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Incidence of Guillain-Barré Syndrome post COVID-19: a systematic review of case reports and case series

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Abstract. – OBJECTIVE: The purpose of this systematic review was to study the incidence, risk factors and patients subjected to Guillain-Barré Syndrome (GBS) after COVID-19.

MATERIALS AND METHODS: For qualitative assessment and assessing the methodological quality, the Cochrane Handbook for Systematic Reviews of Interventions and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA 2020) checklist were utilized. Data from PubMed, Cochrane, Embase, CINAHIL, Medline, ResearchGate, and Scopus were searched. The relevant studies involved patients with confirmed COVID-19 diagnosis by RT-PCR, and GBS diagnosis based on typical clinical symptoms and/or confirmatory diagnostic results. A total of 12 English relevant articles (6 papers were case reports and 8 were case series with a total of 32 patients) published in a peer-reviewed journal from 2019 to 2021 were included. Following the review methodology, two independent raters were responsible for retrieving, extracting and checking for data eligibility. Demographic characteristics are presented as frequencies and percentages. Based on distribution of values, continuous data were expressed as median and interquartile range (IQR).

RESULTS: Out of 32 patients, 26 patients reported neurological symptoms, 6 cases went unnoticed, 7 cases showed involvement of the cranial nerves, 12 cases did not, and 13 cases went unreported.

CONCLUSIONS: It is too early to draw any conclusions concerning a potential relationship between SARS-CoV-2 infection and GBS. More large-scale observational studies are required to understand the pathogenesis of SARS-CoV-2-associated GBS and to demonstrate a definite causal relationship between GBS and SARS-CoV-2 infection.

Key Words:
Guillain-Barré Syndrome, GBS, COVID-19, Coronavirus, SARS-CoV-2.

Introduction

Coronavirus disease (COVID-19) is a newly discovered infectious disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)[1]. It was originally reported in Wuhan, China on December 31, 2019, and since then has spread worldwide, prompting the World Health Organization to declare a worldwide pandemic on March 11, 2020[2]. Since the SARS-CoV-2 pandemic began, it has been shown[3] that the virus induces lung disease (COVID-19) and affects other organs, including the central and peripheral nervous systems (PNS, CNS), kidneys, intestines, and heart. Guillain-Barré Syndrome (GBS) is a neurological autoimmune disease that French neurologists initially described (Guillain, Barré, and Strohl), and is characterized by progressive and symmetrical limb weakness as well as paresthesia with reduced or absent deep

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tendon reflexes[4]. GBS most occurs because of upper or lower respiratory infections caused by various viruses such as *Campylobacter jejuni*, Epstein-Barr virus, influenza, or cytomegalic virus, and bacteria such as *Mycoplasma Pneumoniae*[5]. Furthermore, it has been associated[6] with a recent outbreak caused by the Zika virus in South America. During the ongoing pandemic of SARS-CoV-2, several reports[3,5] have identified GBS as a neurological complication of COVID-19 disease.

The clinical manifestation of GBS presents with muscle weakness, pain, altered sensations, loss of reflexes, and finally, progressive flaccid paralysis, which is the most serious complication[7]. As a result, early diagnosis and management of GBS induced by COVID-19 are crucial in preventing GBS from progressing to acute respiratory failure and consequently death. GBS has been classified[4,8] into different variants, including acute inflammatory demyelinating polyradiculoneuropathy (AIDP), a motor-sensory demyelinating disorder (AMSAN), and acute motor axonal neuropathy (AMAN). AIDP is recognized as a motor-sensory demyelinating disorder, while both (AMAN), and (AMSAN), are considered axonal disorders. There are also other rare variants of GBS such as Miller Fisher Syndrome (MFS), paraparetic GBS, pharyngeal-cervical-brachial weakness, bilateral facial palsy with paresthesia (BFP), and Bickerstaff brainstem encephalitis (BBE)[8]. The mechanism by which COVID-19 infection triggers GBS progression is unclear. Still, it is thought that an increase in inflammatory cytokines released in response to COVID-19 infection causes CD+4 cells to be activated, which explains the indirect neural damage[9]. GBS associated with COVID-19 is now widely documented; according to Palaiodimou et al[10] the prevalence of GBS cases associated with COVID-19 is 15%[10]. However, the clinical, laboratory, pathophysiology, and electrodiagnostic patterns are still unclear, emphasizing the need for updated research efforts. Understanding the clinical signs and symptoms that raise the suspicion of GBS, as well as the time it takes for symptoms to develop and treatment options, is crucial for improving GBS outcomes in COVID-19 patients and for identifying prophylactic procedures to overcome GBS after COVID-19. The current systematic review aimed to study the incidence, risk factors and subjected patients to GBS post COVID-19.

Materials and Methods

A review of the existing literature followed the preferred reporting items for the systematic review and meta-analysis protocols (PRISMA-P) Statement of 2015[11]. This study was registered in the International prospective register of Systematic Reviews (PROSPERO), with registry number: CRD42022318681. To comply with research guidelines in the health science field, the PRISMA-P guideline was designed to ensure research ethics, transparency, validity, accountability, and reliability that assist in developing new scientific propositions in the field of health science. The protocol adheres to the PRISMA-P guidelines which defined sections into introduction, research question, methodology, search strategy, data extraction, data analysis, results, discussion, and conclusion.

