Review articles

SARS-CoV-2 vaccinations reduce the prevalence of post-COVID Guillain-Barre syndrome

Josef Finsterer a,*, Daniel Matovu b, Fulvio A. Scorzab

a Neurology & Neurophysiology Center, Vienna, Austria
b Disciplina de Neurociência, Universidade Federal de São Paulo/Escola Paulista de Medicina (UNIFESP/EPM), São Paulo, SP, Brasil

HIGHLIGHTS

- SARS-CoV-2 infections can be complicated by Guillain-Barre Syndrome (GBS).
- The prevalence of SARS-CoV-2 associated GBS declined since the introduction of SARS-CoV-2 vaccines.
- The outcome of SARS-CoV-2 associated GBS is worse among those with comorbidities compared to those without.

ARTICLE INFO

Keywords:
SARS-CoV-2
COVID-19
Neuro-COVID Complications
Polyradiculitis
Vaccination

ABSTRACT

Guillain-Barre Syndrome (GBS) has been repeatedly reported as a neurological complication of COVID-19 (post-COVID GBS [PCG]). Whether the introduction of SARS-CoV-2 vaccines reduced the prevalence of PCG is unknown. This narrative review aimed to compare the number of published PCG cases between the second half of 2020 (no vaccination available) with those of the first half of 2021 (vaccination available). A total of 124 articles reported 300 patients with PCG between January 2020 and June 2021. The ages ranged from 7 to 94y. There was male dominance. The latency between the onset of COVID-19 and the onset of PCG ranged from -10 to 90d. Acute, inflammatory, demyelinating polyneuropathy was diagnosed in 171 patients, acute, motor axonal neuropathy in 24, and acute, motor, and sensory axonal neuropathy in 16 patients. Regarding treatment, 241 patients received immunoglobulins, 28 patients’ plasmaphereses, and 7 patients’ steroids. Artificial ventilation was required in 59 patients. Full recovery was achieved in 42 cases, partial recovery in 163 cases, and 17 patients died. The number of published PCG patients fell from 192 in the second half of 2020 to 75 patients in the first half of 2021. It is concluded that the prevalence of PCG has decreased since the introduction of SARS-CoV-2 vaccines. SARS-CoV-2 vaccinations have a positive effect on the prevalence of PCG.

Introduction

Guillain-Barré Syndrome (GBS) is an increasingly perceived complication of SARS-CoV-2 (COVID-19) infections.1 In the first half of 2020, only a few patients with SARS-CoV-2 associated GBS (post-COVID GBS [PCG]) were published.1−9 In the second half of 2020 the number of published PCG patients increased significantly. Since December 2020 several brands of SARS-CoV-2 vaccinations have been launched. It is unknown whether the frequency of PCG has decreased since the introduction of these anti-SARS-CoV-2 vaccines. Therefore, the present narrative, up-to-date review aimed to compare the number, demographics, clinical presentation, therapeutic management, and outcome of PCG in the 6 months before and after vaccine availability (July to December 2020 compared with January 2021 to June 2021) and to answer the question of whether SARS-CoV-2 vaccinations reduce the prevalence of PCG.

Methods

A literature search in the databases PubMed and Google Scholar using the search terms “neuropathy”, “Guillain Barre syndrome”, “polyradiculitis”, “AIDP”, “AMAN”, “AMSAN”, “Miller-Fisher syndrome”, “polyneuritis cranialis”, “cranial nerve”, and “Bickerstaff encephalitis”, in combination with “SARS-CoV-2”, “COVID-19”, and “coronavirus” was conducted. Additionally, reference lists were checked for further articles meeting the search criteria. Included were only

Abbreviations: AIDP, Acute, Inflammatory, Demyelinating Polyneuropathy; AMAN, Acute, Motor Axonal Neuropathy; AMSAN, Acute, Motor and Sensory Axonal Neuropathy; BSE, Bickerstaff encephalitis; CSF, Cerebro-spinal fluid; GBS, Guillaumpe Barre syndrome; IVIG, Intravenous Immunoglobulins; PCB, Pharyngeal, Cervical and Brachial variant; PCG, Post COVID-19 GBS; PNC/MNC, Poly- or Mono-Neuritis Cranialis

*Corresponding author.
E-mail address: fifi1gs1@yahoo.de (J. Finsterer).

https://doi.org/10.1016/j.clinsp.2022.100064
Received 4 January 2022; Revised 8 April 2022; Accepted 30 May 2022

1807-5932/© 2022 Published by Elsevier España, S.L.U. on behalf of HCFMUSP. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/)
original articles detailing individual patients’ data (age, sex, latency between onset of COVID-19 and onset of GBS, GBS subtype, results of CSF investigations, comorbidities, treatment, and outcome) published between January 2020 and June 2021. Excluded from data analysis were reviews, abstracts, proceedings, and editorials. Cohort studies that did not provide sufficient individual data were also excluded.

