Multiple Sclerosis and COVID19

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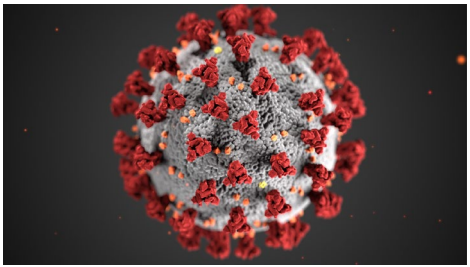
Corona Virus Disease 2019 (COVID19)



- COVID19 is a contagious respiratory illness caused by infection with a new coronavirus called severe acute respiratory syndrome corona virus 2 (SARS-CoV-2)
- COVID-19 appears to spread more easily than flu. It can also take longer before people show symptoms and people can be contagious for longer.
- COVID-19 spreads via a number of routes, involving saliva and other bodily fluids and excretions. These fluids form small droplets and aerosols, which are spread when an infected person breathes, coughs, sneezes, or speaks. The virus may also spread by direct contact. It is unknown how often it spreads via contaminated surfaces.

Symptoms associated with COVID19

- Fever or chills
- Cough
- Shortness of breath or difficulty breathing
- Fatigue
- Muscle or body aches
- Headache
- New loss of taste or smell
- Sore throat
- Congestion or runny nose
- Nausea or vomiting
- Diarrhea

Corona Virus Disease 2019 (COVID19)

- People of any age can get COVID-19, including healthy young adults and children.

- People who are older or have certain underlying medical conditions (ex. chronic lung or kidney disease, obesity, Type 2 diabetes, sickle cell disease, smoking) are at higher risk of getting severe complications from COVID-19 that require hospitalization and even ICU admission.

- People with COVID-19 have had a wide range of symptoms ranging from mild symptoms to severe illness. Symptoms may appear 2-14 days after exposure to the virus.

- A significant number of patients who have recovered from the acute phase of the disease continue to experience a range of effects—known as *long COVID* —for months afterwards. These effects include severe fatigue, memory loss and other cognitive issues, low-grade fever, muscle weakness, and breathlessness.

Risk of COVID19 infection for individuals with MS

- **General Observations** *from multiple registries around the world*: The incidence of COVID19 cases among individuals with MS reflects that of the general population.

- **Risk of contracting COVID19** *UK MS registry* (5,309 subjects): No association was found between disease modifying treatment, MS disease duration or degree of disability and the likelihood of contracting COVID19.

(Older and more disabled people with MS were more likely to self isolate, as were patients treated with monoclonal antibodies or fingolimod.)

Risk factors for poor outcomes secondary to COVID19 infection in people with MS

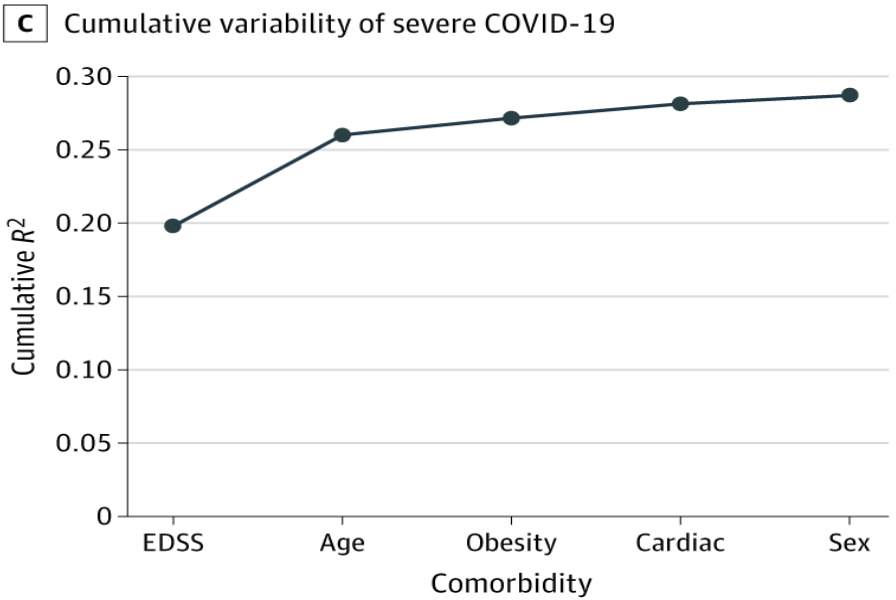
- *Multiple registries around the world*: As in the general population, older age, male sex, race, and co-morbidities (such as cardiovascular disease, obesity and chronic pulmonary disease), are risk factors for worse outcomes

