# LETTER TO THE EDITOR

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# SARS-CoV-2-Associated Guillain-Barre Syndrome is Common but Underrecognised and Underreported

## Sir,

We read with interest the valuable paper by Hanif and coworkers about a 32-year-old *SARS-CoV-2*-positive female, who developed lower limb weakness with reduced tendon reflexes but without any sensory disturbances for 16 days after a positive PCR test for *SARS-CoV-2*.<sup>1</sup> As work-up for Guillain-Barre syndrome (GBS) revealed demyelinating sensori-motor neuropathy and albuminocytologic dissociation in the cerebro-spinal fluid (CSF), the patient was diagnosed with acute inflammatory demyelinating polyneuropathy (AIDP) and underwent plasmapheresis with a beneficial effect.<sup>1</sup> The study is attractive but has some shortcomings.

We disagree with the message that only a few cases with SARS-CoV-2-associated GBS (SAG) had been published so far. By the end of December 2020, at least 220 SAG cases have been published.<sup>2</sup> By the end of June 2021, the number of published SAG cases increased to at least 300 [Finsterer, submitted]. Among these 300 SAG patients, age ranged from 7 to 94 years. The male-to-female ratio was 2.18:1. The period between onset of COVID-19 and the onset of SAG ranged between 10 to 90 days. CSF contained SARS-CoV-2 RNA only in one case. GBS subtypes included patients with AIDP (n=171), acute, motor axonal neuropathy (n=24), acute, motor and sensory axonal neuropathy (n=16), Miller-Fisher syndrome (n=8), poly-/mono-neuritis cranialis (n=3), and the pharyngo-cervico-brachialvariant(n=1).Treatmentincluded intravenous immunoglobulins (IVIGs, n=241), plasmapheresis (n=28), and steroids (n=7). Artificial ventilation was required in 59 patients. Complete recovery was achieved in 42 patients, partial recovery in 163 patients, and 17 patients died.

Missing is the information whether the CSF tested positive or negative for *SARS-CoV-2* RNA. As only two cases were positive for virus RNA in the CSF so far, and only one case for neutralising antibodies,<sup>3</sup> and as SAG is an immunological and not an infectious polyradiculitis, one would expect that the CSF in the index patient was negative for *SARS-CoV-2* as well.

Also, missing is the discussion about GBS due to SARS-CoV-2 vaccinations. Since the introduction of SARS-CoV-2 vaccinations in December 2020, at least 19 patients with post-vaccination GBS had been reported until the end of June 2021.<sup>4</sup> These patients were 20 to 86 years old and male-to-female

ratio was 0.9:1. Post-vaccination GBS developed in all the patients after the first jab. Fourteen patients received AstraZeneca vaccine, four received the Pfizer vaccine, and one patient received the Johnson vaccine. The time from vaccination to onset of GBS amounted to 3-39 days. The patients received IVIGs (n=13), steroids (n=3), or no therapy (n=3). Mechanical ventilation was indicated in 6 patients. The outcome was poor despite immediate adequate treatment.

In conclusion, SAG is not a rare condition and most likely under-recognised and under-reported. Not only the virus triggers SAG but also *SARS-CoV-2* vaccinations. SAG responds favourably to immediate treatment with IVIGs, plasmapheresis, or steroids. The most effective approach appears to be the zipper concept,<sup>5</sup> which relies on the alternate application of IVIGs and plasmapheresis.

## **COMPETING INTEREST:**

The authors declared no competing interest.

## **AUTHORS' CONTRIBUTION:**

JF: Design, literature search, discussion, first draft, and critical comments.

SZ: Literature search, discussion, and critical comments.

All the authors have approved the final version of the manuscript to be published.

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#### **AUTHOR'S REPLY**

Sir,

Thank you for your interest and comment on our article published in the Journal of College of Physicians and Surgeons of Pakistan (JCPSP).<sup>1</sup> At the time of the COVID-19 pandemic, the observations were changing consistently which was making the information obsolete in a short time. The author showed disagreement with rare and under-recognised nature of SAG. COVID-19-induced GBS has indeed been reported several times up till now, but at the time of submission [September 2020], only a few cases had been published. Furthermore, the author elicited the lack of information on the CSF status for SARS-CoV-2 RNA. SARS-CoV-2 was not tested in CSF as this virus has rarely been found in CSF. A study by Miller et al on SARS-CoV-2 in CSF reported that all samples tested for SARS-CoV-2 were negative despite abnormal CSF reports.<sup>2</sup> Similarly, another study in encephalopathic COVID-19 patients did not show SARS-CoV-2.3 Likewise, the author reported that the case lacked information on GBS due to *SARS-CoV-2* vaccination. The author mentioned that the COVID-19 vaccine was introduced in December 2020, although we reported this case a few months before in September 2020, so the world was waiting for the vaccine at that time.

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