Results

By the end of June 2021, a total of 124 articles were found that met the inclusion criteria and described individual patients with PCG (Fig. 1). The first patient with PCG was reported by Zhao et al. in May 2020.10,11 By the end of June 2020, 33 patients with PCG were published (Table 1). From July to December 2020, 192 PCG patients were published (Table 2). From January 2021 to the end of June 2021, a further 75 PCG patients were published (Table 3). The 124 articles published from early January 2020 to late June 2021 reported 300 patients with PCG (Table 4). Relevant data on age, gender, onset before/after COVID-19, latency between COVID-19 and onset of PCG, the subtype of GBS, PCR result in the Cerebrospinal Fluid (CSF), therapy, and outcome are presented in Table 4. The ages of these patients, available from 295 patients, ranged from 7 to 94y. The sex was male in 201 cases and female in 92 cases. The onset of PCG, available in 243 cases, was identified in 233/3/7 patients after/along/before the onset of COVID-19. The latency between the onset of COVID-19 and the onset of PCG ranged from −10 and 90 days. The GBS subtype, reported in 233 cases, was identified as Acute, Inflammatory, Demyelinating Polynromyopathy (AIDP) in 171 patients, as Acute, Motor Axonal Neuropathy (AMAN) in 24, as Acute, Motor and Sensory Axonal Neuropathy (AMSAN) in 16, as Miller-Fisher Syndrome (MFS) in 8 patients, as Poly- or Mono-Neuritis Cranialis (PNC/MNC) in 3, and as Pharyngeal, Cervical, and Brachial (PCB) variant in 1 patient. Bickerstaff Encephalitis (BFE) was not reported in any case. SARS-CoV-2 was only detected in the CSF of a single patient. Therapy of PCG, available in 270 cases, included Intravenous Immunoglobulins (IVIG) in 241 patients, plasmapheresis in 28, steroids in 7, and no therapy in 8 cases. Artificial ventilation was required for 59 patients. The outcome, available from 222 cases, was rated as full recovery (n = 42), a partial recovery (n = 163), or death (n = 17). Comparing patients with and without comorbidities, the incidence of a fatal outcome was higher in those with comorbidities than in those without. Among those with comorbidities, 8 died and among those, without comorbidities, only 5 died. The comparison of the patients published in the second half of 2020 with the patients published in the first half of 2021 showed that the number of publications and thus the number of patients had fallen from 192 to 75 patients in the first half of 2021 (Table 4).

Discussion

The review shows that PCG can be a complication of COVID-19 and suggests that SARS-CoV-2 vaccinations reduce the prevalence of PCG. Whether the prevalence of PCG has really increased since the outbreak of the pandemic is still a matter of debate. Some studies report an increase in the prevalence, others a decrease.12,13 There are also studies that report no change in GBS prevalence since the outbreak of the pandemic.14 Because CSF is devoid of viral RNA in almost all cases and because cytokines are elevated in the CSF in PCG patients,15 an abnormal immune response rather than an infectious cause is the most likely pathophysiology underlying the development of PCG. Because PCG recovery is incomplete at discharge in most cases, PCG has to be classified as a serious complication of COVID-19. The surprising finding that the number of reported PCG patients was lower in the first half of 2021 compared to the second half of 2020 can be asserted by several explanations. First, scientists are no longer interested in the topic as evidence accumulates that PCG is an established

Fig. 1. flowchart of the selection process upon which papers were included or excluded.
Table 1

Patients with PCG as reported by the end of June 2020.

| Age (y) | Sex | Onset | LOO (d) | Subtype | CIC | CM | Therapy | AV | Outcome | Country | Reference |
|---------|-----|-------|---------|---------|-----|----|---------|----|---------|----------|-----------|
| 54      | m   | 8     | AIDP    | nr      | No   | IG | Yes     | Complete USA | Virani 4/20 |
| 71      | m   | 4     | AIDP    | No      | AHT, AAR, LC | IG | Yes     | Death Italy | Alberti 4/20 |
| 46      | m   | A18   | AIDP    | nr      | nr   | No | No      | Partial Iran | Ebrahimzadeh 4/21 |
| 65      | m   | A10   | AIDP    | nr      | nr   | IG | No      | Partial Iran | Ebrahimzadeh 4/21 |
| 61      | f   | B9    | AIDP    | nr      | No   | IG | No      | Complete China | Zha 5/20 |
| 61      | m   | A10   | MFS     | No      | No   | S  | No      | Complete Spain | Julia Caamano 5/20 |
| 76      | f   | A8    | GBS*    | nd      | No   | No | nr      | Death Spain | Marta-Enquita 5/20 |
| 43      | m   | 21    | AIDP    | No      | nr   | IG | No      | Complete France | Biguet 5/20 |
| 71      | f   | A10   | AIDP    | No      | nr   | IG | No      | Partial France | Biguet 5/20 |
| 55      | f   | A14   | AIDP    | nr      | No   | IG | Yes     | Partial Spain | Esteban Molina 5/20 |
| 61      | f   | A7    | AMAN    | No      | nr   | IG | No      | Partial USA | Valiuddin 5/20 |
| 46      | m   | A10   | AIDP    | nr      | nr   | IG | No      | Partial Spain | Velayos Galan 5/20 |
| 58      | m   | AB    | 0       | AIDP    | No   | No | IG      | No Partial Canada | Chan 5/20 |
| 68      | m   | A13   | nr      | nr      | nr   | PE | IG      | Yes Partial USA | Chan 5/20 |
| 84      | m   | 23    | nr      | nr      | nr   | PE | IG      | Partial USA    | Sedaghat 5/20 |
| 65      | m   | 9     | AMSAN   | nd      | DM   | IG | No      | nr Iran | Sedaghat 6/20 |
| 66      | f   | 7     | AIDP    | No      | nr   | IG | Yes     | Complete Italy | Ottaviani 6/20 |
| 54      | f   | 21    | AIDP    | nd      | No   | IG | No      | Complete Germany | Scheid 6/20 |
| 70      | f   | A3    | AMSAN   | No      | RA   | IG | No      | Partial Morocco | El Otmani 6/20 |
| 64      | m   | A11   | AIDP    | nd      | No   | IG | Yes     | nr France | Camdessanche 6/20 |
| 58      | m   | 14    | AIDP    | No      | nr   | IG | No      | Partial USA | Zha 6/20 |
| 54      | m   | A14   | AIDP    | Nd      | nr   | IG | No      | Partial USA | Rana 6/20 |
| 53      | f   | Bnr   | AIDP    | No      | nr   | IG | No      | Partial Turkey | Oguz-Akarso 6/20 |
| 51      | f   | A14   | MFS     | nr      | IG | No      | Partial Spain | Reyes-Bueno 6/20 |
| 68      | m   | A14   | AIDP    | mkf     | IG | PE | Yes     | Partial Austria | Helbok 6/20 |
| 53      | m   | A24   | AIDP    | No      | Nr   | IG | No      | Partial Netherlands | Kollin 6/20 |
| 57      | m   | 6     | AIDP    | No      | AHT, psoriasis | IG | Yes     | Partial UK | Webb 6/20 |
| 21      | m   | 16    | AIDP    | nr      | AHT, DM | PE | No      | Partial USA | Hutchins 6/20 |
| 41      | m   | 10    | AIDP    | nr      | DM   | IG | No      | Partial Iran | Fariz 6/20 |