Search Strategy

The search strategy aimed to find relevant evidence from published articles. A pilot search was conducted before the main search to assist in identifying the relevant search keywords in the literature. In this stage, keywords for searching were: 'Guillain-Barre Syndrome', AND 'COVID-19', OR 'SARS-CoV-2', OR 'Corona virus'. After retrieving the relevant articles, abstracts and texts were analyzed to identify emergent index terms describing these articles. Seven electronic databases were used in the search: PubMed, Cochrane, Embase (The Excerpta Medica database), CINAHIL (Cumulative Index to Nursing and Allied Health Literature), Medline, ResearchGate, and Scopus.

Eligibility Criteria

Included studies had the following criteria: (i) English-language articles published in a peer-reviewed journal with a publication date of 2020 or later, (ii) Full texts available in an online database, (iii) Studies that are classified as a case report or case series and involved patients, (iv) Studies with patients having a positive reverse transcription polymerase chain reaction (RT-PCR) nasopharyngeal or serum antibody test for COVID-19, (v) GBS diagnosis based on typical clinical symptoms and/or confirmatory diagnostic results, such as electrophysiological or cerebrospinal fluid (CSF) investigations. Excluded studies from the further analysis were: (i) Unpublished articles (grey literature) and publications that have not been published in English, (ii) Narrative article reviews, (iii) Studies that involved patients with GBS without COVID-19 or post-COVID-19 vaccine GBS, (iv) Studies that were not related to the

study objectives, (v) Duplicated or overlapped data.

Study Selection Process

Relevant studies were assessed for inclusion criteria by two independent reviewers. The two raters were responsible for retrieving the relevant articles from the above-listed online databases and checking for eligibility. Further on, the two raters agreed on the eligibility of the selected articles (inter-rater reliability). Any discrepancies between the two raters were resolved through discussion with the senior supervisor. Selected articles were stored and managed using Mendeley reference management software version 1.19.8 (available at: https://www.mendeley.com/reference-management/reference-manager).

Data Extraction Process

For this review, data was extracted from each included study by two independent reviewers. Extracted data included the following items: study design, country, year of publication, participant characteristics, clinical presentation, the clinical presentation of GBS and its variants, intervention, treatment, and clinical outcomes. Any discrepancies over data extraction were resolved through a discussion with a third reviewer. The extracted data were stored and recorded in a predesigned excel spreadsheet.

Quality Assessment

Two reviewers checked each of the included studies for methodological quality. Eligible case reports and case series were subjected to quality control and bias assessment by using the Joanna Briggs Institute Critical Appraisal checklist (JBI).

Statistical Analysis

Descriptive statistical analysis was conducted using SPSS version 26 (IBM Corp., Armonk, NY, USA). Categorical variables (demographic characteristics) are presented as frequencies and percentages. Continuous data are expressed as median and interquartile range (IQR) based on the distribution of values.

Results

Study Selection

A total of 185 studies were identified through the initial search in electronic databases. After removing the duplicates, 91 articles were screened *via* assessment of titles and abstracts. Only 32 articles were assessed for eligibility and following full-text assessment. After excluding non-English articles (n=5), cohort studies (n=3), case report presenting GBS cases post-COV-2 vaccine (n=8) and case reports of GBS cases with a probable diagnosis of COVID-19 (n=4), only 12 relevant articles were selected for qualitative assessment and evaluation of the methodological quality in the final analysis. Figure 1 demonstrates the study selection flow using a PRISMA diagram.

Subjects

There were 12 studies discussing Guillain-Barré Syndrome post-COVID-19; six were case reports and the other were case series with a total of 32 included patients (Table I). 9 cases were females and 18 were males, with 5 unreported cases (Figure 2). The median age of patients was 61 years old (IQR=23), with 5 unreported cases (Table II).

Clinical Outcomes

The median onset of neurological symptoms was 10 days (IQR=13) with 2 unreported cases. Four cases had upper limb neurological symptoms, and 6 had lower limb neurological symptoms, while 16 suffered from both upper and lower limb neurological symptoms, with 6 unreported cases (Figure 3). Sixteen patients needed mechanical ventilation and had respiratory affection. Seven cases suffered from cranial nerve involvement, 12 did not suffer from any cranial nerve involvement, with 13 unreported cases (Figure 4). Eighteen cases had full clinical improvement, 5 cases had improved but with residual complications, and 9 cases did not get any improvement (Table III, Figure 5). Nine patients had hypertension, 4 patients were suffering from diabetes mellitus, one patient had cholelithiasis, 1 patient was suffering from chronic kidney disease, and 1 patient was suffering from hypothyroidism, with 19 unreported cases (Table IV, Figure 6).

Table V shows the distribution of cases across the country, including 16 cases from Italy and 5 from India, three from Switzerland, three from Iran, and one each from the United States, the United Kingdom, Turkey, Kuwait, and Morocco.

Discussion

This systematic review aimed to study the incidence, risk factors and patients subjected to GBS post COVID-19. The current review showed

