SIEKIERKO, Nikola, ŻOŁNIEREK, Maja, KOTUSIEWICZ, Wiktoria, LEWANDOWSKI, Mateusz, BIENIA, Grzegorz, LUBCZYŃSKA, Zuzanna, POPRAVKO, Yevheniia & ŚWIĘTOCHOWSKI, Jakub. Guillain-Barre Syndrome linked to SARS-CoV-2 infection – meta-analysis and literature review. Journal of Education, Health and Sport. 2023;25(1):40-56. eISSN 2391-8306. DOI http://dx.doi.org/10.12775/JEHS.2023.25.01.004
https://apcz.umk.pl/JEHS/article/view/43563
https://zenodo.org/record/7886506

The journal has had 40 points in Ministry of Education and Science of Poland parametric evaluation. Annex to the announcement of the Minister of Education and Science of December 21, 2021. No. 32343.
Has a Journal's Unique Identifier: 201159. Scientific disciplines assigned: Physical Culture Sciences (Field of Medical sciences and health sciences); Health Sciences (Field of Medical Sciences and Health Sciences).
Punkty Ministerialne z 2019 - aktualny rok 40 punktów. Załącznik do komunikatu Ministra Edukacji i Nauki z dnia 21 grudnia 2021 r. Lp. 32343. Posiada Unikatowy Identyfikator Czasopisma: 201159.
Przypisane dyscypliny naukowe: Nauki o kulturze fizycznej (Dziedzina nauk medycznych i nauk o zdrowiu); Nauki o zdrowiu (Dziedzina nauk medycznych i nauk o zdrowiu).

The authors declare that there is no conflict of interests regarding the publication of this paper.
Received: 13.04.2023. Revised: 20.04.2023. Accepted: 02.05.2023. Published: 02.05.2023.

Guillain-Barre Syndrome linked to SARS-CoV-2 infection – meta-analysis and literature review

Nikola Siekierko

Szpital Praski pw. Przemienienia Pańskiego

https://orcid.org/0000-0002-1113-7112

Maja Żołnierek

Samodzielny Publiczny Specjalistyczny Szpital Zachodni im. św. Jana Pawła II

https://orcid.org/0000-0002-4860-2508

Wiktoria Kotusiewicz

Wojskowy Instytut Medyczny- Państwowy Instytut Badawczy

https://orcid.org/0000-0003-4033-0648

Mateusz Lewandowski

UNIVERSITY CLINICAL CENTER OF WARSAW MEDICAL UNIVERSITY

https://orcid.org/0000-0002-4968-1770

Grzegorz Bienia

Military Institute of Medicine-National Research Institute

https://orcid.org/0000-0001-9036-5510

Zuzanna Lubczyńska

Szpital Grochowski im. dr med. Rafała Masztaka

https://orcid.org/0000-0002-4860-2508

Yevheniia Popravko

Szpital Praski pw. Przemienienia Pańskiego

https://orcid.org/0000-0002-1164-1802

Jakub Świętochowski

Uniwersyteckie Centrum Kliniczne w Gdańsku

https://orcid.org/0000-0003-3848-6520

Abstract

Background

The novel coronavirus disease-2019 (COVID-19), which is caused by Severe Acute Respiratory Distress Syndrome coronavirus 2 (SARS-CoV2), was originally detected in Wuhan, China in December 2019. In this meta-analysis and literature review, we compared and summarized the clinical presentation, cerebrospinal fluid (CSF) and electromyography (EMG) findings and outcomes in SARS-CoV-2 patients with Guillain-Barre Syndrome (GBS) and its variants.

Methods

We conducted a literature review in February 2023 searching for terms “Guillain-Barre Syndrome and COVID-19", “SARS neurology”, “COVID-19 complications”. We used PubMed and Google Scholar databases inquiring case reports or series of cases published between April 1, 2020, and September 14, 2023.

Results

Of the 52 GBS cases 61,5% (n=32) were male and 39,5% (n=20) were female. The mean age was 57 years old. A total of 75% (n=33) patients presented acute inflammatory demyelinating polyneuropathy (AIDP) variant, 6,8% (n=3) presented acute motor axonal neuropathy (AMAN) variant, 15,9% (n=7) presented acute motor-sensory axonal neuropathy (AMSAN) variant. A total of 85,7% (n=42) of patients were diagnosed with albuminocytological dissociation. During the hospitalization, a total of 30,8% (n=16) required mechanical ventilation. A total of 61,5% (n=32) of patients were treated with a 5-day regimen of intravenous immunoglobulin (IVIG) in dose 0.4 g/kg/day. There were 46,1% (n=24) complete recoveries from GBS, 32,7% (n=17) partial recoveries and 9,6% (n=5) of patients did not respond to treatment. A total of 11,5% (n=6) of patients died.

Conclusion

It is crucial to follow patients with COVID-19 and GBS over time to estimate properly the efficacy of treatment and evaluate the real percentage of recovery and complications.

Keywords: AIDP, AMSAN, COVID-19, GBS, SARS-CoV-2

Abstrakt

Wprowadzenie

Nowa choroba COVID-19, wywoływana przez drugi koronawirus ciężkiego ostrego zespołu oddechowego (SARS-CoV2), została pierwotnie wykryta w miejscowości Wuhan w Chinach w grudniu 2019 roku. W tej metaanalizie i przeglądzie literatury porównano i podsumowywano obraz kliniczny oraz wyniki badania płynu mózgowo-rdzeniowego (CSF) i elektromiografii (EMG) u pacjentów z współistniejącym zakażeniem SARS-CoV-2 z zespołem Guillaina-Barrego (GBS) i jego wariantami.

Metody przeglądu

W lutym 2023 roku przeprowadzono przegląd literatury wyszukując następujące słowa kluczowe: „Zespół Guillaina-Barrego i COVID-19’, „SARS neurologia”, „powikłania COVID-19”. W tym celu użyto bazy danych PubMed i Google Scholar rozpatrując opisy przypadków opublikowanych między 1 kwietnia 2020 roku a 14 września 2023 roku.

