**Guillain-Barre syndrome due to SARS-CoV-2**

**Abstract:**

Keywords: SARS-CoV-2, COVID-19, Guillain-Barre syndrome, nerve conduction, immunoglobulins.

**Letter to the Editor**

With interest we read the article by Sriwastava et al., (2020) about a systematic review following the PRISMA guidelines about patients with polyradiculitis (polyradiculoneuritis, Guillain-Barre syndrome (GBS)) with/without cranial nerve involvement in association with a SARS-CoV-2 infection (COVID-19) (SC2-GBS) (Sriwastava, S. et al., 2020). Among 50 patients with SC2-GBS collected until July 2020, 33 had acute, inflammatory, demyelinating polyneuropathy (AIDP), and the remainder acute, motor axonal neuropathy (AMAN), acute, motor and sensory axonal neuropathy (AMSAN), Miller-Fisher syndrome (MFS), Bickerstaff encephalitis (BFE), or polyneuritis cranialis (PNC) (Sriwastava, S. et al., 2020). It was recommended to carry out long-term follow-up investigations to assess the outcome of these patients (Sriwastava, S. et al., 2020). We have the following comments and concerns.

We do not agree that only 50 patients with SARS-CoV-2 associated GBS have been reported in the first half of 2020. In addition to the 50 patients included in the review, at least 18 other patients were published during this period. These additional patients were reported by “Ghosh et al.,” “Juliao-Caamano et al.,” “Marta-Enguita et al.,” “Galan et al.”, “Oguz-Akarsu et al.,” “Esteban Molina et al.,” “Farzi et al.,” “Paybast et al.,” “Khaliifa et al.,” “Frank et al.,” “Manganotti et al.,” “Wada et al.,” “Garcia-Manzanedo et al.,” and “Naddaf et al.”. By the end of December 2020, >200 SC2-GBS cases have been reported [Finsterer, in preparation].

Though there is evidence that SARS-CoV-2 can trigger GBS, there are conflicting results concerning a suspected increase of the prevalence of GBS since onset of the pandemic. In a study of 47 SC2-GBS patients from the UK, the prevalence of GBS did not increase between March and May 2020 as compared to the years 2016-2019 (Keddie, S. et al., 2020). However, in a retrospective, multicenter study from northern Italy of 34 SC2-GBS patients, the estimated incidence of GBS during March and April 2020 increased from 0.93/100000/y in 2019 to 2.43/100000/y in 2020 (Filosto, M. et al., 2020).

A further limitation refers to the discrepancy between the method and results section. In the method section it is stated that only patients with PCR-confirmed COVID-19 were included (Sriwastava, S. et al., 2020). However, in the results section and in table 2 it is mentioned that 3 AIDP patients and 3 non-AIDP patients were negative by PCR. The discrepancy should be explained. According to the inclusion criteria, these six patients should have been excluded. Furthermore, it is unclear why age ≤18y was an exclusion criterion. GBS in pediatric patients is not at variance from GBS in adults.
Two thirds of the patients required artificial ventilation (Sriwastava, S. et al., 2020). It should be discussed if respiratory insufficiency in these patients was due to involvement of the respiratory muscles in GBS, due to brainstem encephalitis, due to viral pneumonia with acute, respiratory distress syndrome (ARDS), or due to a mixture of the three.

Missing is the treatment patients received for COVID-19. Since some of the drugs applied are potentially neurotoxic (e.g. lopinavir, tocilizumab, chloroquine) (Khanlou, H. et al., 2007; Sugiuira, F. et al., 2009; & Becerra Cuñat, JL et al., 2003), it is crucial to know if any of these compounds were given.

GBS has to be delineated from critical illness neuropathy, from toxic neuropathy, and from any pre-existing neuropathy. We should know if these differentials were excluded in all 50 cases.

In a recent review about 62 patients with SC2-GBS, four patients developed GBS prior to clinical manifestations of COVID-19 (Finsterer, J. et al., 2021). These patients were reported by “Zhao et al.”, “Coen et al.”, and “Chao et al.”. Why were these patients classified as GBS developing after onset of COVID-19 in the present review? SC2-GBS prior to onset of non-neurological manifestations of COVID-19 has been also reported by others (Gale, A. et al., 2020) and is explained by subclinical infection with the virus prior to onset of GBS or the incubation time of SARS-CoV-2, which is up to 14 days (Filosto, M. et al., 2020).

Not discussed in the review were cases in which GBS developed during artificial ventilation on an ICU. Diagnosing GBS during artificial ventilation is challenging (Filosto, M. et al., 2020) but if the neurological exam indicates neuropathy and if patients cannot be weaned successfully from the respirator, GBS should be considered. Early diagnosis of GBS is crucial as the outcome improves with early application of appropriate treatment (Dubey, D. et al., 2016).

We do not agree with the statement that ischemic stroke is among the most frequent manifestations of COVID-19. SARS-CoV-2 associated ischemic stroke is rare and the prevalence of ischemic stroke apparently did not increase since onset of the pandemic (Requena, M. et al., 2020).

In table 1 of the review a paper by “Solomon et al.” is cited as reference 28, which cannot be found in the reference list. There is also no hit for this paper on a PubMed search. When searching the paper by “Ebrahimzadeh et al.”, no entry could be found. The paper by “Mozhdehpanah et al.” cited in table 1, is not accessible either. The reference “Augustina et al.”, listed in table 1, could neither be found in the reference list nor by a PubMed search. However, the paper indexed as reference 45 is erroneously mentioned in table 1 by the given name instead of the surname.

According to the flow-chart of figure 1 of the review, 37 studies were included in the discussion (Sriwastava, S. et al., 2020). However, in the first paragraph of the discussion, 39 studies are mentioned. This inconsistency should be solved.

Overall, SARS-CoV-2 triggers the development of GBS but cannot be found in the CSF. SC2-GBS occurs in each age group and is not at variance with regard to clinical presentation and treatment compared to non-COVID-19 GBS. Outcome of SC2-GBS, however, appears to be worse compared to non-CS2-GBS. Whether the prevalence/incidence of GBS increased since outbreak of the pandemic is under debate but an increasing number of SC2-GBS cases are reported. Alertness for SC2-GBS in non-symptomatic, symptomatic, and ventilated COVID-19 patients is warranted.

REFERENCES