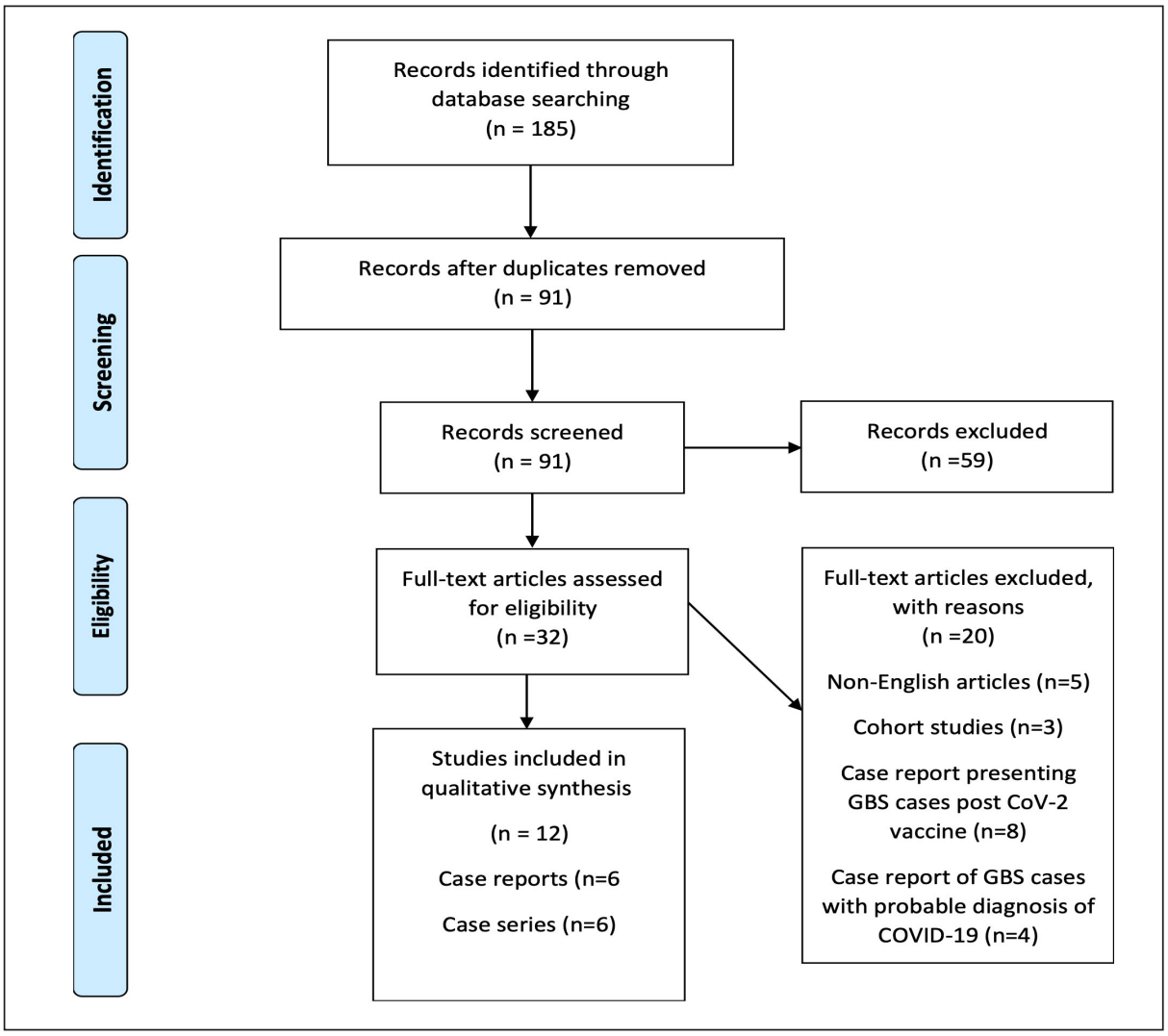


Figure 1. The flowchart of screening of studies.

demographic, clinical characteristics and clinical outcomes of patients with GBS associated with COVID-19. All included patients had GBS with a confirmed SARS-CoV-2 infection[12-23]. COVID-19 had a wide range of neurological symptoms, and GBS may be a significant sequela of the condition. GBS is a common neurological condition, and whether the frequency of GBS is higher in the context of the SARS-CoV-2 pandemic or simply a coincidence of two distinct pathologies must be determined by further examination of the available data[24]. The pathogenic effects of SARS-CoV-2 on the neurological system were likely complex, including systemic illness symptoms, direct neuro-invasion of the central nervous sysetm (CNS), involvement of the peripheral nervous system (PNS) and muscle, and a post-infectious, immune-mediated mechanism[25]. The clinical spectrum and outcomes of neurologic symptoms linked to SARS-CoV-2 infection were wide and varied, implying many underlying pathogenic mechanisms[25].

Male and elderly patients tend to be more affected than the younger generation. This finding could have an impact on SARS-CoV-2 gender epidemiology. In this regard, males typically have a worse COVID-19 outcome than females which could be attributable to a lower life expectancy or greater circulating Angiotensin Converting-Enzyme 2 (ACE2) levels[26]. Many reviews[3,27-29] stated that the majority of involved cases were men and the elderly were more susceptible to GBS post-COVID-19 infection with a mean age of 57 years; however, there are 6 pediatric cases reported[3]. In a previous systemat-

Table I. Overview of included studies.

