilitative and supportive MS care during the pandemic (DeLuca et al., 2020). Additionally, racial and social disparities in the impact of COVID-19 in the US have become evident, with underserved and ethnic minority populations being disproportionately affected (Webb Hooper et al., 2020). These disparities underscore the need to better serve PwMS in these more vulnerable populations.

3. Current evidence on COVID-19 risk and severity in MS

The current state of the evidence suggests that simply having MS does not increase risk of SARS-CoV-2 infection or worsen clinical outcomes compared to those without MS (Evangelou et al., 2020; Parrotta et al., 2020). As with the general population, PwMS with risk factors such as older age, obesity, diabetes, cardiac and pulmonary comorbidities, and potentially physical disability may be at higher risk for more severe outcomes of COVID-19 if they become infected (Louapre et al., 2020; Multiple Sclerosis International Federation, 2020; Sormani et al., 2020). PwMS are therefore advised to follow the same World Health Organization guidelines as the general population including wearing a face mask, maintaining social distancing, and practicing good hygiene (Multiple Sclerosis International Federation, 2020). Those at high risk of severe COVID-19, whether they have MS or not, are advised to be extra vigilant to protect against infection (Louapre et al., 2020; Multiple Sclerosis International Federation, 2020).

Studies evaluating DMT use on infection severity have generally reported mixed results (Louapre et al., 2020; Sormani et al., 2020). An initial analysis of the MS Global Data-Sharing Initiative, which included 1540 PwMS with confirmed or suspected SARS-CoV-2 infection, suggested that anti-CD20 DMTs ocrelizumab and rituximab were associated with higher frequencies of hospital admission, ICU admission, and the need for artificial ventilation compared to dimethyl fumarate and other MS DMTs. However, there did appear to be no association observed between DMTs and risk of death (Simpson-Yap et al., 2020). In contrast, the Covisep registry in France, which included 347 PwMS with confirmed/highly suspected COVID-19 diagnosis, found no association between exposure to DMTs and infection severity (Louapre et al., 2020).

More work is needed to collect well controlled data on use of DMTs in MS and negative outcomes caused by COVID-19. However, to give general guidance, clinical experts have provided their opinions on the potential effect of DMTs used for MS on SARS-CoV-2 infection risk and in general have concluded that INF β and glatiramer acetate “may not” increase infection risk, whereas fingolimod, siponimod, B cell-depleting therapies, alemtuzumab, and cladribine “may” do so (Korsukewitz et al., 2020; Thakolwiboon et al., 2020). The infection risk associated with natalizumab, teriflunomide, and dimethyl fumarate is thus far unclear

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(Korsukewitz et al., 2020; Thakolwiboon et al., 2020).

The evidence to date provides important but early insights on the impact of SARS-CoV-2 on PwMS. However, clinical decision-making during the pandemic should balance potential COVID-19 risks and the consequences of delaying higher efficacy therapies, including unintended outcomes such as worsening disability and increased relapse rate, MRI lesions, and brain atrophy that will persist long after the COVID-19 pandemic.

4. Expert perspectives and future outlook

The risk of SARS-CoV-2 infection and the potential association between infection severity and MS and DMT use has been a particularly highly debated topic of interest since the early days of the pandemic in 2020. With very limited available data, clinical guidance published in the first few months of the pandemic was based on perceived hypothetical risks associated with the mechanism of action of the DMT drug class or general principles of immunologic mechanism of action. Although well-intentioned, such recommendations are not evidence-based and may have inadvertently created confusion and, in some cases, unnecessary changes in clinical care. Cautiously, some MS treatments have been delayed or discontinued, with some experts recommending a shift to less effective DMTs. These clinical decisions may contribute to greater physical and cognitive disability for PwMS in the future. Early data from large centralized databases/registries such as the MS Global Data-Sharing Initiative (QMENTA, 2020) and the COViMS registry (COViMS Registry, 2020) suggest that some of the initial fears concerning SARS-CoV-2 may have been unfounded. Future data from these sources will be important in addressing questions on long-term immunity in PwMS following SARS-CoV-2 infection and, once a COVID-19 vaccine becomes available, will provide insights into the challenges associated with immunizing those on DMTs.

