Letters

Self-diagnosed COVID-19 in people with multiple sclerosis: a community-based cohort of the UK MS Register

INTRODUCTION

In the early phases of the UK COVID-19 outbreak, in the absence of clear evidence about the risks for people with multiple sclerosis (pwMS) and those taking immunomodulatory disease-modifying therapies (DMT), we launched a community-based study as part of the UK MS Register (UKMSR). We intended to capture the picture of COVID-19 among pwMS and their risk of contracting the disease. Here, we report our findings from 17 March to 24 April 2020.

METHODS

The COVID-19 study (clinicaltrials.gov: NCT04354519) is a prospective observational cohort launched on 17 March 2020 as part of the UK MSR (Ethics:16/ SW/0194). PwMS completed a specific COVID-19 related survey which was combined with data held from before the pandemic where available. The primary outcome of the study is participant-reported self-diagnosis of COVID-19. Participants were asked if their diagnosis was confirmed by testing—the available test in the UK was reverse transcriptase-PCR. Participants reported if their sibling without MS, closest in age who was not living with them, had self-diagnosed COVID-19. The likelihood of having COVID-19 was assessed using multivariable regression analysis with the variables: age, gender, ethnicity, MS duration and type, self-isolation and DMTs. DMTs were considered after stratifying based on moderate-efficacy versus high-efficacy therapies (table 1). Disability was assessed using the last recorded web-based Expanded Disability Status Scale (webEDSS) or MS Impact Scale v2 (MSIS-29v2).

RESULTS

As of 24 April, out of 3910 participants, 237 (6.1% (95% CI 5.3% to 6.8%)) reported self-diagnosed COVID-19 among whom 54 (22.8% (17.5% to 28.2%)) also had a diagnosis by a healthcare professional based on symptoms and 37 (15.6% (11.2% to 20.6%)) a confirmed diagnosis by testing. Three participants reported hospitalisation due to COVID-19. No deaths were reported.

Among 1283 siblings without MS, 79 (6.2%) had also reported a diagnosis of COVID-19. Adjusting for age and gender, the likelihood of contracting COVID-19 in pwMS was similar to siblings (OR 1.180 (0.888 to 1.569)).

Seven hundred and fifty-nine of 3812 participants reported that they were self-isolating and that they had been self-isolating for at least 2 weeks before symptom onset if they had COVID-19. Of these, 2 (0.3% (0% to 0.7%)) had self-diagnosed COVID-19 whereas 137 of 3053 participants not self-isolating (4.5% (3.8% to 5.2%)) had the disease (p<0.001). Among participants with confirmed COVID-19, 94.6% (86.5% to 100%) were not self-isolating which was higher than those without the disease (79.9% (78.7% to 81.3%), p=0.023). Self-isolating participants were slightly older than those not self-isolating (p<0.001).

A lower proportion of participants on DMTs were self-isolating compared with those not taking DMTs (18.1% (16.4% to 20%) vs 21.5% (19.6% to 23.3%), p=0.01). Rate of self-isolation in participants taking high-efficacy DMTs was similar to those not taking DMTs and higher than those taking moderate-efficacy DMTs (21.3% vs 21.4% and 16.5%, p=0.993 and p=0.014, respectively). More participants with progressive MS (PMS) were self-isolating compared with relapsing-remitting MS (RRMS) (23.2% (21% to 25.3%) vs 17.9% (16.3% to 19.5%), p<0.001).

Using self-diagnosed and confirmed COVID-19 as outcomes, 3714 and 3618 participants were included in the regression analysis, respectively. Self-isolation predicted a lower likelihood of having self-diagnosed COVID-19 (OR 0.646 (0.016 to 0.259)) but not confirmed COVID-19. Participants on DMTs were less likely to have self-diagnosed COVID-19 (OR 0.640 (CI 0.428 to 0.957)), which remained significant after removing