N	Author/year/ location	Gender and sample size M/F	Outcome measures	Follow-up Duration	Result/ conclusion	QAS
Case report						
1	Taguchi et al[12] 18 Jan 2022 USA	n= 1 (F)	- Onset between COVID-19 and GBS. - Demographic characteristic. - Clinical presentation.	4 Months 6 Months	**Result:** - After 4 months. At the time of discharge rehabilitation, the patient was walking with a walker. - Within 6 months, the patient had achieved complete recovery (walking independently without assistance and complete resolution of facial weakness). **Conclusion:** GBS may developed in COVID-19 patients even months after viral diagnosis and disease resolution. Physicians should be careful not to confuse between late manifestation of GBS and chronic fatigue after COVID-19.	7/8
2	Kanou et al[13] 7 January 2022 UK	n=1 (M)	- Muscle power. - Reflex recovery. - Activities of daily living (ADL).	8 weeks 12 weeks	**Result:** The patient had recovered gradually without the use of any intravenous immunoglobulin or plasmapheresis and had discharged home to continue therapy and had been assessed in outpatient clinic few months post discharge. Patient had improved significantly, & normal power noted during the follow-up with good reflexes recovery and able to walk independently. **Conclusion:** The patient was the first presentation of GBS associated with COVID-19 which had limited disability and was self-resolving in nature. Although nerve conduction studies could not be performed for the patient, but; clinical features, CSF findings and MRI were suggestive of GBS. While immune-mediated destruction of nerve tissues is considered as the pathophysiological mechanism for GBS secondary to COVID-19, further studies were needed to establish the association of GBS and COVID-19.	7/8
3	Mehta et al[14] 30 July 2021 India	n=1 (M)	- Demographic characteristic. - Muscle power. - ICU admission.	Not reported	**Result:** The patient completely recovered and went home walking. Quadriparesis started on day 22 after the infection, with ascending muscle weakness of the LL 3/5, UL 4/5 in next day (on day 23 post-infection). **Conclusion:** Neurological involvement in COVID-19 is common, but GBS is rare, and it should be considered in a patient with quadriparesis or respiratory failure which is out of proportion to the severity of the COVID illness. All patient with GBS should be screened for COVID-19	6/8

Continued

Table I *(Continued)*. Overview of included studies.

N	Author/year/ location	Gender and sample size M/F	Outcome measures	Follow-up Duration	Result/ conclusion	QAS
4	Ackey et al[15] 12 April 2021 Turkey	n=1 (M)	- Disease course progression, (peak, and duration of weakness) and favorable outcomes on discharge.	18 Days 2 Months	**Result:** - The presence of the Albumin cytological dissociation, demyelinating GBS, and favorable outcomes on discharge are the features of GBS associated with SARS-CoV-2 infection. - This patient did not have these typical features of GBS associated with SARS-CoV-2 infection except, presence of albumin cytological dissociation. **Conclusion:** This patient was the youngest patient presenting in axonal GBS associated with SARS-CoV-2 infection. The disease course was severe with rapid progression, an earlier peak, and prolonged duration in weakness.	7/8
5	Kamel et al[15] 18 March 2021 Kuwait	n=1 (M)	- Muscle power by Medical Research Council (MRC). - Nerve conduction studies (NCS). - Comorbidity.	5 Days 1 Month	**Result:** After receiving intravenous immunoglobulins (IVIG) for five days, the patient had marked improvement in walking with unilateral support on the fifth day of infusion with no respiratory or autonomic manifestations on discharge. After 1 month, the patient showed muscle power of Medical Research Council grade 5/5 all over, with marked improvement in deep sensation examination and walking without support. **Conclusion:** Neurologists should be aware of GBS as a complication associated with COVID-19. This patient had a favorable outcome with IVIG without autonomic or respiratory affection.	7/8
6	El Aidouni et al[16] 5 august 2020 Morocco	n=1 (M)	- Muscle power. - ICU admission. - Cranial nerve involvement. - NCS. - Electromyography.	1 Month 3 Months 6 Months	**Result:** - On day 28 of GBS, patient showed significant improvement in muscles power of both upper and lower limbs and stayed in the intensive care unit. The patient was transferred to the rehabilitation center after 2 months. - The rate of recovery was approximatively 80% and the lower limb muscle power was regained after 6 months. **Conclusion:** This case report suggested the probable causal link between COVID-19 and GBS. This association prompted for further researches that may help in an early diagnosis and early treatment in order to improve morbidity and mortality.	7/8

Continued

Table I *(Continued)*. Overview of included studies.

N	Author/year/ location	Gender and sample size M/F	Outcome measures	Follow-up Duration	Result/ conclusion	QAS
Case series						
1	Abolmaali et al[17] 1 November 2020 Iran	n=3 2 (M), 1 (F)	- Muscle power by MRC. - ICU admission. - Mortality.	2 Weeks	**Result:** Three cases of GBS during the active phase of COVID-19 reported severe symptoms and fast progression of quadriplegia and facial diplegia after 2 days. - Mild muscle weakness 2-3/5. - All cases admitted to ICU. - One case died due to severe autonomic dysfunction. **Conclusion:** A severe and rapid progression of GBS appears as a neurological complication of COVID-19 could be possibly occurred during the active phase of the disease.	8/10
2	Nanda et al[18] 10 September 2020 India	n=4 3 (M), 1 (F)	- Muscle power by MRC. - NCS.	Discharged after 7-10 days	**Result:** - Muscle power 3 to 4+/5 lower limb. - NCS was suggested to severe demyelinating sensori-motor polyneuropathy in two cases and pure motor demyelinating polyneuropathy in other two cases and affecting all 4 limbs. **Conclusion:** Physicians should be aware of the association of GBS with COVID-19, as early diagnosis and treatment could lead to a favorable outcome. It is also important to differentiate GBS from critical illness neuropathy and respiratory distress secondary to COVID-19. Incorrect diagnosis could lead to a significant increase in morbidity.	9/10
3	Garnero et al[19] 02 September 2020 Italy	n=6 4 (M), 2 (F)	- Muscle power by MRC. - GBS-DS. - Requirement of mechanical ventilation	15-45 days	**Result:** - All GBS patients with pneumonia developed respiratory failure and three patients needed mechanical ventilation. Two patients developed autonomic dysfunction. - MRC score and GBS-DS were calculated after an average of 26.34 days of follow-up after the end of therapy. **Conclusion:** Not only can SARS-CoV-2 infection cause GBS, but it can also affect the outcome of patients with non-COVID-19 related GBS due to the effects of the pandemic on the health organization.	7/10

Continued

Table I *(Continued)*. Overview of included studies.