Based on the available evidence, treatment should be similar to that

provided prior to the pandemic: individualized to each person's clinical profile, taking into account factors such as age, MS disease course, current disease activity, and comorbidities. For many PwMS, treatment may likely remain unchanged unless contrary evidence emerges. All patients, whether they have MS or not, should be educated on risk factors for more severe outcomes of COVID-19 if they become infected. Vaccinations should be discussed as an integral part of MS care, particularly in relation to how some DMTs such as anti-CD20s may impact effective immune responses to routine vaccines as well as the potential SARS-CoV-2 vaccine in the future. During patient encounters, whether virtual or in person, MS care teams should make a focused effort to address patients' fears about the effect that their MS and DMTs may have on their infection risk and outcomes. Clinicians should educate their patients about their risks based on clinical evidence and facts, rather than on hypotheticals, to ensure an informed, evidence-based, shared decision-making approach to MS care. Additionally, MS care teams should actively engage with patients during their encounters to assess any impacts the pandemic has had on their psychosocial well-being and to ensure their supportive care needs are being met. It is crucial that we continue to assess, diagnose, follow-up, monitor, and treat PwMS as frequently and as carefully as we did before the pandemic. Advances in telemedicine should be leveraged for all aspects of MS care to compensate for necessary distancing requirements.

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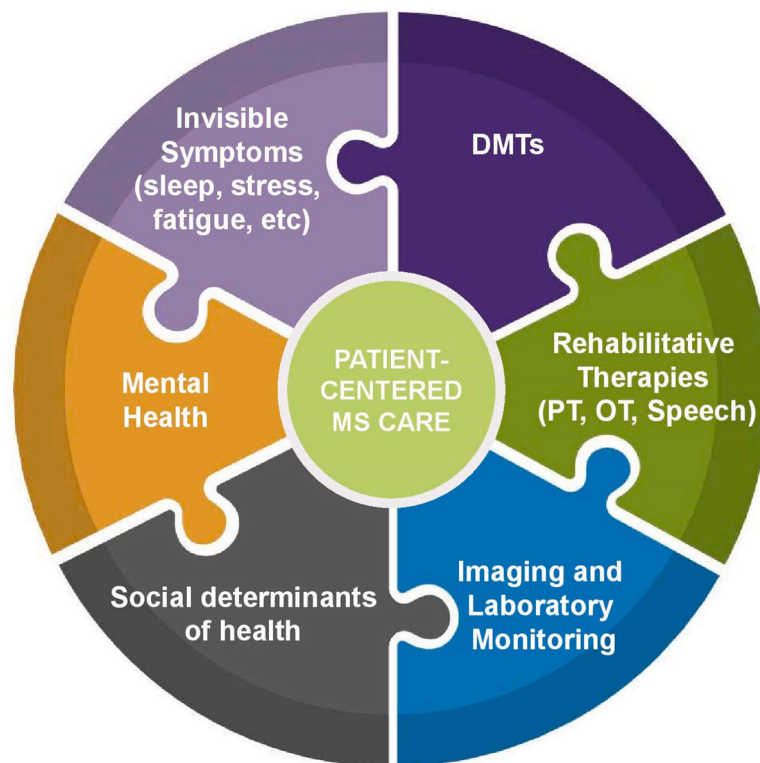


Fig. 1. Multifaceted aspects for patient-centric MS care during and post-COVID-19 pandemic. Telemedicine should be leveraged for all aspects of MS care, whenever permissible, to compensate for necessary limitations to in-person interactions with the MS care teams. DMTs, disease modifying therapies; OT, occupational therapy; PT, physical therapy.

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