Wyniki

Z 52 przypadków GBS 61,5% (n=32) stanowili mężczyźni, a 39,5% (n=20) kobiety. Średnia wieku wynosiła 57 lat. Łącznie u 75% (n=33) pacjentów wystąpił wariant ostrej demielinizacyjnej polineuropatii zapalnej(AIDP), u 6,8% (n=3) wariant ostrej ruchowej neuropatii aksonalnej (AMAN), u 15,9% (n=7) wariant ostrej ruchowo-czuciowej neuropatii aksonalnej (AMSAN). Łącznie u 85,7% (n=42) pacjentów rozpoznano rozszczepienie komórkowo-białkowe. W trakcie hospitalizacji 30,8% (n=16) pacjentów wymagało wentylacji mechanicznej.

61,5% (n=32) pacjentów otrzymało 5-dniowy schemat dożylnej immunoglobuliny (IVIG) w dawce 0,4 g/kg mc./dobę. 46,1% (n=24) całkowicie wyzdrowiało z GBS, 32,7% (n=17) wyleczyło się częściowo, a 9,6% (n=5) pacjentów nie odpowiedziało na leczenie. Łącznie zmarło 11,5% (n=6) pacjentów.
Wnioski
Kluczowym jest obserwowanie pacjentów z współistniejącym zakażeniem SARS-CoV-2 z zespołem Guillaina-Barrego (GBS) aby prawidłowo oszacować skuteczność leczenia i ocenić rzeczywisty procent wyzdrowień i powikłań.

Słowa kluczowe: AIDP, AMSAN, COVID-19, GBS, SARS-CoV-2

Abbreviations: AIDP, Acute inflammatory demyelinating polyneuropathy; AMSAN, Acute motor-sensory axonal neuropathy; AMAN, Acute motor axonal neuropathy; CoV, coronavirus; COVID-19, novel coronavirus disease-2019; COVID-19, Coronavirus infectious disease-2019; GBS, Guillain-Barre Syndrome; SARS-CoV-2, Severe Acute Respiratory Distress Syndrome coronavirus 2; PE, plasmapheresis; IVIG, Intravenous immunoglobulin; IL, Interleukin; EMG, Electromyography; CSF, Cerebrospinal fluid; RT-PCR, Reverse transcriptase polymerase chain reaction; WHO;, World Health Organization; SARS, severe acute respiratory distress syndrome; MERS, Middle East respiratory syndrome

1. Introduction

The novel coronavirus disease-2019 (COVID-19), which is caused by SARS-CoV2, was originally detected in Wuhan, China in December 2019. Due to virus' rapid spread worldwide, it promptly led to the announcement of the pandemic on March 11, 2020, by the World Health Organization (WHO). By now, January 2023, there have been 664 873 023 confirmed cases of COVID-19, including 6 724 248 deaths, reported to WHO. [1] It is the greatest and the most severe pandemic since the 1918 influenza pandemic.[2] Despite Europe being currently the leader in number of COVID-19 cases, both Americas emerge as the first continents in the number of deaths statistics.[1]

Nevertheless, SARS-CoV-2 is not the first coronavirus that humanity needs to cope with. Two outbreaks of these microorganisms have already occurred, including severe acute respiratory syndrome (SARS) in 2002 as well as Middle East respiratory syndrome (MERS) in 2012. [3] What is important, both SARS and MERS cause not only respiratory failure, but also have a definite affinity to neurons and are proven to cause damage to the nervous system. There are multiple theories on how CoV infects the human nervous system, including direct infection, blood circulation pathway, neuronal pathway, hypoxia injury, immunological factors, or the role of angiotensin-converting enzyme. [2] Several papers indicate the viruses' threatening potential and underestimated clinical effect. [4,5,6,7] Unfortunately, according to the study conducted by Peeri et al.[3], we did not draw proper conclusions from the past epidemics, and we were ill-prepared for the full-scale pandemic.

A great number of studies explore the most frequent complications of COVID-19. [10, 11] The prevailing neurological manifestations among infected patients are ischemic stroke, encephalitis and Guillain-Barre Syndrome.[7] Teixeira-Vas et al. [8] found that patients in critical state suffering from COVID-19 are more likely to develop neurological complications than other individuals in comparable condition without COVID-19. These findings encouraged us to focus on one of these neurological complications which is Guillain-Barre Syndrome and to investigate the risk factors and course of GBS in patients with COVID-19 infection.

Guillain-Barre Syndrome is an acute, immune-based polyradiculoneuropathy which influences predominantly motor, but also sensory and autonomic nerves. It presents a wide range of clinical manifestations. The most perilous condition, that may occur in up to 30% of patients, is respiratory failure due to phrenic nerve paralysis. It requires mechanical ventilation and intensive care unit admission. It is extremely important for physicians to be aware of that danger especially when it comes to COVID-19 patients. [12, 13]

The variants of GBS include motor demyelinating disorder named Acute inflammatory demyelinating polyradiculoneuropathy (AIDP); axonal disorders including Acute motor axonal neuropathy (AMAN), and Acute motor and sensory axonal neuropathy (AMSAN). Some rare variants of GBS are Miller Fisher Syndrome

(MFS), paraparetic GBS, pharyngeal-cervical-brachial weakness, bilateral facial palsy with paresthesia (BFP), Bickerstaff brainstem encephalitis (BBE). [13, 14]

Analyzing a total of 23 case reports and 8 case series comprising 52 patients with COVID-19 and GBS worldwide, we conducted a meta-analysis to outline the clinical characteristics, CSF and EMG findings, courses of disease and treatment outcomes in SARS-CoV-2 patients with GBS and its variants. Based on EMG findings and the Brighton criteria, which are useful when diagnosing GBS, we investigated the distribution of GBS variants including AIDP, AMAN, AMSAN and other mixed or atypical forms of GBS.

2. Methods

2.1 Study design

We conducted a literature review in February 2023 searching for terms “Guillain-Barre Syndrome and COVID-19", “SARS neurology”, “COVID-19 complications”. We used PubMed and Google Scholar databases to inquire about case reports or series of cases published between April 1, 2020, and September 14, 2023.

2.2. Inclusion criteria

The inclusion criteria for the case reports and case series included: 1) Patient age >18 years 2) RT-PCR nasopharyngeal or serum antibody positive test or confirmed COVID-19 diagnosis in a previous month 3) GBS diagnosis confirmed by clinical evaluation and at least one of the diagnostic tests performed: cerebrospinal fluid (CSF) study or EMG examination.

2.3. Exclusion criteria

The exclusion criteria for the studies included: 1) Patient age <18 years 2) Patients with no confirmation of COVID-19 diagnosis at the moment or in a previous month 3) Missing both diagnostic tests: CSF study and EMG 4) Studies in languages other than English

This resulted in a total of 52 cases from 31 studies as the final count for our review.