N	Author/year/ location	Gender and sample size M/F	Outcome measures	Follow-up Duration	Result/ conclusion	QAS
4	Manganotti et al[20] 6 July 2020 Italy	n=5 4 (M), 1 (F)	-NCS - Clinical presentation.	Not reported	**Result:** IVIG therapy was found to be effective and safe to treat the reported peripheral. neurological symptoms, with a good recovery in most of the patients. **Conclusion:** The use of clinical neurophysiology is better to detect abnormalities, establish the diagnosis, and promote the use of certain medications, such as IVIG, to manage these essential neurological symptoms.	8/10
5	Toscano et al[21] 17 April 2020 Italy	n=5	- NCS. - Requirement of mechanical ventilation.	4 Weeks	**Result:** Electrophysiological studies showed low compound muscle action potential amplitudes, and two patients had prolonged motor distal latencies. Generally, findings were consistent with an axonal variant of GBS in three patients and with a demyelinating process in two patients. Two patients received mechanical ventilation. **Conclusion:** It is not possible to determine whether severe deficits and axonal involvement are typical features of COVID-19-associated GBS. So, GBS with COVID-19 should be distinguished from critical illness neuropathy and myopathy, which tend to appear later in the course of critical illness than GBS.	8/10
6	Lascano et al[22] 2020 Switzerland	n=3 3 (F)	GBS-DS	5 Weeks	**Result:** Full recovery was observed in one patient, another one was able to walk with assistance and the last remained bedridden but was able to rise to standing up (GBS disability score at five weeks follow-up was 1/6, 3/6 and 4/6 respectively). **Conclusion:** The exact mechanism underlying SARS-CoV-2-associated GBS is still unclear and these observations support the hypothesis that SARS-CoV-2 triggers GBS via a secondary immune-mediated mechanism rather than a direct viral neuropathic damage.	8/10

Figure 2. Gender across the patients.

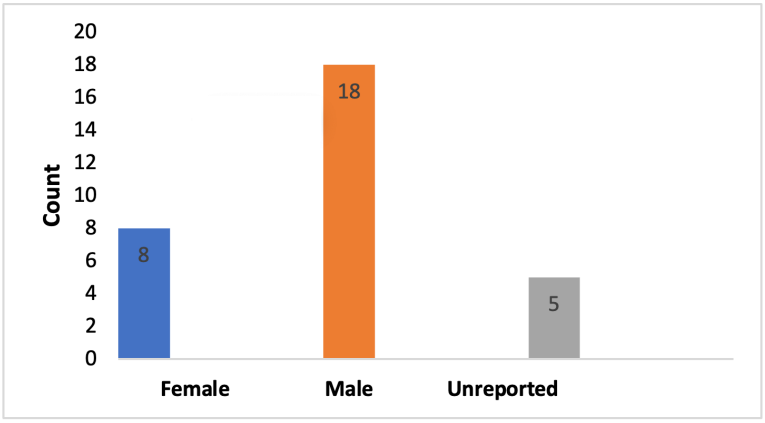


Table II. Median ages and onset of neurological symptoms of 32 patients.

		Median	IQR	Not reported
Age in years		61	23	5 cases
Onset of neurological symptoms (days)		10	13	2 cases
Gender, N (%)	Female	9	28%	5 cases
	Male	18	56%	

IQR: Inter quartile range.

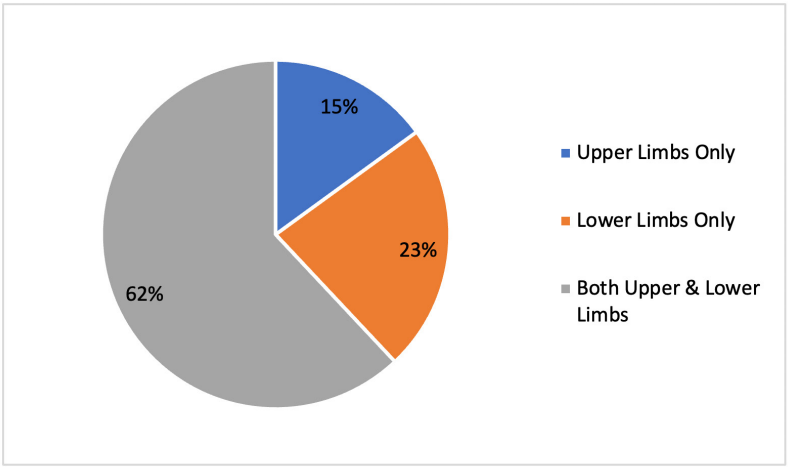


Figure 3. Area of affection across the patients.

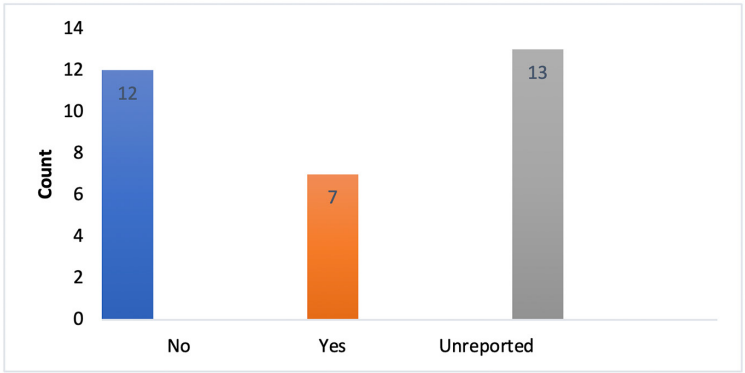


Figure 4. Involvement of cranial nerve across the patients.