A, Onset of GBS after onset of non-neurological manifestations, AAR, Aortic Aneurysm Repair, AHT, Arterial Hypertension; AL, Alcoholism; AV, Artificial Ventilation; B, Onset of GBS before onset of non-neurological manifestations; CA, Carcinoma; CHD, Coronary Heart Disease; CIC, CoV2 in CSF; CM, Comorbidities, COPD, Chronic Obstructive Pulmonary Disease; DM, Diabetes; f, female; GBS*, no NCSs reported; HLP, Hyperlpidemia; IG, Immunoglobulins; LC, Lung Cancer; LOO, Latency between onset of GBS and COVID-19 respectively vice versa; m, male; nd, not done; nr, not reported, NTX, Renal Transplantation; pc, personal communication; PCB, Pharyngeal, Cervical, Brachial variant of GBS; PE, Plasma Exchange; PNC, Polyneuritis Cranialis; RA, Rheumatoid Arthritis; RI, Renal Insufficiency; RSD, Reflex Sympathetic Dystrophy; S, Steroids, & antibodies positive in CSF.

Table 2

Patients with PCG as reported from July to December 2020.

| Age (y) | Sex | Onset | LOO (d) | Subtype | CIC | CM | Therapy | AV | Outcome | Country | Reference |
|---------|-----|-------|---------|---------|-----|----|---------|----|---------|----------|-----------|
| 56      | f   | A15   | AIDP    | No      | Nr   | IG | Yes     | Partial Spain | Sancho-Saldana 7/20 |
| 70      | f   | A23   | AIDP    | nd      | No   | IG | Yes     | Nr Italy | Padroni 7/20 |
| 75      | m   | B10   | AIDP    | No      | No   | IG | No      | Complete Swiss | Coen 7/20 |
| 64      | m   | A23   | AIDP    | No      | No   | IG | No      | Complete France | Arnaud 7/20 |
| 36      | m   | A4    | MFS     | nr      | Nr   | IG | No      | Complete USA | Lantos 7/20 |
| 55      | m   | A20   | AIDP    | No      | Nr   | IG | Yes     | Partial Italy | Assini 7/20 |
| 60      | m   | A3    | AMSAN   | No      | Nr   | IG | Yes     | Partial Italy | Assini 7/20 |
| 58      | m   | A16   | AIDP    | nr      | AHT | PE | No      | Complete Iran | Payback 7/20 |
| 14      | f   | Anr   | nr      | nr      | No   | IG | No      | Complete Iran | Payback 7/20 |
| 49      | m   | A14   | AIDP    | No      | No   | IG | No      | Complete UK | Tiet 7/20 |
| 68      | m   | A5    | AIDP    | nr      | AHT, HLP | IG | No      | Complete Italy | Agosti 7/20 |
| 11      | m   | A21   | AIDP    | nr      | No   | IG | No      | Complete Saudi | [Khaila 7/20] |
| 65      | m   | Anr   | AMAN    | No      | No   | IG | No      | Partial Brazil | Frank 7/20 |
| 72      | m   | A18   | AIDP    | No      | Nr   | IG | Yes     | Partial Italy | Manganothi 7/20 |
| 72      | m   | A30   | AIDP    | No      | Nr   | IG | Yes     | Partial Italy | Manganothi 7/20 |
| 49      | f   | A14   | AIDP    | No      | Nr   | IG | No      | Partial Italy | Manganothi 7/20 |
| 94      | m   | A33   | AIDP    | nr      | Nr   | S  | No      | Partial Italy | Manganothi 7/20 |
| 76      | m   | A22   | AIDP    | No      | Nr   | IG | Yes     | Partial Italy | Manganothi 7/20 |
| 64      | m   | Anr   | nr      | nr      | DM   | IG | Yes     | Complete Japan | Wada 7/20 |
| 77      | m   | Anr   | AIDP    | nr      | AHT, HLP | IG | no      | Complete Spain | Garcia-Manzano 7/20 |
| 75      | m   | nr    | nr      | No      | Spinal trauma | IG | no      | Complete USA | Elkhousy 7/20 |
| 37      | nr   | 10    | nr      | nr      | nr   | nr   | nr      | Belgium | Guilmot 7/20 |
| 51      | m   | A12   | AIDP    | No      | No   | IG | Yes     | Partial Germany | Pfeiferkon 7/20 |
| 65      | m   | 3     | AIDP    | nr      | No   | IG | No      | Complete Germany | Lamp 7/20 |
| 12      | m   | 7     | AIDP    | nr      | Nr   | IG | Yes     | Death Tanzania | Manji 7/20 |
| 66      | f   | A30   | AIDP    | nr      | DM, AHT, arthritis | IG | No      | Partial Iran | Mozhadehipanah 7/20 |
| 55      | f   | A31   | AMSAN   | No      | COPD | IG | Yes     | Death Iran | Mozhadehipanah 7/20 |
| 70      | m   | A15   | AMAN    | nr      | Nr   | IG | No      | Partial Spain | Guijarro-Castro 7/20 |