2.5. Data acquisition

From the selected studies, we extracted the following variables for our analysis: study type, date of publication, country of origin on the case, age, gender, GBS variant and clinical symptoms, diagnostic tests for SARS-CoV-2 infection including RT-PCR nasopharyngeal and serum antibodies, time between COVID-19 symptom onset and initial symptoms of GBS, requirement of mechanical ventilation, treatment including intravenous immunoglobulins (IVIG) protocol and plasma exchange (PE), cerebrospinal fluid (CSF) study including total protein levels and cell levels, EMG/ENG findings, and the recovery rate.

2.6. Data analysis

In our analysis we examined the mean and median age, gender percentage and some chronic diseases distribution amongst patients with or post COVID-19 infection and GBS. We analyzed the most frequent clinical symptoms and variants of GBS recognizing EMG studies’ results. We also explored GBS therapies and their results by checking the percentage of recovered or partially recovered patients.

3. Results

A total of 52 patients presently infected with SARS-CoV-2 or with a recent history of COVID-19 infection were used for analysis from the 33 case reports and case series published in 19 countries. Table 1. shows a detailed schedule of studies with information on their individual country, type of study (case report or case series), number of patients in the study, their age, gender, type of GBS variant.

Table 1.

S.NO.	AUTHOR	COUNTRY	TYPE OF STUDY	NO. OF PATIENT	AGE	GENDER	GBS VARIANT
1	E Agosti et al. [15]	Italy	Case report	1	68	M	AIDP
2	A Noon et al. [16]	USA	Case report	1	46	F	other
3	U Ilyas et al. [17]	USA	Case report	1	62	M	other
4	T Ahmad et al. [18]	Syria	Case series	2	49, 34	2M	Other, AMSAN
5	K F Miyajan et al. [19]	Saudi Arabia	Case Report	1	66	M	AMSAN
6	M M Al.-Zadjali et al. [20]	Oman	Case Report	1	72	M	AIDP
7	M Khaja et al. [21]	USA	Case Report	1	44	M	BFP
8	S Sharma et al. [22]	Nepal	Case Report	1	27	M	AIDP
9	A P Ivan et al. [23]	Romania	Case Series	9	56, 65, 67, 56, 56, 41, 51, 39, 51	7M, 2W	7 AIDP, 2 AMAN
10	A K Devarakonda et al. [24]	USA	Case Report	1	63	M	AIDP

11	G Cea et al. [25]	Chile	Case Series	3	48, 31, 62	3F	2AIDP, AMAN
12	R P Rane et al. [26]	USA	Case Report	1	62	F	Other
13	V Zivkovicet al. [27]	Serbia	Case Report	1	57	F	AIDP
14	K Carpenter et al. [28]	USA	Case Series	3	55, 67, 46	2M, F	AMSAN, 2 other
15	D Nigatu et al. [29]	Ethiopia	Case Report	1	70	M	AMSAN
16	N Kaeley et al. [30]	India	Case Report	1	40	F	AIDP
17	E Toy et al. [31]	Nigeria	Case Report	1	68	M	other
18	H Zhao et al. [32]	China	Case Report	1	61	F	AIDP
19	Z Sedaghat et al. [33]	Iran	Case Report	1	65	M	AIDP
20	D Ottaviani et al. [34]	Italy	Case Report	1	66	F	Mixed AIDP/AMSAN
21	P Alberti et al. [35]	Italy	Case Report	1	71	M	AIDP
22	M Padroni et al. [36]	Italy	Case Report	1	70	F	AIDP
23	M Coen et al. [37]	Switzerland	Case Report	1	70	M	AIDP

24	H El Otmani et al. [38]	Morrocco	Case Report	1	70	F	AIDP
25	E Scheidl et al. [39]	Germany	Case Report	1	54	F	AIDP
26	N Riva et al. [40]	Italy	Case Report	1	60	M	AIDP
27	A Assini et al. [41]	Italy	Case Series	2	55,60	2M	AIDP, AMSAN
28	K Bigaut et al. [42]	France	Case Series	2	48, 70	M, F	2 AIDP
29	J L Chan et al. [43]	Canada	Case Report	1	58	M	AIDP
30	G Toscano et al. [44]	Italy	Case Series	5	77, 23, 55, 76, 61	4M, F	3 AIDP, 2 AMSAN
31	A M Lascano [45]	Switzerland	Case Series	3	52, 63, 61	3F	3 AIDP

M – Male; F – Female; AIDP- Acute Inflammatory demyelinating polyneuropathy; AMSAN - Acute motor and sensory axonal neuropathy; AMAN - Acute motor axonal neuropathy; BFP- Bifacial weakness with paresthesia;

Of the 52 cases, 12 were from Italy, 9 from Romania, 8 from the US, 4 from Switzerland, 3 from Chile, 2 each from Syria and France, and 1 each from Nigeria, India, Ethiopia, Serbia, Canada, Germany, Morocco, China, Iran, Saudi Arabia, Oman and Nepal. The mean age of the patients was 57 years old, whereas the medium age was 60 years old. Of all 52 cases, 61.5% (n=32) of patients were male and 39.5% (n=20) were female. Based on EMG study results and clinical characteristics, 84.6% of patients (n=44) were of a specified GBS variant. In this group 75% (n=33) presented the AIDP variant, 6.8% (n=3) presented the the AMAN variant, 15.9% (n=7) presented the AMSAN variant and 2.27% (n=1) was diagnosed with other GBS variant which was not analyzed.

We explored 36 case reports and case series which included patients' medical history. Then, we analyzed the most frequent chronic illnesses that the patients presented. Studies showed that 19.4% (n=7) of cases suffered from diabetes mellitus type 2, 30.6% (n=11) of cases had hypertension, 13.9% (n=5) of patients were obese, 13.9% (n=5) had dyslipidemia and 36.1% (n=13) denied any chronic diseases. We also examined GBS symptoms distribution amongst patients. 92.3% (n=48) presented lower limbs weakness, 73% (n=38) presented upper limbs weakness, 86.5% (n=45) had areflexia, 28.8% (n=15) showed paresthesia, 33.3% (n=17) suffered from facial paralysis. Autonomic disorders including urinary incontinence or retention and fecal incontinence,

were present in 11.5% (n=6) of patients, dysphagia in 17.3% (n=9), dysarthria in 13.4% (n=7), sensory deficits in 32.7% (n=17) and respiratory failure, probably as a result of phrenic nerve paralysis in 13.4% (n=7) patients.

