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Correspondence

Estimating the risk of COVID-19 in multiple sclerosis patients in Buenos Aires, Argentina



On March 11, 2020, the WHO declared the COVID-19 pandemic (WHO Director-General's opening remarks at the media briefing on COVID-19 - 11 2020). In Argentina, according to the National Ministry of Health, as of June 3rd, the confirmed cases of COVID-19 were 19,268 (Reporte Diario Vespertino Nro 162, 2020). Most of the cases are concentrated in the Metropolitan Area of Buenos Aires (MABA), which is the megalopolis that comprises the Autonomous City of Buenos Aires and the surrounding conurbation of the province of Buenos Aires. The MABA has a population of 12,806,866 inhabitants, and 15,555 cases of COVID-19 (80.7% of national cases), which determines a cumulative incidence of 121.4 cases / 100,000 inhabitants for this region, since the beginning of the epidemic up to June 3rd (Reporte Diario Vespertino Nro 162, 2020).

Multiple sclerosis (MS) patients may have an increased risk of infections mainly due to immunosuppression caused by some of the prescribed drug therapies (Willis and Robertson, 2020). Both immunosuppression and certain neurological conditions, including MS, have been identified as risk factors for the development of severe forms and COVID-19-related death (OpenSAFELY Collaborative et al., 2020).

The demand for data on the impact of the novel coronavirus on people with MS grows rapidly and information is crucial. Currently, there are many registries ongoing around the world trying to describe the frequency and the evolution of SARS-CoV-2 infection in MS patients. (<https://musc-19.dibris.unige.it/>, <https://msdataalliance.com/>).

Those registries also try to identify the estimated risk of infection in MS patients. In Argentina, there is an ongoing registry to identify the number of affected MS patients with COVID-19 as well as the evolution; however, no estimation about the risk of SARS-CoV-2 infection was done to provide evidence-based decisions.

Here we report the results of an investigation with the scope of estimating the risk of SARS-CoV-2 infection in patients with MS in the MABA.

For the analysis estimation we used the prevalence of MS previously reported for the MABA. The MABA refers to the megalopolis composed by the Autonomous City of Buenos Aires and the surrounding area of the province of Buenos Aires - namely the adjacent 24 municipalities. This includes an area of 4,758 km² and 12,806,866 inhabitants. The method applied was the capture-recapture method cross-matching registries from 6 MS Centers and the estimated prevalence was 38.2 per 100,000 inhabitants (95% confidence interval [CI] 36.1– 41.2) (Cristiano et al., 2016).

Under the assumption that both events, MS and COVID-19 are independent and follow a random distribution, following Bayes' theorem (Bayes, 1763), the probability that a subject has both events can be calculated according to the formula:

$P(A \cap B) = P(A) \cdot P(B)$. where the probability of observing both events, under the assumption of independence, is equal to the product of the probability of event A by the product of the probability of event

B. Although it is known that cases of COVID-19 in the MABA are not randomly distributed, but there are transmission clusters (Reporte Diario Vespertino Nro 162, 2020), since that there are no data available regarding the distribution of MS cases within this area, we maintained this assumption in order to make the estimates.

Due to under-diagnosis in COVID-19 cases, the observed number of cases may be less than the actual number. We estimated the proportion of under-diagnosed cases of COVID-19 to calculate the total number of people infected, as described by Russell et al. (Russell et al., 2020). For the estimate of under-diagnosis in the MABA, we assumed that the level of under-diagnosis is homogeneous throughout the country. With the total cases obtained, we then estimated the probability of finding a patient with MS infected with SARS-CoV-2 as described before.

The estimated probability of observing a subject with MS and COVID-19 is 4.64 cases / 10 million inhabitants. In our country, it has been estimated that only 15% of total cases have been diagnosed (95% CI 11-29) (Russell et al., 2020), which would set the total number of people with COVID-19 at 128,453 and in the MABA would be 103,700 cases (95% CI 53,637-141,409). With this estimated number of total cases, the probability of finding a person with MS and COVID-19 is 38.3 / 10 million inhabitants (95% CI 15.9 - 42.2 / 10 million inhabitants). Taking into account the MABA population, the absolute number of people with COVID-19 and MS would be 49 (95% CI 20.3-54). These estimates would represent that every 2116.3 cases of COVID-19, there could be expected one patient with MS infected.