(continued)
Table 2 (Continued)

| Age (y) | Sex | Onset | LOO (d) | Subtype | CIC | CM | Therapy | AV | Outcome | Country | Reference |
|---------|-----|-------|---------|---------|-----|----|---------|----|---------|---------|-----------|
| 34      | m   | A     | 4       | PNC     | nr   | AIDP | IG      | No | Partial | USA     | Dinkin 8/20 |
| 71      | f   | A     | Days    | PNC     | nr   | AIDP | no      | No | Partial | USA     | Dinkin 8/20 |
| 58      | f   | A     | 6       | AIDP    | No   | No   | PE      | No | Complete | USA     | Nadaf 8/20  |
| 56      | f   | A     | 7       | AIDP    | No   | AHT, thyroxin ↓ | nr | No     | Partial | Germany | Pelea 8/20  |
| 61      | f   | A     | 7       | AMAN    | No   | AHT, DM, HLP, CA | S, PE | No     | No       | USA | Maideniuc 8/20 |
| 50      | m   | A     | 3       | MFS, PNC| No   | No   | IG      | No | Complete | Spain   | Gutierrez-Oritz 8/20 |
| 39      | m   | A     | 3       | MFS, PNC| No   | No   | No      | No | No       | Spain   | Gutierrez-Oritz 8/20 |
| 47      | m   | A     | 10      | AIDP    | No   | Nr   | IG      | No | Complete | Greece 8/20 |
| 70      | f   | A     | 90      | nr      | nr   | RSD  | IG      | No | Complete | USA     | Defabio 8/20 |
| 57      | m   | A     | 17      | AIDP    | No   | Nr   | IG      | no | Partial | Italy   | Zito 8/20   |
| 63      | m   | A     | 1       | MFS     | nr   | No   | no      | No | No       | USA     | Su 8/20   |
| 65      | m   | A     | 5       | AIDP    | nr   | DM, AHT| IG  | Yes     | Death   | Sudan | Sidig 8/20 |
| 62      | m   | A     | 12      | m      | COPD, sleep apnea | IG | Yes     | Partial | UK | Jones 8/20  |
| 65      | m   | A     | 17      | AIDP    | No   | No   | IG      | No | Complete | Italy   | Riva 9/20  |
| 52      | f   | A     | 15      | AIDP    | No   | Nr   | IG      | No | Partial | USA     | Swiss | Luciano 9/20 |
| 63      | f   | A     | 7       | AIDP    | nr   | nr   | IG      | No | No       | Complete | Spain | Luciano 9/20 |
| 61      | f   | A     | 22      | AIDP    | No   | nr   | IG      | No | No       | Switzerland 9/20 |
| 74      | f   | A     | nr      | AIDP    | No   | Lymphoma | IG  | No     | Partial | Spain | Fernandez-Domingo 9/20 |
| 53     | 1m  | A   | 0.5–28  | AIDP    | No  | n = 4 | nr | IG, n = 15 | nr | Partial, Italy, n = 17 | Foresti 9/20 |

A, Onset of GBS after onset of non-neurological manifestations; AAR, Aortic Aneurysm Repair; AHT, arterial hypertension; AL, Alcoholism; AV, Artificial Ventilation; B, Onset of GBS before onset of non-neurological manifestations; CA, Carcinoma; CHD, Coronary Heart Disease; CIC, CoV2 in CSF; CM, Comorbidities; COPD, Chronic Obstructive Pulmonary Disease; DM, Diabetes; f, female; GBS*, No NCSs reported; HLP, Hyperlipidemia; IG, Immunoglobulins; LC, Lung Cancer; LOO, Latency between Onset of GBS and COVID-19 respectively vice versa; m, male; nd, not done; nr, not reported, NTX, Renal Transplantation; pc, personal communication; PCB, Pharyngeal, Cervical, Brachial variant of GBS; PE, Plasma Exchange; PNC, Polyneuritis Cranialis; RA, Rheumatoid Arthritis; RI, Renal Insufficiency; RSD, Reflex Sympathetic Dystrophy; S, Steroids, ↓ antibodies positive in CSF.