RT-PCR test or serum antibodies analysis were performed in 90.4% (n=47) of patients resulting in 89.4% (n=42) positive RT-PCR nasopharyngeal, 4.3% (n=2) negative RT-PCR nasopharyngeal, 4.3% (n=2) positive IgG and IgM antibodies and 2.1% (n=1) negative serum antibodies. Patients with a negative test result were included in the study based on recent, confirmed COVID-19 infection.

On the admission to the hospital 84.6% (n=44) of patients had COVID-19 symptoms including fever, cough and fatigue. 15.4% (n=8) were asymptomatic when it comes to upper respiratory infection symptoms.

A total of 94.2% (n=49) patients had CSF study performed. 85.7% (n=42) of these patients were diagnosed with albuminocytological dissociation which consists of elevated protein levels and normal cell count in the cerebrospinal fluid. This outcome is characteristic for GBS based on the Brighton criteria. Despite that, the lack of ACD in CSF study should not exclude GBS as a probable diagnosis.[14]

A number of 80.8% (n=42) patients had a significant history of upper respiratory tract infection which was confirmed to be COVID-19 or was highly probable of that. The mean number of days between COVID-19 symptoms onset and the beginning of GBS symptoms was 15. The median was 11 days.

During the hospitalization, a total of 30.8% (n=16) required mechanical ventilation.

We examined several protocols of treatment of GBS from which we extracted three most frequent – IVIG administered in dose 0.4 g/kg/day for 5 days, IVIG administered in dose 2 g/kg/day for 5 days and the same IVIG regimen enriched with 5 plasma exchanges (PE). Other treatments included 0.4 g/kg IVIG administered for less than 5 days, with various amounts of plasma exchange. A total of 61.5% (n=32) of patients were treated with 5 days regimen of IVIG in a dose of 0.4 g/kg/day, 9.6% (n=5) were treated with 5 days regimen of IVIG in dose 2 g/kg/day, and 7.7% (n=4) received IVIG in dose 0.4 g/kg/day and 5 PE. There were 21.1% (n=11) of patients who received other treatment or did not receive any due to financial reasons or lack of consent.

We divided the treatment results into 4 categories: recovery, which means the complete return to physical health; partial recovery, which includes patients who required rehabilitation, but were able to walk, no recovery, which means no measurable improvement in patient's symptoms and deceased, which consist of patients who suffered from respiratory failure and died. A total of 46.1% (n=24) of patients entirely recovered from GBS, 32.7% (n=17) of patients experienced only partial recovery and 9.6% (n=5) of patients did not respond to the treatment. During the hospitalization a total of 11.5% (n=6) of patients died.

Table 2. presents patients' chronic diseases, PCR-RT nasopharyngeal or antibodies test results, time between COVID-19 infection and GBS symptoms onset, CSF study results, treatment and its outcome.

Table 2.

S.NO.	PATIENT'S HISTORY	PCR-RT/ ANTIBODIES	TIME BETWEEN COVID-19 AND GBS	CSF STUDY	TREATMENT	RESULTS
1	Dyslipidemia, benign prostatic hypertrophy, hypertension, abdominal aortic aneurysm	positive	15	ACD	IVIG 0.4 5 days	recovery
2	DM2, dyslipidemia, obesity	no test conducted	60	normal	IVIG 0.4 5 days	recovery

3	DM2, hypertension, dyslipidemia, CAD	positive	6	ACD	IVIG 0.4 5 days +5PE	partial recovery
4	not known	positive	2	ACD	2PE	deceased
5	not known	positive	21	ACD	4PE	partial recovery
6	Hypertension, psychiatric illness	positive	22	ACD	IVIG 0.4 5 days	partial recovery
7	Hypertension, CAD	positive	-	ACD	IVIG 0.4 5 days	recovery
8	Hypertension, asthma	positive	-	ACD	IVIG 0.4 5 days	recovery
9	not known	positive	14	ACD	IVIG 0.4 5 days	recovery
10	no	positive	11	normal	IVIG 0.4 5 days	partial recovery
11	Hypertension, DM2, obesity	positive	-	ACD	IVIG 0.4 5 days +5PE	partial recovery
12	no	positive	1	ACD	IVIG 0.4 5 days	partial recovery
13	hypertension	positive	14	ACD	IVIG 0.4 5 days	recovery
14	no	positive	7	Not performed	IVIG 0.4 5 days	deceased
15	Obesity, dyslipidemia, history of AMSAN	positive	-	Not performed	IVIG 0.4 5 days	recovery
16	Hypertension, obesity	positive	21	ACD	IVIG 0.4 5 days	recovery

17	stroke central core disease, DM2	positive	6	ACD	IVIG 0.4 5 days	partial recovery
18	epilepsy	positive	7	ACD	IVIG 0.4 5 days +5PE	partial recovery
19	Hypertension, chronic obstructive pulmonary disease obesity	positive	35	ACD	IVIG 0.4 5 days	recovery
20	DM2 wth polyneuropathy, liver failure	positive	-	ACD	IVIG 2g 5 days	partial recovery
21	no	positive	-	ACD	IVIG 2g 5 days	recovery
22	non-specific colitis, sensory polyneuropathy	positive	12	ACD	IVIG 2g 5 days	partial recovery
23	not known	antibodies negative	21	ACD	IVIG 0.4 5 days	recovery
24	no	positive	4	ACD	IVIG 0.4 5 days	deceased
25	DM2, peripheral neuropathy	no test conducted	weeks	ACD	4 PE	recovery
26	not known	no test conducted	5	ACD	5 PE	recovery
27	no	positive	60	ACD	5 PE	recovery
28	no	positive	4	ACD	no treatment	recovery
29	no	no test conducted	12	normal	no treatment	recovery

30	hairy cell leukemia	positive	35	ACD	IVIG 5 days	0.4	recovery
31	not known	positive	-	ACD	no treatment		recovery
32	DM2	positive	14	Not performe d	IVIG 5 days	0.4	recovery
33	hypertension	negative	10	ACD	IVIG 5 days	0.4	deceased
34	Hypertension, abdominal aortic aneurysm, lung cancer	positive	7	ACD	IVIG 5 days	0.4	deceased
35	not known	positive	24	ACD	IVIG 5 days	0.4	deceased
36	not known	positive	10	ACD	IVIG 5 days	0.4	partial recovery
37	rheumatoid arthritis	positive	3	ACD	IVIG 5 days	2g	no recovery
38	no	negative	21	ACD	IVIG 5 days	0.4	recovery
29	no	positive antibodies	20	normal	IVIG 5 days	0.4	recovery
40	not known	positive	-	normal	IVIG 5 days	0.4	recovery
41	not known	positive	-	normal	IVIG 5 days	0.4	partial recovery
42	not known	positive	21	ACD	IVIG 5 days	2g	recovery

