Caspian Journal of Neurological Sciences
"Caspian J Neurol Sci"
Journal Homepage: http://cjns.gums.ac.ir

Research Paper: Guillain-Barré Syndrome During the COVID-19 Pandemic and Pre-pandemic Periods

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Citation Besharati A, Saberi A, Ghorbani Shirkouhi S, Ashraf A, Hatamian H, Eslami Kenarsari H, et al. Guillain-Barré Syndrome During the COVID-19 Pandemic and Pre-pandemic Periods. Caspian J Neurol Sci. 2022; 8(1):33-38. https://doi.org/10.32598/CJNS.8.28.213.2

Running Title Guillain-Barré Syndrome & COVID-19

https://doi.org/10.32598/CJNS.8.28.213.2

Article info:
Received: 31 Aug 2021
First Revision: 05 Sep 2021
Accepted: 09 Oct 2021
Published: 01 Jan 2022

ABSTRACT

Background: Guillain-Barré Syndrome (GBS) is an autoimmune disease that may occur after infections. As Coronavirus Disease 2019 (COVID-19) may bring about GBS, it is important to assess the effect of the COVID-19 pandemic on this disease

Objectives: This study aimed to compare the distribution and characteristics of GBS during and before the COVID-19 pandemic in an academic referral hospital in the north of Iran.

Materials & Methods: This retrospective study assessed GBS distribution and characteristics during the COVID-19 pandemic period (from March 2020 to the end of February 2021) and before the pandemic (from March 2019 to the end of February 2020) on 5340 patients referred to the Neurology Ward of Poursina Hospital of Guilan Province, in Iran.

Results: There was no significant difference between GBS distribution during (0.03%) and before (0.04%) the COVID-19 pandemic (P=0.413). There were also no differences between the two periods regarding the gender (P=0.659) and age (P=0.417) of the patients. The most common subtype of GBS during the COVID-19 pandemic was Acute Motor and Sensory Axonal Neuropathy (AMSAN) (71.4%). In both periods, the most common type of treatment was intravenous administration of immune globulin. There was no significant difference between the two periods (P=0.838) regarding the patients' treatment response.

Conclusion: The distribution of GBS, its subtypes, type of treatment, and response to treatment were not different between the two study periods.

Keywords: COVID-19, Guillain-Barré syndrome, Autoimmune diseases

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Highlights

- There is no difference between the demographic parameters, type of treatment, and treatment to therapy in patients with GBS during and before the COVID-19 pandemic.

- AMSAN (acute motor and sensory axonal neuropathy) was the most prevalent subtype of GBS during the COVID-19 pandemic.

- The rate of complete recovery in the COVID-19 pandemic period was lower than that before the pandemic.

Introduction

Guillain-Barré syndrome (GBS) is the most common cause of acute flaccid paralysis worldwide [1]. In two-thirds of the patients, a probable recent infection and respective neuroinflammation cause the syndrome [2, 3]. GBS is divided into four main subtypes: Acute Inflammatory Demyelinating Polyneuropathy (AIDP), axonal subtypes such as Acute Motor Axonal Neuropathy (AMAN), acute motor and sensory axonal neuropathy (AMSAN), and Miller-Fisher Syndrome (MFS) [4, 5]. Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) has different degrees of neurotropism. The S glycoprotein of the virion is attached to angiotensin-converting enzyme 2 receptors on the host cells, and endocytosis occurs [6].

Coronavirus Disease 2019 (COVID-19) has Central Nervous System (CNS) manifestations [7], such as arterial and venous stroke [7-12] and myelitis [13, 14]. In addition, COVID-19 brings about various Peripheral Nervous System (PNS) manifestations [15]. COVID-19 may involve the PNS even before the resolution of pneumonia, thus meeting acute polyradiculoneuropathy diagnostic criteria [16]. There is a cytokine storm in COVID-19. Patients with COVID-19 show elevated levels of interferon gamma-induced protein 10, granulocyte-macrophage colony-stimulating factor, monocyte chemoattractant protein 1, and circulating interleukin-2 (IL-2), IL-8, and IL-17 [17]. SARS-CoV-2 can bind to Toll-like receptors and result in the synthesis and release of IL-1 [18, 19]. In COVID-19, an increased level of IL-6 is also seen [20]. The PNS involvement in COVID-19 may be caused by the SARS-CoV-2 dysregulating systemic immune response [15].

GBS has been reported after COVID-19 [15] and may be caused by dysregulation of the immune system arising from COVID-19 [21]. A systematic review argued that the time interval between the onset of COVID-19 symptoms and GBS might range from 8 to 24 days. A typical GBS with a predominantly demyelinating subtype on electrophysiological studies was found in most patients. In addition, mechanical ventilation was required for 44% of patients, despite the death of 11% of the patients [22]. In the present study, we assessed the distribution and characteristics of GBS patients during the COVID-19 pandemic period and compared them with those before the pandemic.