A, Onset of GBS after onset of non-neurological manifestations; AAR, Aortic Aneurysm Repair; AHT, arterial hypertension; AL, Alcoholism; AV, Artificial Ventilation; B, Onset of GBS before onset of non-neurological manifestations; CA, Carcinoma; CHD, Coronary Heart Disease; CIC, CoV2 in CSF; CM, Comorbidities; COPD, Chronic Obstructive Pulmonary Disease; DM, Diabetes; f, female; GBS*, No NCSs reported; HLP, Hyperlipidemia; IG, Immunoglobulins; LC, Lung Cancer; LOO, Latency between Onset of GBS and COVID-19 respectively vice versa; m, male; nd, not done; nr, not reported, NTX, Renal Transplantation; pc, personal communication; PCB, Pharyngeal, Cervical, Brachial variant of GBS; PE, Plasma Exchange; PNC, Polyneuritis Cranialis; RA, Rheumatoid Arthritis; RI, Renal Insufficiency; RSD, Reflex Sympathetic Dystrophy; S, Steroids, ↓ antibodies positive in CSF.
Table 3
Patients with PCG reported from 1.1.2021 to 30.6.2021.

| Age (y) | Sex | Onset | LOO (d) | Subtype | CIC | CM | Therapy | AV | Outcome | Country | Reference |
|---------|-----|-------|---------|---------|-----|----|---------|----|---------|---------|-----------|
| 72      | m   | A     | 12      | nr      | nr   | No | IG      | No | Partial | Morocco | Mansour 1/21 |
| 36      | f   | A     | 42      | nr      | nr   | nr | No      | IG | No      | Complete | Morocco 1/21 |
| 62      | m   | A     | 20      | nr      | nr   | No | IG      | Yes | Partial | Italy   | Colonna 1/21 |
| 46      | m   | A     | 53      | nr      | nr   | nr | No      | IG | No      | UK      | Raahimi 1/21 |
| 55      | f   | A     | nr      | nr      | nr   | nr | AHT     | IG, | S      | nr      | Death     | Goel 2/21 |
| 17      | m   | A     | nr      | nr      | nr   | No | IG      | S, | nr      | Death    | Morocco   | Goel 2/21 |
| 35      | m   | A     | 16      | nr      | nr   | nr | No      | IG | No      | Complete | USA       | Yakobov 3/21 |
| 36      | f   | A     | 18      | nr      | nr   | nr | Obesity | IG | No      | Partial | USA       | Dufour 3/21 |
| 39      | f   | A     | 14      | nr      | nr   | nr | AIDP    | PE | No      | Partial | Colombia  | MacKenzie 3/21 |
| 53      | m   | A     | 9       | AMAN    | nr   | nr | PE      | No | Partial | USA     | Brown 3/21 |
| 45      | m   | A     | nr      | nr      | nr   | nr | No      | IG, | S      | nr      | Death     | India 2/21 |
| 53-65 (15) | 13m | A   | 18      | nr      | nr   | nr | No      | IG | Yes     | Partial | Italy     | Avenali 3/21 |
| 72      | f   | A     | 12      | nr      | nr   | nr | nr      | IG | No      | Complete | USA       | Yakobov 3/21 |
| 57      | m   | A     | 12      | AIDP    | nr   | nr | IG      | No | Partial | Italy   | Avenali 3/21 |
| 35-81   | 17m | A   | 28.5    | AIDP    | nr    | nr | nr      | IG | No      | Italy    | Uncini 3/21 |
| 5       | m   | A     | 28      | AMAN    | nr   | nr | IG      | No | Partial | Chile   | Sandovall 3/21 |
| 71      | f   | A     | 8       | nr      | nr   | nr | AIDP    | IG | Yes     | Partial | Belgium  | Paradise 4/21 |
| 52      | f   | A     | nr      | nr      | nr   | nr | AIDP    | IG | Yes     | Partial | Switzerland | Epiney 4/21 |
| 70      | m   | A     | nr      | AMAN    | nr   | nr | nr      | IG | No      | Partial | Switzerland | Epiney 4/21 |
| 34      | f   | A     | 9       | AMANS   | nr   | nr | IG      | No | Partial | Turkey   | Tekin 4/21 |
| 70      | m   | nr    | nr      | nr      | nr   | nr | nr      | IG | Yes     | Partial | Iran      | Nejad 5/21 |
| 22      | f   | A     | 7       | AIDP    | nr    | nr | nr      | IG | No      | Partial | Philippines | Garcia 5/21 |
| 7       | m   | B     | 12      | AMAN    | nr    | nr | IG      | No | Partial | India   | Das 5/21   |
| 27      | m   | A     | 5       | AMAN    | nr    | nr | IG      | No | Complete | India   | Khan 6/21  |
| 35      | f   | A     | 9       | AIDP    | nr    | nr | nr      | IG | No      | Complete | India     | Khan 6/21  |
| 40      | f   | A     | 20      | AIDP    | nr    | nr | nr      | IG | No      | Complete | India     | Khan 6/21  |
| 50      | m   | A     | 2       | AMANS   | nr    | nr | nr      | IG | No      | Complete | India     | Khan 6/21  |
| 29      | f   | A     | 9       | AIDP    | nr    | nr | nr      | IG | No      | Complete | India     | Khan 6/21  |
| 62      | m   | nr    | nr      | AMANS   | nr    | nr | nr      | IG, | PE     | No      | Partial   | Iran 6/21   |
| 70      | m   | A     | 15      | AMAN    | nr    | nr | nr      | IG | No      | Partial | Turkey    | Koca 6/21   |
| 34      | m   | A     | 10      | AIDP    | nr    | nr | nr      | IG | No      | Partial | Egypt     | Khedir 6/21 |
| 65      | m   | A     | 5       | AIDP    | nr    | nr | nr      | IG | No      | Partial | Egypt     | Khedir 6/21 |
| 49      | f   | A     | 3       | AMAN    | nr    | nr | nr      | PE, | IG     | No      | Partial   | Egypt     | Khedir 6/21 |
| 45      | m   | A     | 14      | AIDP    | nr    | nr | nr      | S  | No      | Partial | Egypt     | Khedir 6/21 |
| 55      | f   | A     | 14      | AMAN    | nr    | nr | IG      | No | Partial | Egypt    | Khedir 6/21 |
| 11      | f   | A     | nr      | AMAN    | nr    | nr | IG, | S, PE | Yes     | Partial | India     | Khera 6/21 |

