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 UKMSR (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 a reported 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 0.064 (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

Table 1 Distribution of individual disease-modifying therapies (DMTs) among participants of the COVID-19 study

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.

self-isolating participants (OR 0.633 (0.402 to 0.998)). High-efficacy DMTs reduced the likelihood of self-diagnosed COVID-19 compared with no DMTs (OR 0.540 (0.311 to 0.938)) but not compared with moderate-efficacy DMTs. There was no significant association between taking DMTs and having confirmed COVID-19. It was not possible to do a formal statistical test for the association between individual DMTs and COVID-19 due to small numbers (table 1).

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-29v2 (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.

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,[2] 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.

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,[3] 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.[4 5]

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.

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