| DMT                  | Total (n=3907), n (%) | Self-diagnosed COVID-19 (n=236), n (%) | Confirmed COVID-19 (n=37), n (%) |
|----------------------|----------------------|---------------------------------------|---------------------------------|
| None                 | 2088 (53.4)          | 116 (49.2)                            | 11 (29.7)                       |
| Beta-interferons*    | 232 (5.9)            | 11 (4.7)                              | 1 (2.7)                         |
| Glatiramer acetate*  | 196 (5)              | 18 (7.6)                              | 3 (8.1)                         |
| Dimethyl fumarate*   | 446 (11.4)           | 32 (13.6)                             | 7 (18.9)                        |
| Teriflunomide*       | 93 (2.4)             | 2 (0.8)                               | 0 (0)                           |
| Fingolimod*          | 235 (6)              | 15 (6.4)                              | 4 (10.8)                        |
| Siponimod           | 3 (0.1)              | 0 (0)                                 | 0 (0)                           |
| Ocrelizumab†         | 193 (4.9)            | 14 (5.9)                              | 4 (10.8)                        |
| Natalizumab†         | 231 (5.9)            | 19 (8.1)                              | 5 (13.5)                        |
| Cladribine†          | 73 (1.9)             | 2 (0.8)                               | 0 (0)                           |
| Alemtuzumab†         | 93 (2.4)             | 5 (2.1)                               | 2 (5.4)                         |
| HSCT†                | 2 (0.1)              | 0 (0)                                 | 0 (0)                           |
| Mitoxantrone†        | 0 (0)                | 0 (0)                                 | 0 (0)                           |
| Others†              | 16 (0.4)             | 2 (0.8)                               | 0 (0)                           |
| Unknown              | 6 (0.2)              | 0 (0)                                 | 0 (0)                           |

*Defined as moderate-efficacy DMTs.
†Defined as high-efficacy DMTs.

Including rituximab, ofatumumab, ublituximab, vedolizumab, ponesimod, azathioprine, mycophenolate mofetil and methotrexate.

HSCT, hematopoietic stem cell transplantation.
The observation that self-isolating pwMS had a lower risk of COVID-19 was not unexpected. We found older pwMS and those with PMS were less likely to have COVID-19. This could be because they were self-isolating more. Similar to previous reports, we found evidence that pwMS with any ethnicity other than white had a higher chance of contracting COVID-19, but larger numbers are required to confirm this.

When this study launched, there was no accurate or accessible test to diagnose COVID-19. Therefore, we decided to set a diagnosis of COVID-19 made by participants, based on their symptoms, as the primary outcome of the study. This approach has also been adopted in other large-scale studies and is in line with the UK government policy not to seek medical advice for mild symptoms of COVID-19.1,3

In conclusion, during a period with strict precautions in place to prevent the spread of COVID-19, pwMS and those taking DMTs are not at an increased risk of contracting the disease.

DISCUSSION

We report initial findings of an ongoing community-based COVID-19 study in a large UK-wide population of pwMS which coincided with the peak of the COVID-19 outbreak in the UK.1 We show that pwMS taking immunomodulatory treatments do not have an increased risk of contracting COVID-19. We did not find individual DMTs to be noticeably over-represented among pwMS with COVID-19.

The incidence of COVID-19 in our population of pwMS was not higher than that of the general population, and pwMS were not at a higher risk of having COVID-19 compared with their siblings without MS. The low hospitalisation rate in our population is possibly due to its patient-reported nature where hospitalised pwMS would fail to respond to the surveys.

Younger age was associated with increased likelihood of having self-diagnosed (OR 1.043 (1.022 to 1.064)) and confirmed (OR 1.048 (1.009 to 1.087)) COVID-19.

Participants with PMS were less likely to have self-diagnosed (OR 0.429 (0.241 to 0.763)) or confirmed (OR 0.119 (0.015 to 0.967)) COVID-19 compared with those with RRMS, but this effect disappeared after excluding participants who were self-isolating.

Including webEDSS (n=2808) and physical MSIS-29-v2 (n=3192) as additional predictors in the analysis showed no significant association with the likelihood of contracting COVID-19.

The gender distribution was similar between participants with and without COVID-19. More participants with self-diagnosed COVID-19 reported themselves as having any ethnicity other than white compared with those without the disease (6.9% (3.9% to 10.1%) vs 3.8% (3.2% to 4.4%), p=0.019). Gender and ethnicity did not affect the likelihood of having COVID-19.
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