Table III. Clinical characteristics of patients (32 patients).

		N	%	Not reported
Onset of neurological symptoms (days)	Median (IQR)	10	(13)	2 cases
Area of affection	Both UL and LL	16	50%	6 cases
	LL	6	19%	
	UL	4	13%	
Need for mechanical ventilation and respiratory affection	No	16	50%	0 cases
	Yes	16	50%	
Involvement of cranial nerves	No	12	38%	13 cases
	Yes	7	22%	
Clinical improvement	Yes	18	56%	0 cases
	Yes, with residual complications	5	16%	
	No	9	28%	
Received intervention				0 cases
Intravenous immunoglobulins (IVIg)		23	72%	
Intravenous immunoglobulins (IVIg), followed by plasma exchange (PLEX)		3	9%	
Intravenous immunoglobulins (IVIg)+ Methylprednisolone		1	3%	
Plasma exchange (PLEX)		2	6%	
Plasma exchange (PLEX) followed by intravenous immunoglobulins (IVIg)		2	6%	
Did not receive treatment		1	3%	

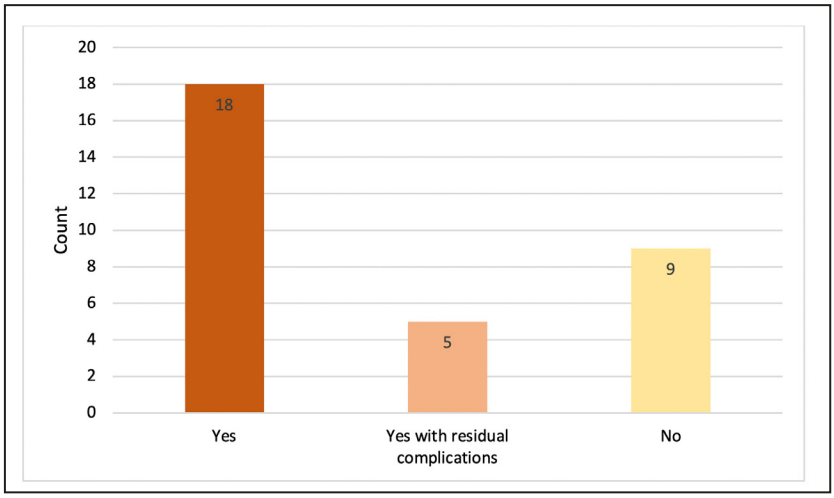
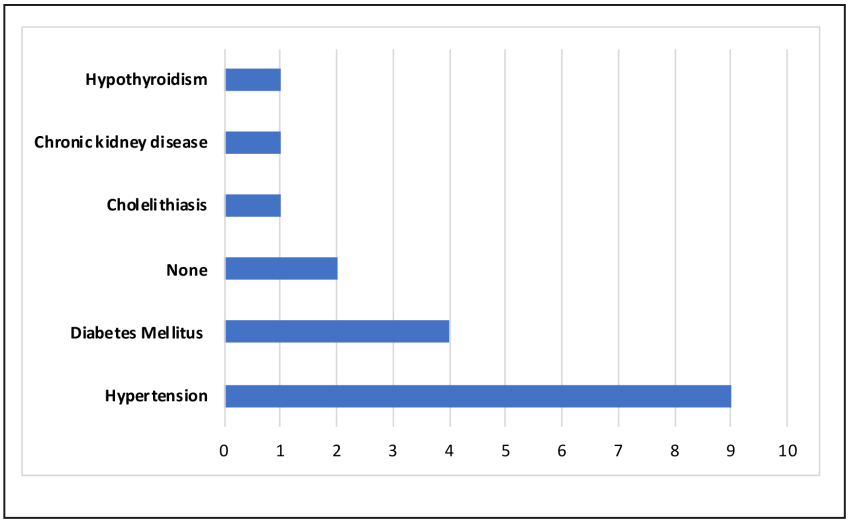


Figure 5. Clinical improvement across the patients.

Table IV. Reported comorbidities for patients in the included studies.

	N	%	Not reported
Hypertension (HTN)	9	28%	19
Diabetes mellitus (DM)	4	13%	
None	2	6%	
Cholelithiasis	1	3%	
Chronic kidney disease	1	3%	
Hypothyroidism	1	3%	

Figure 6. History of patients.