43	obesity	positive	10	ACD	IVIG 5 days	2g	partial recovery
44	no	positive	-	ACD	IVIG 5 days	0.4	no recovery
45	not known	positive	7	ACD	IVIG 2 days	0.4	no recovery
46	not known	positive	10	ACD	IVIG 5 days	0.4	partial recovery
47	not known	positive	10	ACD	IVIG 2 days	0.4	no recovery
48	not known	positive	5	ACD	IVIG 5 days	0.4	partial recovery
49	not known	positive antibodies	7	ACD	IVIG 5 days +5PE	0.4	no recovery
50	no	positive	15	ACD	IVIG 5 days	0.4	partial recovery
51	DM2	positive	7	normal	IVIG 5 days	0.4	recovery
52	no	positive	22	ACD	IVIG 5 days	0.4	partial recovery

DM2 – diabetes mellitus type 2; ACD – albuminocytological dissociation, IVIG – intravenous immunoglobulins, PE - plasmapheresis

4. Discussion

In the current study, we analyzed and reviewed a total of 52 cases of GBS with COVID-19 from 31 studies identified worldwide through different case series and reports.

Studies in COVID-19 patients have implicated a connection between GBS and SARS-CoV-2. A large Italian study of 1200 patients admitted with SARS-CoV-2 reported an incidence of 0.42% for GBS, which is much more frequent than in the general population.[44] The most frequent variant of GBS in our study was AIDP, which is consistent with the literature in general, as nearly 66% of GBS cases identified worldwide were AIDP. [46]

A latency period between COVID-19 symptoms and GBS symptoms onset has been explored in some papers. A recent study by Caress et al. revealed an average latency of 11 days from the beginning of COVID-19 infection to the GBS symptoms presentation, [47] which is congenial to our result (mean of 15 days, median of 11 days). There are some papers reporting GBS in SARS-CoV-2 individuals who had no upper respiratory tract infection symptoms. [20, 21, 23, 28] Furthermore, Zhao et al. and Cea et al. also reported cases where the latency period was 0 days as GBS symptoms preceded COVID-19 symptoms.[25,32]

The postponement of GBS neurological features is related to the pathogenesis of GBS in SARS-CoV-2 infection. It is proved that there are autoantibodies produced as an immune response to epitopes to the infectious agents that then cross-react with similar component of peripheral nerve. It leads to delayed damage to the peripheral nerve causing demyelination.9 This process was already determined in GBS patients, in which the presence of anti-GM1 antibodies was significantly associated with *C. jejuni* infections. [48]

One of the criteria supporting a diagnosis of GBS is CSF protein elevation and CSF cell count <10/mm3. This albuminocytologic dissociation (ACD) is observed in up to 90% of all patients during the third week of the disease course. [49.] We observed ACD result in CSF study in 85,7% of individuals.

Another supportive criterion of GBS is electrophysiologic features of demyelination. Despite that, it is also known that the criteria have their limitations and can often underestimate axonal pathology. The electrophysiology of GBS is a dynamic process and a single nerve conduction study may not reflect the proper pathophysiology. [14 66]

There are some papers which confirm the efficacy of intravenous immunoglobulin (IVIG) and plasma exchange (PE) and do not favor any of them. [50] If we compare these treatments regarding their mechanisms of action, we notice that IVIG inhibits macrophage activation, prevents antibodies from binding to neurons and complement from activation and dimerizes antiganglioside IgG antibodies, whereas PE damages antiganglioside IgG antibodies and inflammatory cytokines. [51 52 53] In our analysis IVIG appeared to be the most often prescribed in GBS in regimen of 0.4 g/kg per day, for five consecutive days. As Beydoun et al. investigated, it is the most frequently chosen therapy in GBS due to its simple procedure and machine-independent attribute. [54] IVIG is not only easy to administer, but it also significantly hastens recovery. [50] Nevertheless, according to Greene-Chandos and Torbey [55] patients may need another dose of IVIG due to treatment-related fluctuation, which is a sudden deterioration of a patient's condition following treatment-induced improvement. It is associated with disease lasting beyond the effect of immunotherapy and may concern about 10% of patients. [56]

In our analysis, PE as a sole treatment was implemented in 9.6% (n=5) of cases and PE along with a high dose of IVIG was administered in 7.7% (n=4) of cases. Worldwide, PE is administered in around 4% of GBS patients, except from several countries (the United States 15%, Malaysia 33%, and Italy 30%). Also, there is a cohort of patients who are not responding to IVIG therapy and about 10% of these individuals are shifted to PE regimen. [52] The usual PE regimen is 5 sessions with 40–50 ml plasma/kg per session within 7–14 days [53] so the treatment is slightly longer than IVIG protocol. Despite the general good tolerance, PE also poses the risk of treatment-related fluctuation. [55]

All in all, IVIG and PE seem to carry comparable risks of adverse events. The procedure of PE is relatively complicated and a specialized team is needed to perform it.[57] According to Charra et al. [58], if we take into consideration mechanically ventilated patients with GBS, they present shorter hospitalization and motility recuperation when treated with IVIG rather than PE, which suggests the superiority of IVIG to PE in ICU patients. The cost of therapy is relative, depending on national valuation, for instance in the United States PE is associated with longer hospitalization (17.78 vs. 10.24 days), and greater cost ($149,143 vs. $103,223) as compared with IVIG [54], whereas in Bangladesh a full course of IVIG costs about $ 12,000–16,000 and conventional PE within 5 days costs about $ 4,500–5,000. [59]

