



Guillain-Barré syndrome associated with SARS-CoV-2 vaccination: how is it different? a systematic review and individual participant data meta-analysis

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Purpose: An association between Guillain-Barré syndrome (GBS) and severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) vaccination has been reported. We aimed to summarize the clinical features of GBS associated with SARS-CoV-2 vaccination and determine the contrasting features from coronavirus disease-19 (COVID-19) associated GBS and GBS following other causes.

Materials and Methods: We performed PubMed search for articles published between 1 December 2020 and 27 January 2022 using search terms related to “SARS-CoV-2 vaccination” and “GBS”. Reference searching of the eligible studies was performed. Sociodemographic and vaccination data, clinical and laboratory features, and outcomes were extracted. We compared these findings with post-COVID-19 GBS and International GBS Outcome Study (IGOS) (GBS from other causes) cohorts.

Results: We included 100 patients in the analysis. Mean age was 56.88 years, and 53% were males. Six-eight received non-replicating virus vector and 30 took messenger RNA (mRNA) vaccines. The median interval between the vaccination and the GBS onset was 11 days. Limb weakness, facial palsy, sensory symptoms, dysautonomia, and respiratory insufficiency were seen in 78.65%, 53.3%, 77.4%, 23.5%, and 25%, respectively. The commonest clinical and electrodiagnostic subtype were sensory-motor variant (68%) and acute inflammatory demyelinating polyneuropathy (61.4%), respectively. And 43.9% had poor outcome (GBS outcome score ≥ 3). Pain was common with virus vector than mRNA vaccine, and the latter had severe disease at presentation (Hughes grade ≥ 3). Sensory phenomenon and facial weakness were common in vaccination cohort than post-COVID-19 and IGOS.

Conclusion: There are distinct differences between GBS associated with SARS-CoV-2 vaccination and GBS due to other causes. Facial weakness and sensory symptoms were commonly seen in the former and outcomes poor.

Keywords: Guillain-Barre syndrome, SARS-CoV-2, COVID-19, SARS-CoV-2 vaccination, Meta-analyses



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Introduction

The recent pandemic of coronavirus disease-2019 (COVID-19) is a serious infectious disease caused by the novel severe acute respiratory syndrome coronavirus (SARS-CoV-2). As on 19 September 2022, the World Health Organization (WHO) COVID-19 dashboard showed 608,328,548 confirmed cases of COVID-19 and 6,501,469 (1.068%) confirmed deaths globally [1]. Massive vaccination programs against COVID-19 were initiated worldwide to limit the pandemic. Guillain-Barré syndrome (GBS) has been

reported as an adverse event following immunization against SARS-CoV-2 [2]. The exact incidence of GBS association with vaccination against SARS-CoV-2 is undetermined. Analysis of the linked National Immunoglobulin Database/National Immunization Management System suggests that first-dose ChAdOx1 nCoV-19 vaccination is associated with an excess GBS risk of 0.576 (95% confidence interval [CI], 0.481–0.691) cases per 100,000 doses [3]. A nationwide study in Mexico showed an overall incidence of 1.19/1,000,000 doses (95% CI, 0.97–1.45 among recipients of 81 million doses of seven vaccines) [4]. However, the protection provided by these vaccines outweighs the risk of developing GBS. The recent multicenter Dutch study found no increased risk of GBS recurrence following SARS-CoV-2 vaccination [5].

Previous systematic reviews on the association between GBS and SARS-CoV-2 vaccination included patients from either one or a few countries [6]. Moreover, these studies have not described the clinical characteristics of GBS following SARS-CoV-2 infection in detail and the contrasting aspects of this entity from GBS due to other causes [7,8]. We aimed to do a systematic review and individual participant data meta-analysis to characterize the GBS associated with vaccination against SARS-CoV-2 infection and to determine whether there are any differences in clinical characteristics when compared to GBS due to other predisposing risk factors. This

systematic review is relevant as we may have to live with COVID-19 and vaccination against SARS-CoV-2 infections.

Materials and Methods

Search strategy and selection criteria

This review and meta-analysis was conducted in accordance with Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) 2020 guidelines [9]. PRISMA flow chart are provided in Fig. 1. PRISMA checklist is provided in Supplement 1. This review was registered at PROSPERO (registration number: CRD42022311831). We systematically searched MEDLINE through PubMed using a comprehensive search strategy for studies published between 1 December 2020 and 27 January 2022 with search filters “Human” and “English language”. We used a combination of the search terms related to “SARS-CoV-2 vaccination” and “GBS”. Full search terms used are provided in Supplement 2. We manually conducted a forward and backward reference search of the remaining articles at the end of screening the PubMed database for any relevant citations using Google Scholar. We have excluded articles published after 27 January 2022 in forward citation searching. We re-run the search prior to the final analysis on 28 September 2022. We have included all the case reports, case series, and cross-sectional studies from all

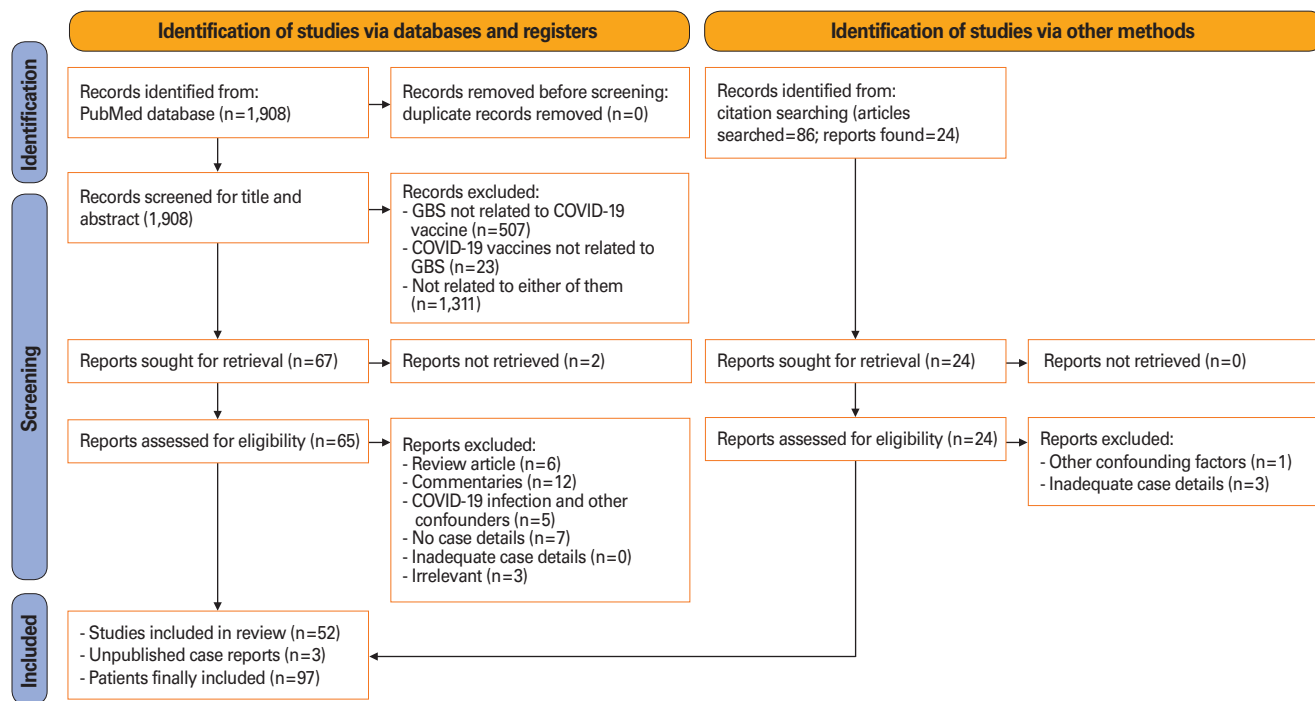


Fig. 1. Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) flow chart. GBS, Guillain-Barré syndrome; COVID-19, coronavirus disease 19.

the world regions irrespective of age, gender, and ethnicity and excluded review articles, editorials, commentaries, opinions, viewpoints, and perspectives from the analysis. However, we included letters to editors or comments that reported original case/patient information. Two authors (R.C. and B.R.) independently screened the titles and abstracts of all retrieved articles to identify eligible studies for final inclusion. The lead author (Y.M.R.) resolved the disagreement between the two reviewers, and the reasons for exclusion were recorded. We also report three unpublished cases of GBS associated with vaccination against SARS-CoV-2 infection admitted to CARE Hospital, Hyderabad between 16 January 2021 and 27 January 2022.

