Assessment of Guillain-Barre Syndrome Cases in Brazil in the COVID-19 Era

To the Editor:

There has been amounted evidence of the neuroinvasive potential of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The main neurological manifestations reported include dizziness, headache, hypogeusia, hyposmia, muscle damage, ischemic, and hemorrhagic stroke.[1] Guillain-Barre syndrome (GBS) represents the most common cause of acute symmetrical flaccid limb weakness. GBS encompasses a wide range of clinical syndromes with an acute inflammatory polyradiculoneuropathy.[2] GBS is one of the neurological complications that has been found in patients with previous diagnosis of coronavirus disease-2019 (COVID-19).[3]

The possible mechanism that has been associated with GBS in patients with COVID-19 is similar to the pathogenesis involved in typical GBS, consisting of demyelination of peripheral nerve roots. Peripheral nerve damage can be caused by the immune response to SARS-CoV-2, driven by the production of self-reactive antibodies (antiganglioside).[4] It is recognized that viral infections can disrupt immune tolerance by exposing antigen epitopes that induce crossreactive antibodies. There are many reports indicating antigenic mimicry between viral and human proteins that cause autoimmune diseases. As autoimmune diseases are linked to a deregulated immune system, this dysregulation can lead to damage and dysfunction in target organs. Autoimmune and immune-mediated diseases can play a pathogenic role in COVID-19 and some patients have reported the appearance of autoimmune diseases such as GBS and lupus erythematosus after coronavirus infection.[5]

To investigate the impact of the pandemic of COVID-19 in the GBS diagnosis in Brazil, the main goal of this study was compare data from the Brazilian Unified Health System (SUS) on the number of annual GBS cases between the prepandemic period (March 2018 to May 2019) and the pandemic (March 2020 to May 2021), from the 5 Macroregions of Brazil (North, Northeast, Southeast, South, and Midwest), representing the Brazilian States (26 States and the Federal District), through data extracted and analyzed from the public database of SUS (http://tabnet.datasus.gov.br/cgi/tabcgi.exe?sia/cnv/qauf.def).

Table 1 shows the increase in GBS diagnosis in all five Brazilian Macroregions since the pandemic period began, ranging from +27.5% in the North region and +1.6% in the Midwest region. In Brazil the rise reached +15,8% diagnosis of GBS, representing more than 240 cases during COVID-19 pandemic compared with the prepandemic period. Table 2 shows the comparison between the mean incident rates of GBS in the prepandemic and transpandemic periods, across Brazilian geographic macroregions and for the country as a whole. The incident rates of GBS diagnoses significantly increased in the pandemic period throughout Brazil (incidence rate ratio = 1.16, 95% confidence interval: 1.08-1.24, $P < 0.0001$), especially in regions Northeast and Southeast.

The literature also includes reports on the correlation between COVID-19 and GBS.[3] A systematic review analyzed 73 cases of GBS that included only patients who had a laboratory test confirming the COVID-19 infection.[6] The authors revealed that most patients showed respiratory and systemic symptoms, and developed GBS manifestations after COVID-19.[6] Vaccination has been investigated as a possible trigger for GBS.[7] A study carried out in United Kingdom in the first wave of COVID-19, did not show a significant increase on GBS cases and, therefore, no relation between the diseases,[8] which differs from this present data, that shows a significant increase in the

TABLE 1. Difference in the Number of Guillain-Barre Syndrome Cases in All 5 Brazilian Geographical Regions Between the Prepandemic Period (March 2018 to May 2019) and the Pandemic Period (March 2020 to May 2021)

Region	Prepandemic Period	Pandemic Period	Difference	%
North	109	139	+30	+27.5
Northeast	251	319	+68	+27.1
Southeast	614	752	+138	+22.5
South	410	419	+9	+2.2
Midwest	183	186	+3	+1.6
Total	1567	1815	+248	+15.8

TABLE 2. Incident Cases of Guillain-Barre Syndrome Cases Per Million Population in Brazilian Macroregions According to the Periods Prepandemic and Pandemic Periods

Regions of Brazil	COVID-19 Cases Per Million Pop	2017-2019 GBS Incidence Rate (95%CI)	2020-2021 GBS Incidence Rate (95%CI)	Incidence Ratio (95%CI)	*P**
North	100,618	6.2 (5.0-7.4)	7.8 (6.6-9.2)	1.27 (0.98-1.65)	0.057
Northeast	84,509	4.4 (3.8-4.9)	5.6 (5.0-6.2)	1.26 (1.07-1.50)	0.0044
Southeast	95,790	7.1 (6.6-7.5)	8.7 (8.1-9.3)	1.22 (1.09-1.36)	0.0002
South	139,995	13.9 (12.6-23)	14.2 (12.9-15.7)	1.02 (0.88-1.17)	0.754
Midwest	141,915	11.7 (10.0-13.5)	11.9 (10.2-13.7)	1.01 (0.82-1.25)	0.875
Total	103,032	7.0 (6.9-7.6)	8.4 (8.0-8.7)	1.16 (1.08-1.24)	< 0.001

*P-value obtained by χ^2statistic.
CI indicates confidence interval; COVID-19, coronavirus disease-2019; GBS, Guillain-Barre syndrome; Pop, population.

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number of GBS cases during the COVID-19 pandemic.

A recent study reported the time to onset of GBS symptoms in patients with COVID-19 was 5 to 10 days, similar interval observed when GBS occurs during or after other infections.[9] In contrast, cerebrospinal fluid protein levels appear higher in COVID-19 patients.[10] The treatment given for these cases used immunoglobulin IV or plasmapheresis, supportive care, and antiviral drugs.[4]

The pandemic period has significantly increased the number of GBS diagnoses in Brazil, and measures to raise the control of this disease must be carried out. In addition, physicians and patients who have already undergone COVID-19 should be aware of this this possible relation between COVID-19 and GBS increased cases.

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