A, Onset of GBS after onset of non-neurological manifestations; AAR, Aortic Aneurysm Repair; AHT, Arterial Hypertension; AL, Alcoholism; AV, Artificial Ventilation; B, Onset of GBS before onset of non-neurological manifestations; CA, Carcinoma; CHD, Coronary Heart Disease; CIC, CoV2 in CSF; CM, Comorbidities; COPD, Chronic Obstructive Pulmonary Disease; DM, Diabetes, f, female; GBS*, No NCSs reported; HLP, Hyperlipidemia; IG, Immunoglobulins; LC, Lung Cancer; LOQ, Latency between onset of GBS and COVID-19 respectively vice versa; m, male; nd, not done; nr, not reported; NTX, Renal Transplantation; pc, personal communication; PCB, Pharyngeal, Cervical, Brachial variant of GBS; PE, Plasma Exchange; PNC, Polyneuritis Cranialis; RA, Rheumatoid Arthritis; RI, Renal Insufficiency; RSD, Reflex Sympathetic Dystrophy, S, Steroids, & antibodies positive in CSF.

Table 4
Comparison of PCG patients between first and second half of 2020 and the first half of 2021.

|                      | 1st half 2020 | 2nd half 2020 | 1st half 2021 | Total |
|----------------------|---------------|---------------|---------------|-------|
| Number of publications| 25            | 74            | 25            | 124   |
| Number of patients (n)| 33            | 192           | 75            | 300   |
| Age (years)          | 21–84 (28/33) | 8–94 (192/192) | 7–81 (75/75) | 7–94  |
| Sex                  |               |               |               |       |
| M                    | 18            | 133           | 50            | 201   |
| F                    | 10            | 57            | 25            | 92    |
| Nr                   | 5             | 2             | 0             | 7     |
| A/B                  |               |               |               |       |
| After                | 30            | 131           | 72            | 233   |
| Before               | 2             | 4             | 1             | 7     |
| Together with        | 1             | 2             | 0             | 3     |
| Nr                   | 0             | 55            | 2             | 57    |
| Latency (days)       | –9 to 24      | –10 to 90     | 1–42          | –10 to 90 |
| Subtypes             |               |               |               |       |
| AIDP                 | 22            | 94            | 55            | 171   |
| AMAN                 | 4             | 11            | 9             | 24    |
| AMANS                | 2             | 9             | 5             | 16    |
| MPS                  | 2             | 6             | 2             | 8     |
| PNC/MNC              | 0             | 3             | 0             | 3     |
| PCB                  | 0             | 1             | 0             | 1     |
| Nr                   | 3             | 68            | 6             | 77    |

(continued)
complication of COVID-19. The interest in publishing established facts is therefore understandably low. Second, editors are no longer interested in publishing case reports or case series for the same reason. Third, COVID-19 patients were more severely ill than before in the first half of 2021 and therefore died prematurely before they could develop GBS. However, there is no evidence to support this speculation. In most registries, mortality from COVID-19 did not increase with the occurrence of more virulent variants of the virus. Fourth, the prevalence of PCG is actually declining either due to improved strategies to treat COVID-19 or due to the effect of vaccination. Since COVID-19 treatment has not changed and has not become more causal and effective than months before, the former speculations are rather unlikely. So if the prevalence of PCG has really decreased, a positive effect of vaccinations is conceivable.