ic review conducted by Uncini et al[26], 42 patients were reported with GBS-associated COVID-19 infection. Most reported cases were men (64.3%), and the mean age of those patients was 57.5 years; the onset between COVID-19 infection and GBS was 11.5 days[26]. Comorbidities were recorded[3,28] in various ways, with no clear indication of disease prevalence and some cases with history free of illness. In the current systematic review, a number of sixteen cases were recorded (16/32) from Italy[20-22]. Most reported cases[3,10,26] are from Europe, mainly from Italy and Spain. One systematic review[29] and meta-analysis included 45 articles from 16 countries that had reported 61 SARS-CoV-2-associated GBS patients. Most articles (97.7%) came from high- and upper-middle-income countries[29]. It is unclear why SARS-CoV-2-associated GBS cases in low-income nations go unnoticed; this could be due to a variety of factors, including a lack of financial and human resources. It is also possible that cases from various countries go unreported or unpublished. In comparison to alternative therapeutic approaches, IVIg therapy appears to have been favored for SARS-CoV2-associated GBS. Most of the patients were given IVIg and had good outcomes. However, this intervention protocol is expensive for all patients in low-income countries[27-29]. No models can predict prognosis or the need for mechanical ventilation in SARS-CoV-2-GBS patients. Due to worsening GBS or COVID-19, mechanical or non-invasive ventilation was used in 21.4% (15/70) and 7.1% (5/70) of the patients, respectively[28]. Abu-Rumeileh et al[27] (n=68) reported that 72.1% (49/68) of the cases showed clinical improvement with partial or complete remission, 10.3% (7/68) of the cases showed no improvement, 11.8% (8/68) required critical care therapy, and 5.8% (4/68) died[27]. Finsterer and Scorza[3] conducted a systematic review of 220 patients with GBS-associated SARS-CoV-2 from 95 published papers. Most of the studies included in this review did not specify whether respiratory failure in SARS-CoV-2-GBS patients was caused by brainstem encephalitis, respiratory muscle involvement in GBS, pneumonia that became acute, respiratory distress syndrome (ARDS), pulmonary embolism, heart failure, or a combination of these conditions[3]. However, determining the etiology of respiratory failure is crucial because therapy and outcomes might vary greatly between various disorders[3]. Regarding cranial nerve involvement, 18 of the 61 individuals had facial palsy, whereas 11 had bulbar palsy[29]. One report[30] was a case of a 61-year-old male patient who developed facial diplegia 10 days after the onset of fever and respiratory symptoms and was treated with low doses of oral prednisone, with the recovery of both sides after two weeks. Symptoms including smell, taste, vision, and sudden hearing loss, vertigo, swallowing difficulties, and face hypoesthesia, subside com-

Table V. Patients Location (Country).

Region	N	%
Italy	16	**50%**
India	5	**15.6%**
Switzerland	3	**9.3%**
Iran	3	**9.3%**
USA	1	**3.1%**
UK	1	**3.1%**
Turkey	1	**3.1%**
Kuwait	1	**3.1%**
Morocco	1	**3.1%**

pletely during the first month of infection so cranial nerve affection may be due to the viral infection itself because it also was seen in many COVID-19 patients. Reduced nerve conduction velocities, a delayed or non-existent F wave, and attenuation of action potential amplitude were seen in electrophysiological tests, suggesting demyelination or axonal polyneuropathy. The NCS revealed the existence of AIDP (which was more common) as well as GBS axonal subtypes[31,32].

Conclusions

It is still too early to confirm any conclusions about a possible link between SARS-CoV-2 infection and GBS. More large-scale observational studies are needed to understand the pathogenesis of SARS-CoV-2-associated GBS and establish a clear causal link between GBS and SARS-CoV-2 infection.

Conflict of Interests
The authors declare that they have no conflict of interests.

Ethics Approval
Not applicable

Informed Consent
Not applicable.

Availability of Data and Materials
The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Authors' Contributions
All authors have participated in writing the manuscript.

References

1) Velavan TP, Meyer CG. The COVID-19 epidemic. Trop Med Int Health 2020; 25: 278-280.
2) Cucinotta D, Vanelli M. WHO Declares COVID-19 a Pandemic. Acta Biomed 2020; 91: 157-160.
3) Finsterer J, Scorza FA. Guillain-Barre syndrome in 220 patients with COVID-19. Egypt J Neurol Psychiatr Neurosurg 2021; 57: 55.
4) van den Berg B, Walgaard C, Drenthen J, Fokke C, Jacobs BC, van Doorn PA. Guillain-Barré syndrome: pathogenesis, diagnosis, treatment and prognosis. Nat Rev Neurol 2014; 10: 469-482.
5) Caress JB, Castoro RJ, Simmons Z, Scelsa SN, Lewis RA, Ahlawat A, Narayanaswami P. COVID-19-associated Guillain-Barré syndrome: The early pandemic experience. Muscle Nerve 2020; 62: 485-491.
6) Cao-Lormeau VM, Blake A, Mons S, Lastère S, Roche C, Vanhomwegen J, Dub T, Baudouin L, Teissier A, Larre P, Vial AL, Decam C, Choumet V, Halstead SK, Willison HJ, Musset L, Manuguerra JC, Despres P, Fournier E, Mallet HP, Musso D, Fontanet A, Neil J, Ghawché F. Guillain-Barré Syndrome outbreak associated with Zika virus infection in French Polynesia: a case-control study. Lancet 2016; 387: 1531-1539.
7) Nguyen TP, Taylor RS. Guillain Barre Syndrome. [Updated 2022 Jul 4]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022.
8) Willison HJ, Jacobs BC, van Doorn PA. Guillain-Barré syndrome. Lancet 2016; 388: 717-727.
9) Chen Z, John Wherry E. T cell responses in patients with COVID-19. Nat Rev Immunol 2020; 20: 529-536.
10) Palaiodimou L, Stefanou MI, Katsanos AH, Fragkou PC, Papadopoulou M, Moschovos C, Michopoulos I, Kokotis P, Bakirtzis C, Naska A, Vassilakopoulos TI, Chroni E, Tsiodras S, Tsivgoulis G. Prevalence, clinical characteristics and outcomes of Guillain-Barré syndrome spectrum associated with COVID-19: A systematic review and meta-analysis. Eur J Neurol 2021; 28: 3517-3529.
11) Moher D, Shamseer L, Clarke M, Ghersi D, Liberati A, Petticrew M, Shekelle P, Stewart LA; PRISMA-P Group. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. Syst Rev 2015; 4: 1-9.
12) Taguchi M, Bonner K, Memon AB. Late-Onset Guillain-Barré Syndrome and Right Facial Nerve Palsy after COVID-19 Infection. Case Rep Neurol 2022; 14: 12-18.
13) Kanou S, Wardeh L, Govindarajan S, Macnay K. Guillain-Barre syndrome (GBS) associated with COVID-19 infection that resolved without treatment in a child. BMJ Case Rep 2022; 15: 1-4.
14) Mehta SK, Sunder A. Getting paralysed after COVID: Guillain-Barre syndrome. J Family Med Prim Care 2021; 10: 2706-2708.
15) Akçay N, Menentoğlu ME, Bektaş G, Şevketoğlu E. Axonal Guillain-Barre syndrome associated with SARS-CoV-2 infection in a child. J Med Virol 2021; 93: 5599-5602.
16) Kamel WA, Ismail II, Al-Hashel JY. Guillain-Barre syndrome following COVID-19 infection: first case report from Kuwait and review of the literature. Dub Med J 2021; 4: 107-111.
17) El Aidouni G, Touihar S, Merbouh M, Aabdi M, El Kaouini A, Bouabdallaoui A, Es-Saad O, Bkiyar H, Housni B. Guillain Barre syndrome as a com-