Data analysis

Data extraction was done using Microsoft Excel (Microsoft Corp., Redmond, WA, USA), independently by two authors (R.C. and B.R.). The lead author (Y.M.R.) cross-checked and finalized any discrepancies. We excluded duplicates using EndNote reference management software ver. 20.4.1 (Clarivate Analytics, Philadelphia, PA, USA). We extracted the individual patient-level data from each of the studies: demographic characteristics, vaccination details, the time interval between vaccination and onset of symptoms, clinical characteristics, clinical subtype, electrophysiological subtype, Brighton's level of certainty, clinical severity, respiratory insufficiency, autonomic dysfunction, cerebrospinal fluid (CSF), and the outcome at the last follow-up. Diagnosis of GBS was based on the National Institute of Neurological Disorders and Stroke, and the diagnostic certainty was assessed using the criteria of Brighton [10,11]. The association with vaccination was considered when the patient developed GBS within 8 weeks of vaccination. Motor weakness was expressed as a Medical Research Council (MRC) sum score and ranged from 0 (tetraparalytic) to 60 (normal strength) [12]. Clinical severity of the disease at admission and nadir was assessed using Hughes's grading system and MRC sum score. We defined nadir as the highest Hughes disability grade or the lowest MRC sum score [13]. Data from the nerve conduction studies were used to determine the electrophysiological subtypes of GBS: acute inflammatory demyelinating polyneuropathy (AIDP), acute motor axonal neuropathy (AMAN), and acute motor-sensory axonal neuropathy (AMSAN) [14]. When the data is insufficient, the patient is categorized as inconclusive categories. Erasmus GBS Respiratory Insufficiency Score at admission was used to predict the probability of re-

spiratory insufficiency in individual patients with GBS [15]. Two authors (Y.M.R. and S.R.Y.) independently assessed the quality of the included studies using the Joanna Briggs Institute (JBI) Critical Appraisal Checklist for case reports, case series, and cross-sectional studies [16]. Disagreements were solved by consulting a third reviewer (J.M.K.J.).

We compared the demographic, clinical, electrodiagnostic, cerebrospinal fluid, and outcomes of the present cohort with a published COVID-19-associated GBS study by Hasan et al. [17], a systematic review and individual participant data meta-analysis similar to our study, which was aimed to determine clinical, serological, and electrodiagnostic features and outcomes of COVID-19-associated GBS. This comparison was made as sometimes both risk factors may co-exist in a given individual. A similar comparison was also made against a published non-COVID-19 GBS cohort. We used the International GBS Outcome Study (IGOS) cohort for the latter [18]. IGOS is a worldwide prospective study initiated by the Inflammatory Neuropathy Consortium and Peripheral Nerve Society on the disease course and outcome in GBS.

For statistical analysis, we used IBM SPSS Statistics ver. 21.0 (IBM Corp., Armonk, NY, USA). Based on the distribution of values, continuous data were expressed as mean \pm standard deviation or as the median and interquartile range (IQR). We used the Student t-test or the Mann-Whitney U test to compare continuous variables and the chi-square test or Fisher exact test for categorical variables. Differences were considered statistically significant at $p < 0.05$. Complete clinical data were unavailable in all the 100 patients with GBS linked to vaccination against SARS-CoV-2 infection. Proportions and statistical significance were calculated for the available clinical data.

Results

We identified 1,908 articles from the PubMed database and excluded 1,841 after screening for title and abstract. Sixty-seven papers were sought for retrieval, out of which 65 were assessed for eligibility and 33 were excluded due to various reasons outlined in Fig. 1. Citation searching using Google Scholar found 24 articles, of which four were excluded due to insufficient case details. We included 100 patients from 52 articles (and our three unpublished cases) in the final analysis and depicted in the study selection figure (Fig. 1). All of the included articles are tabulated (Table 1) [19-70]. We have excluded one case each from the case series of Bonafacio et al.

Table 1. Studies included in the systematic review

| No. | Study | Country | Study design | No. of cases | Vaccine received | Type of GBS | Quality assessment |
|-----|---------------------------------|----------------|--------------|--------------|----------------------|------------------------|--------------------|
| 1 | Kim et al. [19] (2022) | South Korea | Case series | 13 | R virus vector; mRNA | AMAN; AIDP | 10/10 |
| 2 | Nishiguchi et al. [20] (2021) | Japan | Case report | 1 | mRNA | Normal | 8/8 |
| 3 | Michaelson et al. [21] (2021) | USA | Case report | 1 | mRNA | NA | 7/8 |
| 4 | Kim et al. [22] (2021) | USA | Case report | 1 | mRNA | AIDP | 8/8 |
| 5 | Malamud et al. [23] (2021) | USA | Case report | 1 | mRNA | AIDP | 8/8 |
| 6 | Hughes [24] (2021) | USA | Case report | 1 | mRNA | AIDP | 8/8 |
| 7 | Tutar et al. [25] (2021) | Turkey | Case report | 1 | Inactivated virus | AMSAN | 8/8 |
| 8 | Mckean et al. [26] (2021) | Malta | Case report | 1 | R virus vector | AIDP | 8/8 |
| 9 | Razok et al. [27] (2021) | Qatar | Case report | 1 | mRNA | AIDP | 8/8 |
| 10 | Galvez et al. [28] (2021) | Columbia | Case report | 1 | Inactivated virus | AIDP | 8/8 |
| 11 | Maramttom et al. [29] (2021) | India | Case series | 7 | R virus vector | AIDP; AMSAN | 9/10 |
| 12 | Waheed et al. [30] (2021) | USA | Case report | 1 | mRNA | NA | 7/8 |
| 13 | Finsterer et al. [31] (2021) | Austria | Case report | 1 | R virus vector | AIDP | 8/8 |
| 14 | Masuccio et al. [32] (2021) | Italy | Case report | 1 | mRNA | AIDP | 7/8 |
| 15 | Matameh et al. [33] (2021) | Qatar | Case report | 1 | mRNA | AMAN | 8/8 |
| 16 | Allen et al. [34] (2021) | UK | Case series | 4 | R virus vector | Normal; NA | 8/10 |
| 17 | Ogbebor et al. [35] (2021) | USA | Case report | 1 | mRNA | NA | 7/8 |
| 18 | Marquez Loza et al. [36] (2021) | USA | Case report | 1 | R virus vector | AIDP | 8/8 |
| 19 | Patel et al. [37] (2021) | UK | Case report | 1 | R virus vector | Inconclusive | 8/8 |
| 20 | Hasan et al. [38] (2021) | UK | Case report | 1 | R virus vector | AIDP | 8/8 |
| 21 | Bonifacio et al. [39] (2021) | UK | Case series | 4 | R virus vector | AIDP; NA | 9/10 |
| 22 | Censcak et al. [40] (2021) | Czech Republic | Case report | 1 | mRNA | AIDP | 8/8 |
| 23 | Biswas et al. [41] (2021) | India | Case report | 1 | R virus vector | AIDP | 8/8 |
| 24 | Nasuelli et al. [42] (2021) | Italy | Case report | 1 | R virus vector | AIDP | 8/8 |
| 25 | Dang et al. [43] (2021) | Australia | Case report | 1 | R virus vector | Inconclusive | 8/8 |
| 26 | Min et al. [44] (2021) | South Korea | Case series | 2 | R virus vector | AIDP; normal | 7/10 |
| 27 | Dalwadi et al. [45] (2021) | USA | Case report | 1 | mRNA | AMAN | 7/8 |
| 28 | Fukushima et al. [46] (2021) | Japan | Case report | 1 | mRNA | Inconclusive | 8/8 |
| 29 | Kanabar et al. [47] (2021) | UK | Case series | 2 | R virus vector | AIDP | 7/10 |
| 30 | Morehouse et al. [48] (2021) | USA | Case report | 1 | R virus vector | AMSAN | 8/8 |
| 31 | Bax et al. [49] (2021) | Italy | Case series | 2 | mRNA; R virus vector | AIDP; AMSAN | 9/10 |
| 32 | Ling et al. [50] (2021) | Canada | Case report | 1 | R virus vector | AIDP | 8/8 |
| 33 | Prasad et al. [51] (2021) | USA | Case report | 1 | R Virus vector | AIDP | 8/8 |
| 34 | Kim et al. [52] (2021) | South Korea | Case report | 1 | mRNA | Inconclusive | 8/8 |
| 35 | Badoiu et al. [53] (2021) | France | Case report | 1 | R virus vector | NA | 7/8 |
| 36 | Bouattour et al. [54] (2021) | Tunisia | Case report | 1 | mRNA | AIDP | 8/8 |
| 37 | Trimboli et al. [55] (2021) | Italy | Case report | 1 | mRNA | AIDP | 8/8 |
| 38 | Chun et al. [56] (2021) | South Korea | Case series | 2 | mRNA | AMSAN; AIDP | 7/10 |
| 39 | Scendoni et al. [57] (2021) | Italy | Case report | 1 | mRNA | AIDP | 8/8 |
| 40 | Kripalani et al. [58] (2021) | India | Case report | 1 | R virus vector | AIDP | 8/8 |
| 41 | Introna et al. [59] (2021) | Italy | Case report | 1 | R virus vector | AMSAN | 8/8 |
| 42 | Osowicki et al. [60] (2021) | Australia | Case series | 13 | R virus vector | AIDP; inconclusive; NA | 6/10 |
| 43 | James et al. [61] (2021) | India | Case series | 3 | R virus vector | AMSAN; AIDP | 6/10 |
| 44 | Rossetti et al. [62] (2021) | UK | Case report | 1 | R virus vector | NA | 7/8 |
| 45 | Abicic et al. [63] (2021) | Croatia | Case report | 1 | mRNA | Normal | 8/8 |
| 46 | Rao et al. [64] (2021) | USA | Case report | 1 | mRNA | AIDP | 8/8 |