In general, SARS-CoV-2 vaccinations not only have advantages but are sometimes accompanied by side effects, such as GBS. Whether the prevalence of GBS as a side effect of SARS-CoV-2 vaccinations is higher compared to other vaccinations or whether PSG resulted in an overall increase in GBS prevalence is a matter of controversy. In a recent population-based historical rate comparison study and self-controlled case series analysis, only 11 PSG cases were observed after the first Astra Zeneca Vaccination (AZV) dose and only 5 PSG cases after the second dose. Fewer than 5 PCG cases were reported among those who received the BioNtech Pfizer Vaccine (BPV) and no PCG cases among those who received the Johnson & Johnson Vaccine (JJV). In a recent analysis of the US Vaccine Adverse Reporting System (VAERS) fewer than 1 PCG case per 1000,000 vaccine doses were reported within 42 days of vaccination in a period from January 2021 to 14th June 2021. In this study neurological side effects were within 42 days of vaccination in a period from January 2021 and therefore died prematurely before they could develop GBS. However, there is no evidence to support this speculation. In most registries, mortality from COVID-19 did not increase with the occurrence of more virulent variants of the virus. Fourth, the prevalence of PCG is actually declining either due to improved strategies to treat COVID-19 or due to the effect of vaccination. Since COVID-19 treatment has not changed and has not become more causal and effective than months before, the former speculations are rather unlikely. So if the prevalence of PCG has really decreased, a positive effect of vaccinations is conceivable.

In general, SARS-CoV-2 vaccinations not only have advantages but are sometimes accompanied by side effects, such as GBS. Whether the prevalence of GBS as a side effect of SARS-CoV-2 vaccinations is higher compared to other vaccinations or whether PSG resulted in an overall increase in GBS prevalence is a matter of controversy. In a recent population-based historical rate comparison study and self-controlled case series analysis, only 11 PSG cases were observed after the first Astra Zeneca Vaccination (AZV) dose and only 5 PSG cases after the second dose. Fewer than 5 PCG cases were reported among those who received the BioNtech Pfizer Vaccine (BPV) and no PCG cases among those who received the Johnson & Johnson Vaccine (JJV). In a recent analysis of the US Vaccine Adverse Reporting System (VAERS) fewer than 1 PCG case per 1000,000 vaccine doses were reported within 42 days of vaccination in a period from January 2021 to 14th June 2021. In this study neurological side effects were observed more frequently after use of the JJV than after the use of the BPV or the Moderna vaccine. In a recent systematic review and meta-analysis of 48 publications reporting 2110,441,600 participants, the pooled incidence of PCG was 3.09 per 1 million people within six weeks of vaccination, which corresponds to 2.47 cases per 100,000 person year. The pooled incidence was higher as compared to patients who received the influenza vaccine. Regarding the treatment of PCG, it is not at a variance of that applied in patients with non-SARS-CoV-2 associated GBS. However, it is currently unknown whether the therapy is just as effective as in non-SARS-CoV-2 associated GBS. Recently, an emerging new treatment strategy for GBS has been proposed that may affect the prevalence of PCG (“zipper strategy”). The approach is based on the combination of IVIG alternating with PE. The therapy is based on the idea that PE eliminates the autoantibodies and cytokines and administering IVIG immediately after PE neutralizes those antibodies that are newly formed or transfused from tissue. The subsequent PE session eliminates the antibodies away. This new approach can improve the outcome of PCG patients. Since PCG strongly influences the outcome of SARS-CoV-2 infections and since the outcome of PCG is worse among those with than without comorbidities, PCG needs to be recognized early and comorbidities sufficiently treated to improve the overall outcome of COVID-19 patients.

Limitations

A limitation of the study is that publication dates do not necessarily reflect the dates when patients were diagnosed and treated. A further limitation is the design. A prospective, multicentre design is more appropriate than a retrospective design to assess a putative vaccination effect. Among the 7 patients in whom GBS seemingly preceded the viral infection, symptoms of the infection were either not adequately acknowledged or the infection initially remained asymptomatic.

Future directions

Future studies should focus on the question if SARS-CoV-2 vaccinations really reduce the frequency of SARS-CoV-2 infection-associated complications. More generally, they should assess if vaccinations improve the outcome of COVID-19 and reduce the rate of long-COVID, the frequency, and duration of hospitalizations, including the Intensive Care Unit (ICU), and if they reduce mortality.

Conclusions

The present study enriches the current literature as it shows that the prevalence of PCG appears to have decreased since the introduction of SARS-CoV-2 vaccines. To assess if SARS-CoV-2 vaccinations really reduce the prevalence of PCG, prospective, multicentre studies are urgently needed. If such studies confirm the results of the index study,
vaccinations should be advocated and encouraged provided they are safe for everyone.

Declarations

Ethics approval and consent to participate: not applicable
Consent for publication: not applicable
Availability of data and material: all data reported are available from the corresponding author
Funding: none received

Conflicts of interest

The authors declare no conflicts of interest.

Acknowledgments

None.