GBS presents as muscle weakness which may also include respiratory muscles weakness (oropharyngeal, laryngeal, tongue, retropharyngeal, intercostal, and diaphragmatic weakness). It provokes the loss of airway protection, ineffective cough, and multiple pulmonary complications. [60] Another difficulty is bulbar palsy and dysautonomia which weakens the secretion clearing process and thus enlarges the risk of pulmonary infection and respiratory failure. [61] In our study a total of 30,8% (n=16) patients required mechanical ventilation (MV). Shang et al. [62] explored that up to 30% of patients with GBS develop respiratory failure requiring intensive care unit (ICU) admission and MV. Nevertheless, decision-making of intubation and MV in patients with GBS and respiratory failure require a multispecialty team as emergency intubation may lead to life-threatening complications. Respiratory failure may be observed when one of the following criteria is met: (a) vital capacity (VC) < 20 ml/kg, (b) maximal inspiratory pressure (MIP) < 30 cmH2O, (c) maximal expiratory pressure (MEP) < 40 cmH2O. [63] A higher intubation risk can occur in shorter duration from symptom onset to hospital admission,

bulbar, facial or neck weakness, and severe muscle weakness at the admission. [64] Furthermore, quick progression of motor weakness, the involvement of both peripheral and axial muscles, ineffective cough, bulbar muscle weakness, dysphagia and a sudden decrease in VC at admission or during ICU stay are the key indicators for the upcoming need for MV in GBS patients. [65]

5. Conclusions

In this systematic meta-analysis and review, we compared and summarized the clinical presentation, CSF and EMG findings and outcomes in SARS-CoV-2 patients with GBS and its variants. The mean patients' age was 57 and the median age was 60. Patients were mostly male and predominantly did not have any chronic diseases. The most frequent symptoms were upper and lower limbs weakness and areflexia. All the patients had a positive RT-PCR nasopharyngeal swab, positive serum anti-SARS antibodies or had a history of COVID-19 infection in a few weeks time. The mean interval between COVID-19 infection and GBS symptoms onset was around 15 days and the median was 11. CSF study mainly indicated albuminocytological dissociation. EMG examination showed the dominance of the AIDP variant of GBS. The majority of patients were treated with IVIG and some of them received the additional PE treatment. The literature does not indicate the best possible therapy for GBS and the choice depends on the medical team's decision and experience. The outcome was generally positive, but not all the patients regained full mobility and some of them required rehabilitation. What is missing in the analyzed case reports and case series is long-term prognosis in patients with GBS and COVID-19 so it would be valuable to follow these patients over time to properly estimate the frequency of complications in this condition.

Bibliography

1.WHO coronavirus (COVID-19) dashboard. WHO Coronavirus (COVID-19) Dashboard With Vaccination Data. Accessed January 26, 2023. https://covid19.who.int/

2.Taubenberger JK, Morens DM. 1918 Influenza: the Mother of All Pandemics. *Emerging Infectious Diseases*. 2006;12(1). doi:10.3201/eid1201.050979

3.Peeri NC, Shrestha N, Rahman MS, et al. The SARS, MERS and novel coronavirus (COVID-19) epidemics, the newest and biggest global health threats: what lessons have we learned? *International Journal of Epidemiology*. 2020;49(3):717-726. doi:10.1093/ije/dyaa033

4.Wu Y, Xu X, Chen Z, et al. Nervous system involvement after infection with COVID-19 and other coronaviruses. *Brain, Behavior, and Immunity*. 2020;87. doi:10.1016/j.bbi.2020.03.031

5.Li Y, Bai W, Hashikawa T. The neuroinvasive potential of SARS-CoV2 may play a role in the respiratory failure of COVID-19 patients. *Journal of Medical Virology*. 2020;92(6). doi:10.1002/jmv.25728

6.Baig AM, Khaleeq A, Ali U, Syeda H. Evidence of the COVID-19 Virus Targeting the CNS: Tissue Distribution, Host–Virus Interaction, and Proposed Neurotropic Mechanisms. *ACS Chemical Neuroscience*. 2020;11(7). doi:10.1021/acschemneuro.0c00122

7.Berger JR. COVID-19 and the nervous system. *Journal of Neurovirology*. 2020;26(2). doi:10.1007/s13365-020-00840-5

8.Teixeira-Vaz A, Rocha JA, Reis DA e, et al. Critical COVID-19 and neurological dysfunction - a direct comparative analysis between SARS-CoV-2 and other infectious pathogens. *Revista Brasileira de Terapia Intensiva*. 2022;34(3). doi:10.5935/0103-507X.20220229-en

9.Ellul MA, Benjamin L, Singh B, et al. Neurological associations of COVID-19. *The Lancet Neurology*. 2020;19(9). doi:10.1016/S1474-4422(20)30221-0

10.Chams N, Chams S, Badran R, et al. COVID-19: A Multidisciplinary Review. *Frontiers in Public Health*. 2020;8. doi:10.3389/fpubh.2020.00383

11.Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *Lancet (London, England)*. 2003;395(10229). doi:10.1016/S0140-6736(20)30566-3

12.Ottaviani D, Boso F, Tranquillini E, et al. Early Guillain-Barré syndrome in coronavirus disease 2019 (COVID-19): a case report from an Italian COVID-hospital. *Neurological Sciences*. 2020;41(6). doi:10.1007/s10072-020-04449-8

13.Shang P, Feng J, Wu W, Zhang HL. Intensive Care and Treatment of Severe Guillain–Barré Syndrome. *Frontiers in Pharmacology*. 2021;12. doi:10.3389/fphar.2021.608130

14.Willison HJ, Jacobs BC, van Doorn PA. Guillain-Barré syndrome. *The Lancet*. 2016;388(10045):717-727. doi:10.1016/S0140-6736(16)00339-1

15.Agosti E, Giorgianni A, D'Amore F, Vinacci G, Balbi S, Locatelli D. Is Guillain-Barrè syndrome triggered by SARS-CoV-2? Case report and literature review. *Neurological Sciences*. 2021;42(2). doi:10.1007/s10072-020-04553-9

16.Noon A, Malhi JK, Wong CK. Atypical Guillain-Barré Syndrome Presenting After COVID-19 Infection. *Cureus*. 2022;14(9). doi:10.7759/cureus.29521

17.Ilyas U, Umar Z, Bhangal R, Shah D, Fayman B. Guillain-Barré Syndrome: A Sequela of the Original COVID-19 Infection or Vaccination. *Cureus*. 2022;14(8). doi:10.7759/cureus.28044

18.Ahmad T, Hamdan S, Saadeh I. Guillain–Barré Syndrome Associated with COVID-19: Two Cases from a Public Hospital in Damascus, Syria. *Case Reports in Medicine*. 2022;2022. doi:10.1155/2022/9722736