This is the first study that estimated the possible number of affected MS patients with COVID-19 to raise awareness to the community as well as to provide health decisions based on the current evidence.

A possible limitation of the estimation is the COVID-19 under-diagnosis in Argentina. The COVID-19 under-diagnosis could be due to different factors such as: testing policies, the availability of diagnostic tests and the existence of subclinical or asymptomatic cases. In Buenos Aires City, in isolated patients in outpatient centers, it was determined that out of 110 confirmed cases, 80 were asymptomatic (72.7%) (Boletín Epidemiológico Semanal, 2020). Therefore, regarding the estimated potential cases with MS and COVID-19, some of them may not be aware of SARS-CoV-2 infection.

As the COVID-19 pandemic increases exponentially worldwide, the demand for data on the impact of the virus on MS is rapidly growing. Despite the current effort to identify and follow every MS patient infected with COVID in the Nationwide registry, here we present an important tool to estimate which could be the number of MS patients infected in Argentina.

Founding source

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Declaration of Competing Interest

The authors declares no conflict of interest.

References

- WHO Director-General's opening remarks at the media briefing on COVID-19 - 11, 2020. World health organization. Geneva March 11, 2020. <https://www.who.int/dg/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19-11-march-20>.
- Reporte Diario Vespertino Nro 162. 2020 Situación de COVID-19 en Argentina al 3 de Junio. Ministerio de Salud de la Nación. <https://www.argentina.gob.ar/coronavirus/informe-diario/junio2020>.
- Willis, MD, Robertson, NP., 2020. Multiple sclerosis and the risk of infection: considerations in the threat of the novel coronavirus, COVID-19/SARS-CoV-2. *J. Neurol.* 267, 1567.
- OpenSAFELY Collaborative T, Williamson E, Walker AJ, Bhaskaran K, Bacon S, Bates C, et al. Open safely: factors associated with COVID-19-related hospital death in the linked electronic health records of 17 million adult NHS patients. n.d. <https://doi.org/10.1101/2020.05.06.20092999>.
- Cristiano, E, Patrucco, L, Miguez, J, Giunta, D, Correale, J, Fiol, M, et al., 2016. Increasing prevalence of multiple sclerosis in Buenos Aires. *Argentina. Mult. Scler. Relat. Disord.* 9, 91–94 Sep.
- Bayes, Thomas, 1763. An Essay towards solving a problem in the doctrine of chances. *Philos. Trans. R. Soc. Lond.* 53, 370–418.
- Russel T, Hellewell J, Abbott S, Jarvis CI, van Zandvoort K, Flasche S, et al. Using a delay-adjusted case fatality ratio to estimate under-reporting. *C Repos [Internet]*. 2020 [cited 2020 May 5];1–6. Available from: <https://cmmid.github.io/topics/covid19/current-patterns-transmission/global-time-varying-transmission.html>.
- Boletín Epidemiológico Semanal. Ciudad Autónoma de Buenos Aires. N° 193, Año V / 1 de Mayo de 2020. *Semana Epidemiológica* 16. <https://www.buenosaires.gob.ar/salud/boletines-periodicos/boletines-epidemiologicos-semanales-2018-2019>.

E Cristiano^a, L Patrucco^{b,*}, JI Rojas^c, S Nuñez^d

^a Centro de Esclerosis Múltiple Buenos Aires, Argentina

^b Hospital Italiano Buenos Aires, Argentina

^c Centro de Esclerosis Múltiple, CEMIC, Argentina

^d Infectious Diseases Unit Sanatorio Güemes, Buenos Aires Argentina

E-mail address: lilianapatrucco@gmail.com (L. Patrucco).

* Corresponding author.