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Table 1. Continued

| No. | Study | Country | Study design | No. of cases | Vaccine received | Type of GBS | Quality assessment |
|-----|------------------------------------|---------|--------------|--------------|------------------|-------------|--------------------|
| 47 | da Silva et al. [65] (2021) | Brazil | Case report | 1 | R virus vector | NA | 7/8 |
| 48 | Azam et al. [66] (2021) | UK | Case report | 1 | R virus vector | AIDP | 8/8 |
| 49 | Jain et al. [67] (2021) | USA | Case report | 1 | R virus vector | NA | 7/8 |
| 50 | Nagalli et al. [68] (2021) | USA | Case report | 1 | mRNA | AMSAN | 8/8 |
| 51 | Garcia-Grimshaw et al. [69] (2021) | Mexico | Case series | 2 | mRNA | AIDP; AMAN | 9/10 |
| 52 | Wan et al. [70] (2022) | Canada | Case series | 3 | R virus vector | AIDP | 10/10 |

GBS, Guillain-Barré syndrome; R virus, recombinant virus; AMAN, acute motor axonal neuropathy; AIDP, acute inflammatory demyelinating polyneuropathy; NA, not available; AMSAN, acute motor sensory axonal neuropathy.

[39] and Osowicki et al. [60] and four patients from the case series of Garcia-Grimshaw et al. [69] from the final analysis due to the confounding factors implicated in the causation of GBS (Supplement 3). The geographical distribution of patients is depicted in Supplement 4, and the study characteristics of individual subjects are provided in Supplement 5. Study characteristics of three unpublished cases from our center are provided in Supplement 6. A list of excluded articles from the articles assessed for eligibility, along with reasons, is provided in Supplement 7. The intra-study risk of bias is also provided in Supplements 8 and 9. Fifty studies out of 52 (96.2%) were of good quality, identified by a JBI score ≥ 7 .

Study characteristics of the whole cohort are summarized in Table 2. Most of the patients (84%) were from high and upper-middle-income countries, according to the World Bank country classification 2022. Of the 16 patients from low-middle-income countries, 15 (93.7%) were from India. There were no reports from low-income countries. The mean age of the cohort was 56.88 ± 17.06 years, with a range of 14–90 years, and 53% were males. Of the 100 patients, 68 received non-replicating virus vector vaccines, 30 received messenger RNA (mRNA), and two received inactivated whole virus vaccine. In 80% of patients, GBS followed the first dose of the vaccine. Seventy-nine patients developed GBS after the first dose of either a non-replicating virus vector vaccine or mRNA vaccine (62 versus 17, $p=0.001$). The median interval between the vaccination and the onset of GBS was 11 days, with a range of 1–45 days. Of the 100 patients, 67 fulfilled level 1 or level 2 of the Brighton criteria. Limb weakness with areflexia or hyporeflexia was the commonest presenting feature (70/89, 78.65%). The mean MRC sum score at admission was 51.51 ± 10.59 (range, 16–60), and at nadir, it was 42.13 ± 18.39 (range, 2–60). Unilateral or bilateral facial palsy was seen in 53.3% (48/90). Sensory symptoms or signs were present in 77.4% (66/84). Dysautonomia was present in 23.5% (20/85).

The classical motor-sensory deficit was the commonest GBS subtype seen in 68%, and Miller-Fisher syndrome was the subtype in 4% of patients. Other GBS variants were the subtypes (Paraparetic [8%]; pure motor [3%]; pharyngeal-cervical-brachial [1%]; bilateral facial with paraesthesia [11%]; pure sensory [4%]; and overlap GBS [1%]) in 28% of patients. Twenty-five patients (25%) required mechanical ventilation either at admission or at the nadir. At admission, the clinical details that were permitted to determine EGRIS score were available in 39 patients: 18 (46.2%) had moderate (3–4) or high-risk scores (5–7) to predict respiratory insufficiency within the first week of admission. The disease severity at nadir by Hughes grade was: grade < 2 in 16/69 patients (23.1%) and > 3 in 53/69 patients (76.9%). The electrophysiological subtypes were: AIDP in 51/83 patients (61.4%), AMAN/AMSAN in 16/83 patients (19.2%), and normal in 8/83 patients (9.6%). Albumino-cytological dissociation was present in 65/78 patients (83.3%). The median CSF protein was 110 mg/dL (IQR, 70–167 mg/dL), and the median cell count was 2 (IQR, 0–4). Of the 100 patients, 10 (10%) received no treatment, and no details were available in 13 patients (13%). Fifty-six of the remaining 77 patients received intravenous immunoglobulin (IVIG), four received plasmapheresis, and eight received both treatments. Of the 82 patients with the clinical details available to assess the GBS Outcome Score, 46 patients (56.1%) could walk at the last follow-up. There were two deaths, three patients required long-term ventilation, and 31 (37.8%) were either unable to walk independently or chair or bedbound.