19.Miyajan KF, Alyamani NA, Zafer DO, Tawakul AA. Guillain-Barré Syndrome in an Elderly Patient as a Complication of COVID-19 Infection. *Cureus*. 2021;13(10). doi:10.7759/cureus.19154

20.Al-Zadjali MM, Shibli EA, Maskari MA, Gujjar AR, Asmi AA. Post-COVID-19 Guillain-Barré Syndrome: A case report from Oman. *Sultan Qaboos University Medical Journal*. 2022;22(3). doi:10.18295/squmj.6.2021.090

21.Khaja M, Gomez GPR, Santana Y, et al. A 44-Year-Old Hispanic Man with Loss of Taste and Bilateral Facial Weakness Diagnosed with Guillain-Barré Syndrome and Bell's Palsy Associated with SARS-CoV-2 Infection Treated with Intravenous Immunoglobulin. *The American Journal of Case Reports*. 2020;21. doi:10.12659/AJCR.927956

22.Sharma S, Adhikari A, Ghimire N, Mainali G, Yadav SK, Rajkarnikar R. Guillain-Barré Syndrome associated with SARS-CoV-2 infection in Nepal: A case report. *Annals of Medicine and Surgery*. 2022;80. doi:10.1016/j.amsu.2022.104214

23.Ivan AP, Odajiu I, Popescu BO, Davidescu EI. COVID-19 Associated Guillain–Barré Syndrome: A Report of Nine New Cases and a Review of the Literature. *Medicina*. 2022;58(8). doi:10.3390/medicina58080977

24.Devarakonda AK, Stumpe TR, Saucier AN, Riley T. Neurological Consequences of COVID-19: A Curious Case of Delayed Onset Guillain-Barre. *Cureus*. 2022;14(5). doi:10.7759/cureus.25325

25.Cea G, Romero C, Aguilar S, et al. Guillain-Barré syndrome in patients with SARS-CoV-2 infection. Report of three cases. *Revista médica de Chile*. 149(12):1812-1816. doi:10.4067/s0034-98872021001201812

26.Rane RP, Jain A, Hussain KM, Naik S, Shahab A. A Rare Case of Guillain-Barré Syndrome Associated With SARS-CoV-2 Infection Requiring Mechanical Ventilation. *Cureus*. 2022;14(6). doi:10.7759/cureus.25810

27.Živković V, Gačić EM, Djukić D, Nikolić S. Guillain–Barré syndrome as a fatal complication of SARS-CoV-2 infection – An autopsy case. *Legal Medicine (Tokyo, Japan)*. 2022;57. doi:10.1016/j.legalmed.2022.102074

28.Carpenter K, Iqbal A, Singh R, et al. COVID-19 Infection and Guillain-Barre Syndrome: A Case Series. *Cureus*. 2022;14(2). doi:10.7759/cureus.21998

29.Nigatu D, Tigabu T, Awraris M, Yohannes A, Kebede D. Guillain-Barré Syndrome Associated with SARS CoV-2 Infection: Case Report. *Ethiopian Journal of Health Sciences*. 2022;32(1). doi:10.4314/ejhs.v32i1.21

30.Kaeley N, Kabi A, Pillai A, Shankar T, S alva AMS. Post-COVID-19 Guillain-Barré Syndrome: A Case Report With Literature Review. *Cureus*. 2022;14(1). doi:10.7759/cureus.21246

31.Toy E, Kart K. Intensive care management in guillain barré syndrome accompanying prolonged Covid-19–A case report. *Nigerian Journal of Clinical Practice*. 2022;25(2). doi:10.4103/njcp.njcp_85_21

32.Zhao H, Shen D, Zhou H, Liu J, Chen S. Guillain-Barré syndrome associated with SARS-CoV-2 infection: causality or coincidence? *The Lancet Neurology*. 2020;19(5). doi:10.1016/S1474-4422(20)30109-5

33.Sedaghat Z, Karimi N. Guillain Barre syndrome associated with COVID-19 infection: A case report. *Journal of Clinical Neuroscience*. 2020;76. doi:10.1016/j.jocn.2020.04.062

34.Ottaviani D, Boso F, Tranquillini E, et al. Early Guillain-Barré syndrome in coronavirus disease 2019 (COVID-19): a case report from an Italian COVID-hospital. *Neurological Sciences*. 2020;41(6). doi:10.1007/s10072-020-04449-8

35.Alberti P, Beretta S, Piatti M, et al. Guillain-Barré syndrome related to COVID-19 infection. *Neurology® Neuroimmunology & Neuroinflammation*. 2020;7(4). doi:10.1212/NXI.0000000000000741

36.Padroni M, Mastrangelo V, Asioli GM, et al. Guillain-Barré syndrome following COVID-19: new infection, old complication? *Journal of Neurology*. 2020;267(7). doi:10.1007/s00415-020-09849-6

37.Coen M, Jeanson G, Almeida LAC, et al. Guillain-Barré syndrome as a complication of SARS-CoV-2 infection. *Brain, Behavior, and Immunity*. 2020;87. doi:10.1016/j.bbi.2020.04.074

38.Otmani HE, Moutawakil BE, Rafai MA, et al. Covid-19 and Guillain-Barré syndrome: More than a coincidence! *Revue Neurologique*. 2020;176(6). doi:10.1016/j.neurol.2020.04.007

39.Scheidl E, Canseco DD, Hadji-Naumov A, Bereznai B. Guillain-Barr é syndrome during SARS-CoV -2 pandemic: A case report and review of recent literature. *Journal of the Peripheral Nervous System*. 2020;25(2):204-207. doi:10.1111/jns.12382

40.Riva N, Russo T, Falzone YM, et al. Post-infectious Guillain–Barré syndrome related to SARS-CoV-2 infection: a case report. *Journal of Neurology*. 2020;267(9). doi:10.1007/s00415-020-09907-z

41.Assini A, Benedetti L, Maio SD, Schirinzi E, Sette MD. New clinical manifestation of COVID-19 related Guillain-Barrè syndrome highly responsive to intravenous immunoglobulins: two Italian cases. *Neurological Sciences*. 2020;41(7). doi:10.1007/s10072-020-04484-5

42.Bigaut K, Mallaret M, Baloglu S, et al. Guillain-Barré syndrome related to SARS-CoV-2 infection. *Neurology® Neuroimmunology & Neuroinflammation*. 2020;7(5). doi:10.1212/NXI.0000000000000785