plication of SARS-CoV-2 infection: A case report. Ann Med Surg (Lond) 2021; 68: 1-3.

18) Abolmaali M, Heidari M, Zeinali M, Moghaddam P, Ramezani Ghamsari M, Jamshidi Makiani M, Mirzaasgari Z. Guillain-Barré syndrome as a parainfectious manifestation of SARS-CoV-2 infection: A case series. J Clin Neurosci 2021; 83: 119-122.
19) Nanda S, Handa R, Prasad A, Anand R, Zutshi D, Dass SK, Bedi PK, Pahuja A, Shah PK, Sharma B. Covid-19 associated Guillain-Barre Syndrome: Contrasting tale of four patients from a tertiary care centre in India. Am J Emerg Med 2021; 39: 125-128.
20) Garnero M, Del Sette M, Assini A, Beronio A, Capello E, Cabona C, Reni L, Serrati C, Bandini F, Granata A, Pesce G, Mancardi GL, Uccelli A, Schenone A, Benedetti L. COVID-19-related and not related Guillain-Barré syndromes share the same management pitfalls during lock down: The experience of Liguria region in Italy. J Neurol Sci 2020; 418: 1-5.
21) Manganotti P, Bellavita G, D'Acunto L, Tommasini V, Fabris M, Sartori A, Bonzi L, Buoite Stella A, Pesavento V. Clinical neurophysiology and cerebrospinal liquor analysis to detect Guillain-Barré syndrome and polyneuritis cranialis in COVID-19 patients: A case series. J Med Virol 2021; 93: 766-774.
22) Toscano G, Palmerini F, Ravaglia S, Ruiz L, Invernizzi P, Cuzzoni MG, Franciotta D, Baldanti F, Daturi R, Postorino P, Cavallini A, Micieli G. Guillain-Barré Syndrome Associated with SARS-CoV-2. N Engl J Med 2020; 382: 2574-2576.
23) Lascano AM, Epiney JB, Coen M, Serratrice J, Bernard-Valnet R, Lalive PH, Kuntzer T, Hübers A. SARS-CoV-2 and Guillain-Barré syndrome: AIDP variant with a favourable outcome. Eur J Neurol 2020; 27: 1751-1753.
24) Stoian A, Bălașa R, Grigorescu BL, Maier S, Andone S, Cocuz IG, Bajko Z, Filep CR, Stoian M. Guillain-Barré syndrome associated with Covid-19: A close relationship or just a coincidence? (Review). Exp Ther Med 2021; 22: 1-7.
25) Meppiel E, Peiffer-Smadja N, Maury A, Bekri I, Delorme C, Desestret V, Gorza L, Hautecloque-Raysz G, Landre S, Lannuzel A, Moulin S, Perrin P, Petitgas P, Sellal F, Wang A, Tattevin P, de Broucker T; contributors to the NeuroCOVID registry. Neurologic manifestations associated with COVID-19: a multicentre registry. Clin Microbiol Infect 2021; 27: 458-466.
26) Jin JM, Bai P, He W, Wu F, Liu XF, Han DM, Liu S, Yang JK. Gender Differences in Patients With COVID-19: Focus on Severity and Mortality. Front Public Health 2020; 8: 1-6.
27) Uncini A, Vallat JM, Jacobs BC. Guillain-Barré syndrome in SARS-CoV-2 infection: an instant systematic review of the first six months of pandemic. J Neurol Neurosurg Psychiatry 2020; 91: 1105-1110.
28) Abu-Rumeileh S, Abdelhak A, Foschi M, Tumani H, Otto M. Guillain-Barré syndrome spectrum associated with COVID-19: an up-to-date systematic review of 73 cases. J Neurol 2021; 268: 1133-1170.
29) Hasan I, Saif-Ur-Rahman KM, Hayat S, Papri N, Jahan I, Azam R, Ara G, Islam Z. Guillain-Barré syndrome associated with SARS-CoV-2 infection: A systematic review and individual participant data meta-analysis. J Peripher Nerv Syst 2020; 25: 335-343.
30) Juliao Caamaño DS, Alonso Beato R. Facial diplegia, a possible atypical variant of Guillain-Barré Syndrome as a rare neurological complication of SARS-CoV-2. J Clin Neurosci 2020; 77: 230-232.
31) Koralnik IJ, Tyler KL. COVID-19: A Global Threat to the Nervous System. Ann Neurol 2020; 88: 1-11.
32) Webb S, Wallace VC, Martin-Lopez D, Yogarajah M. Guillain-Barré syndrome following COVID-19: a newly emerging post-infectious complication. BMJ Case Rep 2020; 13: 1-4.