A comparison of characteristics between patients who received non-replicating virus vector and mRNA vaccines is shown in Supplement 10. There was no significant difference in the time interval (vaccination and GBS) between the non-replicating virus vector and the mRNA vaccine. There were no significant differences in the clinical features of the GBS

Table 2. Clinical features, treatment, and outcomes of the whole cohort (all patients=100)

| Characteristic | Value |
|--|-------------|
| Demographic data | |
| Age (yr) (n=99) | 56.88±17.06 |
| Male gender (n=100) | 53/100 (53) |
| Country (n=100) | |
| South Korea | 18 (18) |
| India | 15 (15) |
| UK, Australia | 14 (14) |
| USA | 13 (13) |
| Italy | 7 (7) |
| Canada | 4 (4) |
| Qatar, Mexico, Japan | 2 (2) |
| Malta, Columbia, Croatia, Austria, Czech Republic, France, Brazil, Tunisia, Turkey | 1 (1) |
| Vaccination details | |
| Type of vaccine (n=100) | |
| Non-replicating viral vector | 68 (68) |
| mRNA | 30 (30) |
| Inactivated whole virus | 2 (2) |
| Dose of vaccine (n=100) | |
| First | 80 (80) |
| Second | 15 (15) |
| Not available | 5 (5) |
| Brand of vaccine (n=100) | |
| Oxford-AstraZeneca | 62 (62) |
| Pfizer-N Biotech | 26 (26) |
| Johnson & Johnson | 5 (5) |
| Moderna | 4 (4) |
| Sino vac | 1 (1) |
| Corona vac | 1 (1) |
| Not available | 1 (1) |
| Time interval between vaccination and onset of GBS (n=99) | 11 (8–14) |
| Clinical features | |
| Quadripareisis (n=89) | 48 (54) |
| Paraparesis (n=89) | 17 (19.1) |
| Upper limb weakness only (n=89) | 3 (3.4) |
| Monoparesis (n=89) | 2 (2.2) |
| No weakness (n=89) | 19 (21.3) |
| Sensory symptoms or deficits (n=84) | 65 (77.4) |
| Pain (n=75) | 32 (42.7) |
| Areflexia/hyporeflexia (n=72) | 66 (91.7) |
| Facial palsy (n=90) | 48 (53.3) |
| Bulbar palsy (n=90) | 15 (16.7) |
| Oculomotor weakness (n=90) | 11 (12.2) |
| GBS subtype | |
| Brighton's level of certainty (n=100) | |
| Level 1 | 47 (47) |
| Level 2 | 20 (20) |

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Table 2. Continued

| Characteristic | Value |
|---|--------------|
| Level 3 | 7 (7) |
| Level 4 | 26 (26) |
| Clinical subtype (n=100) | |
| Classical sensorimotor | 68 (68) |
| Pure motor | 3 (3) |
| Paraparetic | 8 (8) |
| Pharyngo-cervico-brachial variant | 1 (1) |
| Bilateral facial palsy with paresthesia | 11 (11) |
| Pure sensory | 4 (4) |
| Miller Fisher syndrome | 4 (4) |
| Overlap GBS | 1 (1) |
| Electrophysiology subtype (n=100) | |
| AIDP | 51 (51) |
| AMSAN | 10 (10) |
| AMAN | 6 (6) |
| Inconclusive | 8 (8) |
| Normal | 8 (8) |
| Not available | 17 (17) |
| Clinical severity | |
| Hughes grade at presentation (n=78) | |
| 0 (Normal) | 1 (1.3) |
| 1 (Minimal symptoms but able to run) | 13 (16.7) |
| 2 (Unable to run) | 8 (10.3) |
| 3 (Unable to walk independently) | 20 (25.6) |
| 4 (Chair or bed bound) | 30 (38.5) |
| 5 (Ventilated) | 6 (7.7) |
| ≥3 (Unable to walk independently) | 56 (71.8) |
| EGRIS score at admission (n=39) | |
| Low risk (0–2) | 21 (53.8) |
| Intermediate risk (3–4) | 15 (38.5) |
| High risk (5–7) | 3 (7.7) |
| MRC sum score at admission (n=53) | 51.51±10.59 |
| Hughes grade at nadir (n=69) | |
| 0 (Normal) | 0 (0) |
| 1 (Minimal symptoms but able to run) | 11 (15.9) |
| 2 (Unable to run) | 5 (7.2) |
| 3 (Unable to walk independently) | 8 (11.6) |
| 4 (Chair or bed bound) | 24 (34.8) |
| 5 (Ventilated) | 21 (30.4) |
| ≥3 (Unable to walk independently) | 53 (76.8) |
| MRC sum score at nadir (n=62) | 42.13±18.39 |
| Dysautonomia (n=85) | 20 (23.5) |
| Respiratory failure (n=100) | 25 (25) |
| Cerebrospinal fluid analysis (n=78) | |
| Albumino-cytological dissociation | 65 (83.3) |
| CSF protein | 110 (70–167) |
| CSF cells | 2 (0–4) |

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Table 2. Continued

| Characteristic | Value |
|--|-----------|
| Anti-ganglioside antibodies (n=51) | 8 (15.7) |
| Therapy (n=100) | |
| Intravenous immunoglobulin alone | 56 (56) |
| Plasma exchange alone | 4 (4) |
| Intravenous immunoglobulin and plasma exchange | 8 (8) |
| Steroids alone | 4 (4) |
| Steroids and intravenous immunoglobulin | 5 (5) |
| None | 10 (10) |
| Not available | 13 (13) |
| GBS outcome score (n=82) | |
| 0 (Normal) | 11 (13.4) |
| 1 (Minimal symptoms but able to run) | 22 (26.8) |
| 2 (Unable to run) | 13 (15.9) |
| 3 (Unable to walk independently) | 12 (14.6) |
| 4 (Chair or bed bound) | 19 (23.2) |
| 5 (Ventilated) | 3 (3.7) |
| 6 (Death) | 2 (2.4) |
| ≤2 (Able to walk independently) | 46 (56.1) |
| ≥3 (Unable to walk independently) | 36 (43.9) |

Values are presented as mean±standard deviation, number, or median (interquartile range). Data is not uniformly available for each patient leading to separate 'N' (number in the parentheses) for each characteristic.

mRNA, messenger RNA; GBS, Guillain-Barré syndrome; AIDP, acute inflammatory demyelinating polyneuropathy; AMSAN, acute motor sensory axonal neuropathy; AMAN, acute motor axonal neuropathy; EGRIS, Erasmus GBS Respiratory Insufficiency Score; MRC, Medical Research Council; CSF, cerebrospinal fluid.

linked to either vaccine except pain. Significantly more patients with GBS linked to non-replicating virus vector vaccine had pain as the clinical feature (58.3% versus 16%, $p=0.00006$). Patients with GBS linked to the mRNA vaccine had the more severe disease at presentation (Hughes stage >3: 91.7% versus 61.5%, $p=0.007$).

We made a comparison between clinical characteristics of GBS associated with SARS-CoV-2 vaccination and a published post-COVID-19 GBS cohort of Hasan et al. [17] (Table 3). Sensory symptoms or signs were present in 65/84 patients (77.4%) with GBS associated with vaccination against SARS-CoV-2 as compared to 18/61 patients (29.5%) with post-COVID-19 GBS ($p<0.0001$). Facial weakness, either unilateral or bilateral, was the presenting feature in 48/90 patients (53.3%) with GBS linked to vaccination against SARS-CoV-2 as compared to 18/61 patients (29.5%) with post-COVID-19 GBS ($p=0.0039$).

A comparison was made between the clinical characteristics of GBS associated with SARS-CoV-2 vaccination and the IGOS study cohort (Table 4) [18]. Limb weakness (quadripara-

resis/paraparesis/bi-brachial/monoparesis) was seen in 826/924 (89.4%) in the IGOS study cohort. In contrast, it was seen in 70/89 patients (78.65%) with GBS associated with vaccination ($p=0.002$). Facial weakness, unilateral or bilateral, was seen in 48/90 patients (53.2%) with GBS associated with vaccination, whereas it was seen in 286/922 patients (31%) in the IGOS study cohort ($p<0.0001$). Sensory symptoms or signs were seen in 65/84 patients (77.4%) with vaccination GBS. In contrast, it was in 543/890 (59%) in the IGOS study cohort ($p=0.001$). The other GBS variants were more represented in patients with GBS linked to vaccination against SARS-CoV-2 when compared to patients in the IGOS study cohort (24/100 [24%] versus 42/744 [6%], $p<0.01$). Axonal neuropathy (AMAN/AMSAN) was the electrophysiological subtype in 16/83 patients (19.28%) with GBS linked to vaccination against SARS-CoV-2, and it was 71/745 (10%) in the IGOS study cohort ($p=0.01$). At the last follow-up, the GBS outcome scale was between 3 and 5 in 34/82 patients (42.5%) with GBS linked to vaccination against SARS-CoV-2 when compared to 129/556 (23.2%) in the IGOS study cohort ($p<0.01$).