Authors' contributions

JF: Design, literature search, discussion, first draft, critical comments, FS, DM: Literature search, discussion, critical comments, final approval.

References

1. Finsterer J, Scorza FA. Guillain-Barre syndrome in 220 patients with COVID-19. Egypt J Neurol Psychiatr Neurosurg 2021;57(1):55.
2. Aladawi M, Elfli M, Abu-Esheh B, Abu Jazar D, Armouti A, Bayoumi A, et al. Guillain Barre syndrome as a complication of COVID-19: a systematic review. Can J Neurol Sci 2022;49(1):36–48.
3. Li X, Wang Y, Wang H, Wang Y. SARS-CoV-2-associated Guillain-Barré syndrome is a para-infectious disease. QJM 2021;114(9):625–35.
4. Zuberbuhler P, Conti ME, León-Cejas L, Maximilliano-González F, Bonardo P, Miquelini A, et al. Guillain-Barre syndrome associated to COVID-19 infection: a review of published case reports. Rev Neurol 2021;72(6):203–12.
5. Finsterer J, Scorza FA, Fiorini AC. SARS-CoV-2-associated Guillain-Barre syndrome in 62 patients. Eur J Neurol 2021;28(1):e10–2.
6. Sansone P, Giaccari LG, Aurilio C, Coppolino F, Esposito V, Fiore M, et al. Post-infectious Guillain-Barré syndrome related to SARS-CoV-2 infection: a systematic review. Life (Basel) 2021;11(2):167.
7. Srivastava S, Kataria S, Tandon M, Patel J, Patel R, Jowkar A, et al. Guillain Barré Syndrome and its variants as a manifestation of COVID-19: a systematic review of case reports and case series. J Neurol Sci 2021;420:117263.
8. Kajumba MM, Kolbs RJ, Kohlai DC, Kaddumukasa M, Kaddumukasa M, Lankowitz DT. COVID-19-associated Guillain-Barre syndrome: atypical para-infectious profile, symp- toms overlap, and increased risk of severe neurological complications. SN Compr Clin Med 2020;2(12):2702–14.
9. Hanan I, Saff-ur-Rahman KM, Hayat S, Papri N, Jahan I, Azam R, et al. Guillain-Barré syndrome associated with SARS-CoV-2 infection: a systematic review and individual participant data meta-analysis. J Peripher Nerv Syst 2020;25(4):335–43.
10. Zhao H, Shen D, Zhou H, Liu J, Chen S. Guillain-Barré syndrome associated with SARS-CoV-2 infection: causality or coincidence? Lancet Neurol 2020;19(5):383–4.
11. Borah P, Deb PK, Chandraascharan B, Goyal M, Bansal M, Hussain S, et al. Neurological consequences of SARS-CoV-2 infection and concurrence of treatment-induced neuro-psychiatric adverse events in COVID-19 patients: navigating the uncharted. Front Mol Biosci 2021;8:627723.
12. Umamathi T, Er S, Koh JS, Goh YH, Chua L. Guillain-Barré syndrome decreases in Singapore during the COVID-19 pandemic. J Peripher Nerv Syst 2021;26(2):235–6.
13. Keddie S, Pakpoor J, Mousele C, Pipis M, Machado PM, Foster M, et al. Epidemiological and cohort study finds no association between COVID-19 and Guillain-Barré syndrome. Brain 2021;144(2):682–93.
14. Fragiel M, Miró O, Llorens P, Jiménez S, Piñera P, Burillo G, et al. Spanish Investigators on Emergency Situations TeAm (SIESTA) network. Incidence, clinical characteristics, risk factors and outcomes of Guillain-Barré in COVID-19. Ann Neurol 2021;89(3):598–603.
15. Gigli GL, Vogrig A, Nilø Fabris M, Biazzo A, Curcio F, et al. HLA and immunological features of SARS-CoV-2-induced Guillain-Barré syndrome. Neurol Sci 2020;41(12):3391–4.
16. Finsterer J, Scorza FA, Scorza CA. Post SARS-CoV-2 vaccine Guillain-Barré syndrome in 19 patients. Clinics (Sao Paulo) 2021;76:e5286.
17. Li X, Raventos B, Roel E, Pintillo A, Martinez-Hernandez E, Delmentri A, et al. Association between covid-19 vaccination, SARS-CoV-2 infection, and risk of immune mediated neurological events: population based cohort and self-controlled case series analysis. BMJ 2022;376:e608373.
18. Frontera JA, Tamborska AA, Doehm MF, Garcia-Azorin D, Gezegen H, Gueth A, et al. Autoimmune and/or post-infectious Guillain-Barré syndrome decreases in Singapore during the COVID-19 pandemic. J Peripher Nerv Syst 2021;26(2):235–6.
19. Wang F, Wang D, Wang Y, Li C, Zheng Y, Guo Z, et al. Population-based incidence of guillain-barre syndrome during mass immunization with viral vaccines: a pooled analysis. Front Immunol 2022;13:782198.
20. Saritas Nakip O, Kesci S, Bayrakci B. Zipper method is the emerging treatment option for severe Guillain-Barré syndrome related COVID-19. Autoimmun Rev 2021;20(7):102841.