- *COVISEP French study* (347 subjects): Patients with severe COVID-19 infections, requiring hospitalization, were older, more neurologically disabled, more likely to be obese, and more frequently had a progressive course compared with patients with COVID-19 who were not hospitalized.

- *MS Global Data Sharing Initiative* (1,540 subjects): Older age, increasing disability and a progressive disease course were associated with a higher rate of hospitalization due to COVID19.

- *COViMS N. American Registry* (858 patients): African American or black MS patients had a 3 fold higher risk for ICU admission or mortality related to COVID19 compared with non-Hispanic white MS patients after adjusting for co-variates

Clinical Characteristics and Outcomes in Patients With Coronavirus Disease 2019 and Multiple Sclerosis



JAMA Neurol. 2020 Sep 1;77(9):1079-1088.

Recovery from COVID19 infection in MS

- *UK MS registry:* 75% of individuals with COVID19 reported that they had recovered. DMTs and physical disability did not affect recovery from COVID-19.

- *Hoffman LaRoche databases (4,300 subjects)* : In the majority of cases, MS patients who contracted COVID19 during treatment with ocrelizumab had recovered or were recovering.

Impact of disease modifying therapies on the course of COVID19 infection

- *COVISEP French study* (347 subjects): Most of the severe COVID19 infections occurred in patient on **no** treatment. *46% of untreated patients vs. 15% of treated patients had more severe complications.* Some severe cases occurred in patients on teriflunomide or rituximab. Patients on injectable DMTs had a lower risk of severe COVID19 than untreated patients.

- *MuSC-19 Italian study* (784 subjects): Over-representation of MS patients on ocrelizumab in the MS COVID19 cohort and under-representation of patients on IFNβ. Patients on αCD20 tx (rituximab, ocrelizumab) were 2.7x more likely to have severe COVID19 versus patients on dimethylfumarate.

- *MS Global Data Sharing Initiative* (1,540 subjects): Compared to other DMTs, Rituximab was associated with higher rates of hospitalization, ICU admission and mechanical ventilation, but not death, in MS patients with COVID19. Ocrelizumab showed similar trends but of lesser magnitude. *Subjects on anti-CD20 antibodies has a 3 fold higher risk of artificial ventilation than subjects on DMF, and a 2 fold higher risk of hospitalization subjects on natalizumab*.

- *Hoffman LaRoche databases* (4,358 subjects on ocrelizumab): Across clinical trials and post-marketing reports where severity was reported, the majority of SARS-COV2 infections in people with MS on ocrelizumab resulted in mild-moderate disease. The majority reported having recovered; case fatality rates similar to untreated patients and the general population.

Effects of MS disease-modifying therapies on effectiveness of vaccinations

- Several studies demonstrated preserved immune responses to multiple vaccine types in people treated with beta-interferons to multiple vaccine types.
- Limited data suggest vaccine responses to be preserved with dimethyl fumarate treatment.
- Vaccine responses were reduced to varying degrees in those treated with glatiramer acetate, teriflunomide, sphingosine-1-phosphate receptor modulators, and natalizumab.
- Antibody vaccine responses were significantly impaired by B cell depleting anti-CD20 monoclonal antibody therapies.

Mult Scler Relat Disord. 2020 Oct;45:102439

Conclusions

- Overall, the incidence of COVID19 in the MS population reflects that of the general population. This includes people with MS on DMT.
- Poor outcomes are associated with the same risk factors as in the general population.
- IFNβ tx may be protective against severe complications of COVID19.
- There is some evidence that anti-CD20 tx (particularly rituximab) is associated with poor outcomes.
- There is conflicting data on ocrelizumab , but collectively the data suggest it imposes less of a risk than rituximab.
- MS patients on certain disease modifying therapies may have a blunted response to the COVID19 vaccine.