Discussion

There were 100 patients with GBS linked to SARS-CoV-2 vaccination during the study period. Most patients (84%) were from high and upper-middle-income countries. There was no representation from low-income countries. The median age was 59 years (IQR, 48–69 years), and males were 53. The lower representation of younger age groups may be related to the vaccination practices prevalent during the study period. GBS linked to SARS-CoV-2 vaccination has been reported with all types of vaccines. In two-thirds of patients (68%), it followed the non-replicating viral vector vaccine. Symptoms of GBS developed after the first dose of the vaccine in 80% of patients. The time interval from vaccination to GBS symptoms onset was 11 days (range, 8–14 days).

This systematic review characterizes the clinical characteristics of GBS linked to vaccination against SARS-CoV-2. Of the 100 patients identified, 67% fulfilled level 1 and level 2 of the Brighton criteria. Limb weakness with areflexia or hyporeflexia was the commonest presenting feature, followed by sensory symptoms or signs, unilateral or bilateral facial weakness, and dysautonomia. Motor-sensory was the commonest clinical subtype, and variants accounted for 24% of patients. AIDP was the commonest electrophysiological subtype. Se-

Table 3. Comparison between GBS associated to SARS-CoV-2 vaccination and post-COVID-19 GBS cohort

| Variable | Present study (n=100) | Post-COVID-19 GBS cohort (n=61) | p-value |
|---|-----------------------|---------------------------------|-------------------|
| Age (yr) | 59 (48–69) | 57 (49–70) | |
| Male | 53/100 (53) | 42/61 (68.9) | 0.04 |
| Time interval between antecedent event and GBS | 11 (8–14) | 14 (9–20) | |
| Clinical features | | | |
| Motor symptoms | 70/89 (78.65) | 53/61 (86.88) | 0.19 |
| Quadriparesis | 48/89 (54) | 30/61 (49.2) | 0.56 |
| Paraparesis | 17/89 (19.1) | 23/61 (37.7) | 0.01 |
| Upper limb weakness only | 3/89 (3.4) | - | - |
| Monoparesis | 2/89 (2.2) | - | - |
| No weakness | 19/89 (21.3) | - | - |
| Sensory symptoms or deficits | 65/84 (77.4) | 18/61 (29.5) | <0.0001 |
| Pain | 32/75 (42.7) | 9/61 (14.8) | 0.0004 |
| Areflexia/hyporeflexia | 66/72 (91.7) | - | - |
| Facial palsy | 48/90 (53.3) | 18/61 (29.5) | 0.0039 |
| Bulbar palsy | 15/90 (16.7) | 11/61 (18.0) | 0.83 |
| Oculomotor weakness | 11/90 (12.2) | - | - |
| Clinical subtype | | | |
| Sensorimotor | 68/100 (68) | 42/61 (68.9) | 0.90 |
| Pure motor | 3/100 (3) | 4/61 (6.6) | 0.27 |
| MFS | 4/100 (4) | 7/61 (11.5) | 0.06 |
| MFS-GBS overlap | 1/100 (1) | - | - |
| Others (PCB, pure sensory, ataxia, or other variants) | 24/100 (24) | 8/61 (13.1) | 0.09 |
| Electrophysiological subtype | | | |
| Axonal (AMAN/AMSAN) | 16/83 (19.28) | 11/53 (21) | 0.80 |
| AIDP | 51/83 (61.4) | 40/53 (75.5) | 0.08 |
| Normal | 8/83 (9.6) | - | - |
| Inconclusive | 8/83 (9.6) | 2/53 (3.8) | 0.20 |
| Inexcitable | - | - | - |
| Brighton's collaboration level of certainty | | | |
| Level 1 | 47/100 (47) | 41/61 (67.2) | 0.01 |
| Level 2 | 20/100 (20) | 17/61 (27.9) | 0.24 |
| Level 3 | 7/100 (7) | 3/61 (4.9) | 0.59 |
| Level 4 | 26/100 (26) | - | - |
| Clinical severity at nadir | | | |
| Dysautonomia | 20/85 (23.5) | - | - |
| Respiratory insufficiency | 25/100 (25) | 17/56 (30.4) | 0.46 |
| MRC sum score at nadir | 48 (30–58.5) | - | - |
| Hughes grade ≤2 | 16/69 (23.1) | - | - |
| Hughes grade ≥3 | 53/69 (76.9) | - | - |
| Albumino-cytological dissociation | 65/78 (83.3) | 42/52 (80.8) | 0.71 |
| CSF protein | 100.65 (70–167) | - | - |
| Anti-ganglioside antibodies | 8/51 (15.7) | 1/26 (3.9) | 0.13 |

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Table 3. Continued

| Variable | Present study (n=100) | Post-COVID-19 GBS cohort (n=61) | p-value |
|--|-----------------------|---------------------------------|--------------|
| GBS specific treatment | | | |
| IVIG | 64/87 (73.6) | 51/55 (92.7) | 0.004 |
| PLEX | 12/87 (13.8) | 4/55 (7.3) | 0.23 |
| IVIG & PLEX | 8/87 (9.2) | 2/55 (3.6) | 0.20 |
| GBS outcome scale at last follow-up | | | |
| ≤2 | 46/82 (56.1) | 34/61 (65.3) | 0.26 |
| 3–5 | 34/82 (42.5) | 16/61 (30.7) | 0.15 |

Values are presented as median (interquartile range) or number. Data is not uniformly available for each patient leading to separate 'N' (number in the parentheses) for each parameter. Statistically significant results are marked in bold.

GBS, Guillain-Barré syndrome; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; COVID-19, coronavirus disease 19; MFS, Miller-Fisher syndrome; PCB, pharyngo-cervico-brachial; AMAN, acute motor axonal neuropathy; AMSAN, acute motor sensory axonal neuropathy; AIDP, acute inflammatory demyelinating polyneuropathy; MRC, Medical Research Council; CSF, cerebrospinal fluid; IVIG, intravenous immunoglobulin; PLEX, plasma exchange.

vere disease (Hughes grade was ≥3) was noted in 76.9%, and 25% required mechanical ventilation. Significantly more patients with GBS linked to non-replicating virus vector vaccine had pain as the clinical feature, and patients who received the mRNA vaccine had more severe disease (Hughes stage ≥3). Pain is a very disabling symptom often seen GBS. Pathophysiology of pain in GBS is largely unknown. It is probably radiculitis, inflammatory factors, and spontaneous abnormal activity in sensory nerve afferents. This isolated finding needs more studies for validation.

Comparison between patients in the IGOS study cohort and the post-COVID-19 vaccine GBS cohort showed more frequent sensory symptoms or signs and facial palsy in the latter. Other GBS variants and axonal forms (AMAN/AMSA) were more frequent in patients with the latter than the former. GBS linked to vaccination against SARS-CoV-2 was associated with poor outcomes compared to the two other forms of GBS.

Ten patients received no treatment, and details were not available in 13 patients. Of the remaining 77 patients, 68 received evidence-based treatments: IVIG, plasmapheresis, or both. Ten patients received intravenous methylprednisolone and oral steroids or oral steroids alone. There were two deaths. GBS linked to vaccination against SARS-CoV-2 is associated with poor outcomes. In this systematic review, two patients required long-term ventilation, and 31 (37.8%) were either unable to walk independently or chair or bedbound.