43.Chan JL, Ebadi H, Sarna JR. Guillain-Barré Syndrome with Facial Diplegia Related to SARS-CoV-2 Infection. *Canadian Journal of Neurological Sciences / Journal Canadien des Sciences Neurologiques*. 2020;47(6):852-854. doi:10.1017/cjn.2020.106

44.Toscano G, Palmerini F, Ravaglia S, et al. Guillain–Barré Syndrome Associated with SARS-CoV-2. *New England Journal of Medicine*. 2020;382(26):2574-2576. doi:10.1056/nejmc2009191

45.Lascano AM, Epiney J -b., Coen M, et al. SARS-CoV-2 and Guillain–Barré syndrome: AIDP variant with a favourable outcome. *European Journal of Neurology*. 2020;27(9). doi:10.1111/ene.14368

46.Berg B van den, Walgaard C, Drenthen J, Fokke C, Jacobs BC, van Doorn PA. Guillain-Barré syndrome: pathogenesis, diagnosis, treatment and prognosis - PubMed. *Nature reviews Neurology*. 2014;10(8). doi:10.1038/nrneurol.2014.121

47.Caress JB, Castoro RJ, Simmons Z, et al. COVID-19–associated Guillain-Barré syndrome: The early pandemic experience. *Muscle & Nerve*. 2020;62(4). doi:10.1002/mus.27024

48.Jacobs BC, van Doorn PA, Tio-Gillen AP, et al. Campylobacter jejuni infections and anti-GM1 antibodies in guillain-barré syndrome. *Annals of Neurology*. 40(2):181-187. doi:10.1002/ana.410400209

49.Dimachkie MM, Barohn RJ. Guillain-Barré Syndrome and Variants. *Neurologic clinics*. 2013;31(2). doi:10.1016/j.ncl.2013.01.005

50.Hughes RA, Swan AV, van Doorn PA. Intravenous immunoglobulin for Guillain-Barré syndrome - Hughes, RAC - 2014. *Cochrane Database of Systematic Reviews*. 2014;(9). doi:10.1002/14651858.CD002063.pub6

51.Shang P, Feng J, Wu W, Zhang HL. Intensive Care and Treatment of Severe Guillain–Barré Syndrome. *Frontiers in Pharmacology*. 2021;12. doi:10.3389/fphar.2021.608130

52.Verboon C, van Doorn PA, Jacobs BC. Treatment dilemmas in Guillain-Barré syndrome. *Journal of Neurology, Neurosurgery & Psychiatry*. 2017;88(4):346-352. doi:10.1136/jnnp-2016-314862

53.Chevret S, Hughes RA, Annane D. Plasma exchange for Guillain-Barré syndrome. *The Cochrane Database of Systematic Reviews*. 2017;2017(2). doi:10.1002/14651858.CD001798.pub3

54.Beydoun HA, Beydoun MA, Hossain S, Zonderman AB, Eid SM. Nationwide study of therapeutic plasma exchange vs intravenous immunoglobulin in Guillain-Barré syndrome. *Muscle & Nerve*. 61(5):608-615. doi:10.1002/mus.26831

55.Greene-Chandos, Torbey. Critical Care of Neuromuscular Disorders : CONTINUUM: Lifelong Learning in Neurology. LWW. https://journals.lww.com/continuum/Abstract/2018/12000/Critical_Care_of_Neuromuscular_Disorders.11.aspx

56.Kleyweg RP, Meché FG van der. Treatment related fluctuations in Guillain-Barré syndrome after high-dose immunoglobulins or plasma-exchange. *Journal of Neurology, Neurosurgery, and Psychiatry*. 1991;54(11). doi:10.1136/jnnp.54.11.957

57.El-Bayoumi MA, El-Refaey AM, Abdelkader AM, El-Assmy MM, Alwakeel AA, El-Tahan HM. Comparison of intravenous immunoglobulin and plasma exchange in treatment of mechanically ventilated children with Guillain Barré syndrome: a randomized study. *Critical Care*. 2011;15(4). doi:10.1186/cc10305

58.Charra B, Hachimi A, Benslama A, Motaouakkil S. Intravenous immunoglobulin vs plasma exchange in treatment of mechanically ventilated adults with Guillain-Barré syndrome. *The Pan African Medical Journal*. 2014;18. doi:10.11604/pamj.2014.18.35.2911

59.Islam B, Islam Z, Rahman S, et al. Small volume plasma exchange for Guillain-Barré syndrome in resource-limited settings: a phase II safety and feasibility study. *BMJ Open*. 2018;8(8). doi:10.1136/bmjopen-2018-022862

60.Hahn AF. The Challenge of Respiratory Dysfunction in Guillain-Barré Syndrome. *Archives of Neurology*. 2001;58(6):871-872. doi:10.1001/archneur.58.6.871

61.Chakraborty, Kramer, Wijdicks, Rabinstein. Dysautonomia in Guillain–Barré Syndrome: Prevalence, Clinical Spectrum, and Outcomes. *Neurocritical Care*. 2019;32(1):113-120. doi:10.1007/s12028-019-00781-w

62.Shang P, Zhu M, Baker M, Feng J, Zhou C, Zhang HL. Mechanical ventilation in Guillain-Barré syndrome - PubMed. *Expert review of clinical immunology*. 2020;16(11). doi:10.1080/1744666X.2021.1840355

63.Lawn ND, Fletcher DD, Henderson RD, Wolter TD, Wijdicks EF. Anticipating mechanical ventilation in Guillain-Barré syndrome - PubMed. *Archives of neurology*. 2001;58(6). doi:10.1001/archneur.58.6.893

64.Green C, Baker T, Subramaniam A. Predictors of respiratory failure in patients with Guillain-Barré syndrome: a systematic review and meta-analysis - PubMed. *The Medical journal of Australia*. 2018;208(4). doi:10.5694/mja17.00552

65.Umer SR, Nisa Q, Kumari M, Abbas S, Mahesar SA, Shahbaz NN. Clinical Features Indicating the Need for Mechanical Ventilation in Patients with Guillain Barre Syndrome. *Cureus*. 2019;11(8):e5520. doi:10.7759/cureus.5520

66.Hadden RDM, Cornblath DR, Hughes RAC, et al. Electrophysiological classification of guillain-barré syndrome: Clinical associations and outcome. *Annals of Neurology*. 44(5):780-788. doi:10.1002/ana.410440512