Table 4. Comparison between GBS associated to SARS-CoV-2 vaccination cohort and IGOS study cohort

| Variable | Present study (n=100) | IGOS study cohort (n=925) | p-value |
|---|-----------------------|---------------------------|-------------------|
| Age (yr) | 59 (48–69) | 51 (33–64) | |
| Male | 53/100 (53) | 552/925 (59.7) | 0.19 |
| Time interval between antecedent event and GBS | 11 (8–14) | - | |
| Clinical features | | | |
| Motor symptoms | 70/89 (78.65) | 826/924 (89.4) | 0.002 |
| Quadriparesis | 48/89 (54) | 677/924 (73) | 0.0002 |
| Paraparesis | 17/89 (19.1) | 105/924 (11) | 0.023 |
| Upper limb weakness only | 3/89 (3.4) | 19/924 (2) | 0.38 |
| Monoparesis | 2/89 (2.2) | 10/924 (1) | 0.30 |
| No weakness | 19/89 (21.3) | 98/924 (11) | 0.0042 |
| Sensory symptoms or deficits | 65/84 (77.4) | 543/890 (59) | 0.0010 |
| Pain | 32/75 (42.7) | 506/923 (55) | 0.039 |
| Areflexia/hyporeflexia | 66/72 (91.7) | 800/920 (87) | 0.24 |
| Facial palsy | 48/90 (53.3) | 286/922 (31) | <0.0001 |
| Bulbar palsy | 15/90 (16.7) | 234/922 (25) | 0.07 |
| Oculomotor weakness | 11/90 (12.2) | 139/922 (15) | 0.47 |
| Clinical subtype | | | |
| Sensorimotor | 68/100 (68) | 453/744 (61) | 0.17 |
| Pure motor | 3/100 (3) | 170/744 (23) | <0.01 |
| MFS | 4/100 (4) | 40/744 (5) | 0.66 |
| MFS-GBS overlap | 1/100 (1) | 39/744 (5) | 0.07 |
| Others (PCB, pure sensory, ataxia, or other variants) | 24/100 (24) | 42/744 (6) | <0.01 |
| Electrophysiological subtype | | | |
| Axonal (AMAN/AMSAN) | 16/83 (19.28) | 71/745 (10) | 0.01 |
| AIDP | 51/83 (61.4) | 390/745 (52) | 0.10 |
| Normal | 8/83 (9.6) | 49/745 (7) | 0.38 |
| Inconclusive | 8/83 (9.6) | 215/745 (29) | 0.0002 |
| Inexcitable | - | 20/745 (3) | - |
| Brighton's collaboration level of certainty | | | |
| Level 1 | 47/100 (47) | - | - |
| Level 2 | 20/100 (20) | - | - |
| Level 3 | 7/100 (7) | - | - |
| Level 4 | 26/100 (26) | - | - |
| Clinical severity at nadir | | | |
| Dysautonomia | 20/85 (23.5) | 228/924 (25) | 0.75 |
| Respiratory insufficiency | 25/100 (25) | 176/925 (19) | 0.15 |
| MRC sum score at nadir | 48 (30–58.5) | 44 (25–53) | |
| Hughes grade ≤2 | 16/69 (23.1) | 172/815 (21.1) | 0.69 |
| Hughes grade ≥3 | 53/69 (76.9) | 643/815 (78.9) | 0.69 |
| Albumino-cytological dissociation | 65/78 (83.3) | 538/823 (67) | 0.003 |
| CSF protein | 100.65 (70–167) | 98 (59–184) | |
| Anti-ganglioside antibodies | 8/51 (15.7) | - | - |
| GBS specific treatment | | | |

(Continued on next page)

Table 4. Continued

| Variable | Present study (n=100) | IGOS study cohort (n=925) | p-value |
|--|-----------------------|---------------------------|-----------------|
| IVIG | 64/87 (73.6) | 669/909 (73.6) | 1.0 |
| PLEX | 12/87 (13.8) | 62/909 (6.8) | 0.01 |
| IVIG & PLEX | 8/87 (9.2) | - | - |
| GBS outcome scale at last follow-up | | | |
| ≤2 | 46/82 (56.1) | 427/556 (76.8) | <0.01 |
| 3–5 | 34/82 (42.5) | 129/556 (23.2) | <0.01 |

Values are presented as median (interquartile range) or number. Data is not uniformly available for each patient leading to separate 'N' (number in the parentheses) for each parameter. Statistically significant results are marked in bold.

GBS, Guillain-Barré syndrome; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; IGOS, International GBS Outcome Study; MFS, Miller-Fisher syndrome; PCB, pharyngo-cervico-brachial; AMAN, acute motor axonal neuropathy; AMSAN, acute motor sensory axonal neuropathy; AIDP, acute inflammatory demyelinating polyneuropathy; MRC, Medical Research Council; CSF, cerebrospinal fluid; IVIG, intravenous immunoglobulin; PLEX, plasma exchange.

GBS has been described following vaccination against many infections [71]. The available evidence for such a causal relationship is not convincing. Biologically it is plausible that a vaccine can cause an immune attack on any component of the peripheral nerve through molecular mimicry. However, there is no known homology between SARS-CoV-2 surface epitopes and peripheral nerve tissue [72]. This systematic review suggests distinct differences in clinical features between GBS associated with vaccination against SARS-CoV-2 and post-COVID-19 GBS, as well as GBS in the IGOS study cohort. Sensory symptoms and signs and unilateral or bilateral facial palsy were frequently noted in patients with GBS associated with vaccination against SARS-CoV-2. Axonal (AMAN/AMSAN) electrophysiological subtype was more common in the GBS associated with vaccination against SARS-CoV-2 and associated with poor outcomes. These findings suggest that vaccine-induced peripheral nerve pathology is more severe and has smaller fiber involvement. The exact explanation for these observations is speculative; maybe the antigen composition in the vaccine is different.

Concerns about the increased association of GBS with vaccines have existed since the 1976 swine influenza vaccine campaign (1 GBS per 100,000 vaccinations) in the United States [73,74]. In a large retrospective study, Baxter et al. [75] found no evidence of an increased risk of GBS following vaccines. Globally, a mass vaccination campaign is on to control COVID-19 caused by SARS-CoV-2 infection using different types of vaccinations, mRNA, non-replicating virus vectors and inactivated whole virus. There has been no evidence of

an increased risk of GBS from the mass vaccination program COVID-19 worldwide [76]. However, GBS risk following COVID-19 vaccination appears to be lower than what was expected from other respiratory virus vaccination [77]. The Mexican study showed an overall incidence of 1.19/1,000,000 vaccinations against SARS-CoV-2 infection (95% CI, 0.97–1.45), with incidence higher among Ad26.COV2-S (3.86/1,000,000 vaccinations; 95% CI, 1.50–9.93). However, in this study, of the 97 patients with GBS observed, 21 patients (21.6%) had other potential predisposing risk factors for GBS [4].

This review has three main strengths. First, we have followed a comprehensive search strategy and rigorous inclusion and exclusion criteria adhering to the revised PRISMA guidelines. Second, more than 95% of the case studies included had good quality. The non-vaccination GBS cohorts used for comparison were representative of all ages, gender, and ethnicity. However, this review also has limitations. First, we know the lack of representation from low-income countries in the vaccination cohort. Second, including a few case series with limited clinical details may have affected the results. Third, EGRIS and MRC sum scores were calculated based on the clinical features described if they were not mentioned in the text. This could have been erroneous.

In conclusion, the study population represents worldwide and ethnic groups except for low-income countries. There are distinct differences in clinical characteristics in patients with GBS associated with SARS-CoV-2 vaccination compared to patients with GBS due to other predisposing risk factors. Unilateral or bilateral facial weakness and sensory symptoms at presentation were more common in patients with GBS associated with SARS-CoV-2 vaccination. The outcomes were poor in patients with GBS associated with SARS-CoV-2 vaccination.

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Supplementary Materials

Supplementary materials are available at Clinical and Experimental Vaccine Research website (<http://www.ecevr.org>).

References

1. World Health Organization. COVID-19 dashboard [Internet]. Geneva: GAVI; 2022 [cited 2022 Sep 21]. Available from: <https://www.gavi.org/covid19>
2. Hanson KE, Goddard K, Lewis N, et al. Incidence of Guillain-Barre syndrome after COVID-19 vaccination in the Vaccine Safety Datalink. *JAMA Netw Open* 2022;5:e228879.
3. Keh RY, Scanlon S, Datta-Nemdharry P, et al. COVID-19 vaccination and Guillain-Barre syndrome: analyses using the National Immunoglobulin Database. *Brain* 2023;146:739-48.
4. Garcia-Grimshaw M, Galnares-Olalde JA, Bello-Chavolla OY, et al. Incidence of Guillain-Barre syndrome following SARS-CoV-2 immunization: analysis of a nationwide registry of recipients of 81 million doses of seven vaccines. *Eur J Neurol* 2022;29:3368-79.
5. Baars AE, Kuitwaard K, de Koning LC, et al. SARS-CoV-2 vaccination safety in Guillain-Barre syndrome, chronic inflammatory demyelinating polyneuropathy, and multifocal motor neuropathy. *Neurology* 2023;100:e182-91.
6. Shao SC, Wang CH, Chang KC, Hung MJ, Chen HY, Liao SC. Guillain-Barre syndrome associated with COVID-19 vaccination. *Emerg Infect Dis* 2021;27:3175-8.
7. Abolmaali M, Rezaia F, Behnagh AK, Hamidabad NM, Gorji A, Mirzaasgari Z. Guillain-Barre syndrome in association with COVID-19 vaccination: a systematic review. *Immunol Res* 2022;70:752-64.
8. Atzenhoffer M, Auffret M, Pegat A, et al. Guillain-Barre syndrome associated with COVID-19 vaccines: a perspective from spontaneous report data. *Clin Drug Investig* 2022;42:581-92.
9. Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ* 2021;372:n71.
10. Asbury AK, Cornblath DR. Assessment of current diagnostic criteria for Guillain-Barre syndrome. *Ann Neurol* 1990;27 Suppl:S21-4.
11. Fokke C, van den Berg B, Drenthen J, Walgaard C, van Doorn PA, Jacobs BC. Diagnosis of Guillain-Barre syndrome and validation of Brighton criteria. *Brain* 2014;137(Pt 1):33-43.
12. Kleyweg RP, van der Meche FG, Schmitz PI. Interobserver agreement in the assessment of muscle strength and functional abilities in Guillain-Barre syndrome. *Muscle Nerve* 1991;14:1103-9.

13. Hughes RA, Newsom-Davis JM, Perkin GD, Pierce JM. Controlled trial prednisolone in acute polyneuropathy. *Lancet* 1978;2:750-3.
14. Ho TW, Mishu B, Li CY, et al. Guillain-Barre syndrome in Northern China: relationship to *Campylobacter jejuni* infection and anti-glycolipid antibodies. *Brain* 1995;118 (Pt 3):597-605.
15. Doets AY, Walgaard C, Lingsma HF, et al. International validation of the erasmus Guillain-Barre syndrome respiratory insufficiency score. *Ann Neurol* 2022;91:521-31.
16. Munn Z, Moola S, Riitano D, Lisy K. The development of a critical appraisal tool for use in systematic reviews addressing questions of prevalence. *Int J Health Policy Manag* 2014;3:123-8.
17. Hasan I, Saif-Ur-Rahman KM, Hayat S, et al. Guillain-Barre syndrome associated with SARS-CoV-2 infection: a systematic review and individual participant data meta-analysis. *J Peripher Nerv Syst* 2020;25:335-43.
18. Doets AY, Verboon C, van den Berg B, et al. Regional variation of Guillain-Barre syndrome. *Brain* 2018;141:2866-77.
19. Kim JE, Min YG, Shin JY, et al. Guillain-Barre syndrome and variants following COVID-19 vaccination: report of 13 cases. *Front Neurol* 2022;12:820723.
20. Nishiguchi Y, Matsuyama H, Maeda K, Shindo A, Tomimoto H. Miller Fisher syndrome following BNT162b2 mRNA coronavirus 2019 vaccination. *BMC Neurol* 2021; 21:452.
21. Michaelson NM, Lam T, Malhotra A, Schiff ND, MacGowan DJ. Miller Fisher syndrome presenting after a second dose of Pfizer-BioNTech vaccination in a patient with resolved COVID-19: a case report. *J Clin Neuromuscul Dis* 2021;23: 113-5.
22. Kim Y, Zhu Z, Kochar P, Gavigan P, Kaur D, Kumar A. A pediatric case of sensory predominant Guillain-Barre syndrome following COVID-19 vaccination. *Child Neurol Open* 2022;9:2329048X221074549.
23. Malamud E, Otallah SI, Caress JB, Lapid DJ. Guillain-Barre syndrome after COVID-19 vaccination in an adolescent. *Pediatr Neurol* 2022;126:9-10.
24. Hughes DL, Brunn JA, Jacobs J, Todd PK, Askari FK, Fontana RJ. Guillain-Barre syndrome after COVID-19 mRNA vaccination in a liver transplantation recipient with favorable treatment response. *Liver Transpl* 2022;28:134-7.
25. Tutar NK, Eyigurbuz T, Yildirim Z, Kale N. A variant of Guillain-Barre syndrome after SARS-CoV-2 vaccination: AMSAN. *Idegyogy Sz* 2021;74:286-8.
26. McKean N, Chircop C. Guillain-Barre syndrome after COVID-19 vaccination. *BMJ Case Rep* 2021;14:e244125.
27. Razok A, Shams A, Almeer A, Zahid M. Post-COVID-19 vaccine Guillain-Barre syndrome: first reported case from Qatar. *Ann Med Surg (Lond)* 2021;67:102540.
28. Arce Galvez L, Ramirez Abadia LA, de los Reyes Guevara CA, Hernandez Orozco JF. Guillain-Barre syndrome after vaccination for COVID-19: the first report in Latin America. *Neurol Perspect* 2021;1:236-8.
29. Maramattom BV, Krishnan P, Paul R, et al. Guillain-Barre syndrome following ChAdOx1-S/nCoV-19 vaccine. *Ann Neurol* 2021;90:312-4.
30. Waheed S, Bayas A, Hindi F, Rizvi Z, Espinosa PS. Neurological complications of COVID-19: Guillain-Barre syndrome following Pfizer COVID-19 vaccine. *Cureus* 2021; 13:e13426.
31. Finsterer J. Exacerbating Guillain-Barre syndrome eight days after vector-based COVID-19 vaccination. *Case Rep Infect Dis* 2021;2021:3619131.
32. Masuccio FG, Comi C, Solaro C. Guillain-Barre syndrome following COVID-19 vaccine mRNA-1273: a case report. *Acta Neurol Belg* 2022;122:1369-71.
33. Matarneh AS, Al-Battah AH, Farooqui K, Ghamoodi M, Alhatou M. COVID-19 vaccine causing Guillain-Barre syndrome, a rare potential side effect. *Clin Case Rep* 2021; 9:e04756.
34. Allen CM, Ramsamy S, Tarr AW, et al. Guillain-Barre syndrome variant occurring after SARS-CoV-2 vaccination. *Ann Neurol* 2021;90:315-8.
35. Ogbekor O, Seth H, Min Z, Bhanot N. Guillain-Barre syndrome following the first dose of SARS-CoV-2 vaccine: a temporal occurrence, not a causal association. *IDCases* 2021;24:e01143.
36. Marquez Loza AM, Holroyd KB, Johnson SA, Pilgrim DM, Amato AA. Guillain-Barre syndrome in the placebo and active arms of a COVID-19 vaccine clinical trial: temporal associations do not imply causality. *Neurology* 2021;96: 1052-4.
37. Patel SU, Khurram R, Lakhani A, Quirk B. Guillain-Barre syndrome following the first dose of the chimpanzee adenovirus-vectored COVID-19 vaccine, ChAdOx1. *BMJ Case Rep* 2021;14:e242956.
38. Hasan T, Khan M, Khan F, Hamza G. Case of Guillain-Barre syndrome following COVID-19 vaccine. *BMJ Case Rep* 2021;14:e243629.

39. Bonifacio GB, Patel D, Cook S, et al. Bilateral facial weakness with paraesthesia variant of Guillain-Barre syndrome following Vaxzevria COVID-19 vaccine. *J Neurol Neurosurg Psychiatry* 2022;93:341-2.
40. Censcak D, Ungermaun L, Stetkarova I, Ehler E. Guillain-Barre syndrome after first vaccination dose against COVID-19: case report. *Acta Medica (Hradec Kralove)* 2021;64:183-6.
41. Biswas A, Pandey SK, Kumar D, Vardhan H. Post coronavirus disease: 2019 vaccination Guillain-Barre syndrome. *Indian J Public Health* 2021;65:422-4.
42. Nasuelli NA, De Marchi F, Cecchin M, et al. A case of acute demyelinating polyradiculoneuropathy with bilateral facial palsy after ChAdOx1 nCoV-19 vaccine. *Neurol Sci* 2021;42:4747-9.
43. Dang YL, Bryson A. Miller-Fisher syndrome and Guillain-Barre syndrome overlap syndrome in a patient post Oxford-AstraZeneca SARS-CoV-2 vaccination. *BMJ Case Rep* 2021;14:e246701.
44. Min YG, Ju W, Ha YE, et al. Sensory Guillain-Barre syndrome following the ChAdOx1 nCov-19 vaccine: report of two cases and review of literature. *J Neuroimmunol* 2021;359:577691.
45. Dalwadi V, Hancock D, Ballout AA, Geraci A. Axonal-variant Guillain-Barre syndrome temporally associated with mRNA-based Moderna SARS-CoV-2 vaccine. *Cureus* 2021;13:e18291.
46. Fukushima T, Tomita M, Ikeda S, Hattori N. A case of sensory ataxic Guillain-Barre syndrome with immunoglobulin G anti-GM1 antibodies following the first dose of mRNA COVID-19 vaccine BNT162b2 (Pfizer). *QJM* 2022;115:25-7.
47. Kanabar G, Wilkinson P. Guillain-Barre syndrome presenting with facial diplegia following COVID-19 vaccination in two patients. *BMJ Case Rep* 2021;14:e244527.
48. Morehouse ZP, Paulus A, Jasti SA, Bing X. A rare variant of Guillain-Barre syndrome following Ad26.COV2.S vaccination. *Cureus* 2021;13:e18153.
49. Bax F, Gigli GL, Belgrado E, Brunelli L, Valente M. Guillain-Barre syndrome following COVID-19 immunization: a report of two cases. *Acta Neurol Belg* 2022;122:1365-7.
50. Ling L, Bagshaw SM, Villeneuve PM. Guillain-Barre syndrome after SARS-CoV-2 vaccination in a patient with previous vaccine-associated Guillain-Barre syndrome. *CMAJ* 2021;193:E1766-9.
51. Prasad A, Hurlburt G, Podury S, Tandon M, Kingree S, Sriwastava S. A novel case of bifacial diplegia variant of Guillain-Barre syndrome following Janssen COVID-19 vaccination. *Neurol Int* 2021;13:404-9.
52. Kim N, Kim JH, Park JS. Guillain-Barre syndrome associated with BNT162b2 COVID vaccination: a first case report from South Korea. *Neurol Sci* 2022;43:1491-3.
53. Badoiu A, Moranne O, Coudray S, Ion IM. Clinical variant of Guillain-Barre syndrome with prominent facial diplegia After AstraZeneca coronavirus disease 2019 vaccine. *J Clin Neuromuscul Dis* 2021;23:115-6.
54. Bouattour N, Hdihi O, Sakka S, et al. Guillain-Barre syndrome following the first dose of Pfizer-BioNTech COVID-19 vaccine: case report and review of reported cases. *Neurol Sci* 2022;43:755-61.
55. Trimboli M, Zoleo P, Arabia G, Gambardella A. Guillain-Barre syndrome following BNT162b2 COVID-19 vaccine. *Neurol Sci* 2021;42:4401-2.
56. Chun JY, Park S, Jung J, et al. Guillain-Barre syndrome after vaccination against COVID-19. *Lancet Neurol* 2022;21:117-9.
57. Scendoni R, Petrelli C, Scaloni G, Logullo FO. Electromyoneurography and laboratory findings in a case of Guillain-Barre syndrome after second dose of Pfizer COVID-19 vaccine. *Hum Vaccin Immunother* 2021;17:4093-6.
58. Kripalani Y, Lakkappan V, Parulekar L, Shaikh A, Singh R, Vyas P. A rare case of Guillain-Barre syndrome following COVID-19 vaccination. *Eur J Case Rep Intern Med* 2021;8:002707.
59. Introna A, Caputo F, Santoro C, et al. Guillain-Barre syndrome after AstraZeneca COVID-19-vaccination: a causal or casual association? *Clin Neurol Neurosurg* 2021;208:106887.
60. Osowicki J, Morgan H, Harris A, Crawford NW, BATTERY JP, Kiers L. Guillain-Barre syndrome in an Australian State using both mRNA and adenovirus-vector SARS-CoV-2 vaccines. *Ann Neurol* 2021;90:856-8.
61. James J, Jose J, Gafoor VA, Smita B, Balaram N. Guillain-Barre syndrome following ChAdOx1 nCoV-19 COVID-19 vaccination: a case series. *Neurol Clin Neurosci* 2021;9:402-5.
62. Rossetti A, Gheihman G, O'Hare M, Kosowsky JM. Guillain-Barre syndrome presenting as facial diplegia after COVID-19 vaccination: a case report. *J Emerg Med* 2021;61:e141-5.
63. Abicic A, Adamec I, Habek M. Miller Fisher syndrome following Pfizer COVID-19 vaccine. *Neurol Sci* 2022;43:1495-7.
64. Rao SJ, Khurana S, Murthy G, Dawson ET, Jazebi N, Haas

- CJ. A case of Guillain-Barre syndrome following Pfizer COVID-19 vaccine. *J Community Hosp Intern Med Perspect* 2021;11:597-600.
65. da Silva GF, da Silva CF, Oliveira RE, et al. Guillain-Barre syndrome after coronavirus disease 2019 vaccine: a temporal association. *Clin Exp Neuroimmunol* 2022;13:92-4.
66. Azam S, Khalil A, Taha A. Guillain-Barre syndrome in a 67-year-old male post COVID-19 vaccination (Astra Zeneca). *Am J Med Case Rep* 2021;9:424-7.
67. Jain E, Pandav K, Regmi P, Michel G, Altshuler I. Facial diplegia: a rare, atypical variant of Guillain-Barre syndrome and Ad26.COVS vaccine. *Cureus* 2021;13:e16612.
68. Nagalli S, Shankar Kikkeri N. Sub-acute onset of Guillain-Barre syndrome post-mRNA-1273 vaccination: a case report. *SN Compr Clin Med* 2022;4:41.
69. Garcia-Grimshaw M, Michel-Chavez A, Vera-Zertuche JM, et al. Guillain-Barre syndrome is infrequent among recipients of the BNT162b2 mRNA COVID-19 vaccine. *Clin Immunol* 2021;230:108818.
70. Wan MM, Lee A, Kapadia R, Hahn C. Case series of Guillain-Barre syndrome after the ChAdOx1 nCoV-19 (Oxford-AstraZeneca) vaccine. *Neurol Clin Pract* 2022;12:149-53.
71. Leonhard SE, Mandarakas MR, Gondim FA, et al. Diagnosis and management of Guillain-Barre syndrome in ten steps. *Nat Rev Neurol* 2019;15:671-83.
72. Keddie S, Pakpoor J, Mousele C, et al. Epidemiological and cohort study finds no association between COVID-19 and Guillain-Barre syndrome. *Brain* 2021;144:682-93.
73. Schonberger LB, Bregman DJ, Sullivan-Bolyai JZ, et al. Guillain-Barre syndrome following vaccination in the National Influenza Immunization Program, United States, 1976-1977. *Am J Epidemiol* 1979;110:105-23.
74. Schonberger LB, Hurwitz ES, Katona P, Holman RC, Bregman DJ. Guillain-Barre syndrome: its epidemiology and associations with influenza vaccination. *Ann Neurol* 1981; 9 Suppl:31-8.
75. Baxter R, Bakshi N, Fireman B, et al. Lack of association of Guillain-Barre syndrome with vaccinations. *Clin Infect Dis* 2013;57:197-204.
76. Jaffry M, Mostafa F, Mandava K, et al. No significant increase in Guillain-Barre syndrome after COVID-19 vaccination in adults: a vaccine adverse event reporting system study. *Vaccine* 2022;40:5791-7.
77. Lahoz Fernandez PE, Miranda Pereira J, Fonseca Risso I, et al. Guillain-Barre syndrome following COVID-19 vaccines: a scoping review. *Acta Neurol Scand* 2022;145:393-8.