Materials and Methods

This retrospective study reviewed medical records of patients referred to the neurology ward of Poursina Hospital in Guilan Province of Iran during the COVID-19 pandemic period (from March 2020 to February 2021) and before the pandemic (from March 2019 to February 2020). Data including subtype of GBS, type of treatment, the response to treatment, and demographic data were collected from the hospital record system. COVID-19 diagnosis had been made based on the lung Computed Tomography (CT) scan and Polymerase Chain Reaction (PCR). The subtype of GBS had been diagnosed based on the Nerve Conduction Velocity (NCV) records in the patients based on Uncini's criteria [23]. Recovery of the patients had been defined as complete (the force or sense of the limbs back to baseline), partial (the force or sense of the limbs changed partially but did not return to baseline), and no recovery (lack of change in the force or sense of the limbs). The force of the limbs had been determined based on Medical Research Council (MRC) score [24]. Recovery had been assessed in all patients one week after discharge. The collected data were analyzed using IBM SPSS for Windows, version 22. (IBM Corp., Armonk, NY, USA). We used a t test and non-parametric test to compare quantitative data. Furthermore, the Mann-Whitney or Chi-square tests were used to compare the qualitative data.

Table 1. Demographic information of the GBS patients and comparing different variables before and during the pandemic

Variables		No. (%)			Fisher Exact Test	P
		Total	Before the Pandemic	COVID-19 Pandemic		
Gender	Male	11(52.4)	8(57.1)	3(42.9)	0.382	0.659
	Female	10(47.6)	6(42.9)	4(57.1)		
GBS subtype	AIDP	6(28.6)	5(35.7)	1(14.3)	2.13	0.421
	AMAN	5(23.8)	4(28.6)	1(14.3)		
	AMSAN	10(47.6)	5(35.7)	5(71.4)		
Treatment	Plasmapheresis	2(9.6)	0(0)	2(28.2)	4.4	0.987
	IVIG	19(90.5)	14(100)	5(71.4)		
Treatment response	No recovery	4(19)	2(14.3)	2(26.8)	0.932	0.838
	Partial recovery	9(42.9)	6(42.9)	3(42.9)		
	Complete recovery	8(38.1)	6(42.9)	2(26.8)		

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COVID-19: Coronavirus Disease of 2019; GBS: Guillain-Barré Syndrome; AIDP: Acute Inflammatory Demyelinating Polyneuropathy; AMAN: Acute Motor Axonal Neuropathy; AMSAN: Acute Motor And Sensory Axonal Neuropathy; IVIG: Intravenous Immunoglobulin.

Results

The GBS was found in 7 cases out of 2252 patients (0.3%), and 14 cases out of 3088 patients (0.4%) admitted to the neurology ward during the COVID-19 pandemic and before the pandemic, respectively. There was no significant difference between the distribution of GBS patients in the pandemic and before the pandemic (P=0.413).

During the COVID-19 pandemic and before the pandemic, the Mean±SD age of the patients with GBS was 53.8±17.2 years (range: 14-80 years). The demographic characteristics of the GBS patients are shown in Table 1. Most GBS patients were men (52.4%). The most common subtype of GBS was AMSAN (47.6%). The most common treatment for the GBS patients was Intravenous Administration Of Immunoglobulin (IVIG) (90.5%). Most GBS patients experienced a partial recovery (42.9%).

The Mean±SD ages of the GBS patients during the COVID-19 pandemic and before the pandemic were 58±15.5 and 51.6±18.1 years, respectively (P=0.417). There was no significant difference in gender distribution between the COVID-19 pandemic period and the pre-pandemic period (P=0.659). During the COVID-19 pandemic, there were 3 male patients (42.9%), compared to 4 female patients (57.1%) (Table 1).There was no significant difference in the distribution of GBS subtypes between the two periods (P=0.421). During the COVID-19 pandemic period, the most common subtype of GBS was AMSAN (71.4%). However, before the pandemic period, AMSAN (35.7%) and acute inflammatory demyelinating polyneuropathy (AIDP) (35.7%) were the most common subtypes (Table 1).

There was no significant difference between the two studied periods (P=0.987) in the distribution of GBS treatment. In both periods, the IVIG was the most common treatment given to the GBS patients (Table 1).

There was no significant difference in the distribution of response to treatment and recovery rate between the COVID-19 pandemic and the before the pandemic period (P=0.838). In the COVID-19 pandemic period, most GBS patients had partial recovery (42.9%); nevertheless, before the pandemic, most of the patients had partial (42.9%) and (42.9%) complete recovery (Table 1).

During the COVID-19 pandemic, lung involvement was observed in 42.9% of the GBS patients confirmed by CT scans. During the COVID-19 pandemic period, PCR tests were performed in 57% of the GBS patients, of which 42.9% were found to be positive. Clinical signs of COVID-19 during the pandemic period were observed in only two GBS patients (28.5%) (Table 2).

Table 2. Distribution of positive PCR results and suspected clinical signs of COVID-19 during the pandemic period

Variables	Result	No. (%)
Lung involvement (CT scan)	Positive	3(42.9)
PCR	Positive	3(42.9)
	Negative	1(14.2)
	Undone	3(42.9)
Suspected clinical signs	Yes	2(28.5)

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COVID-19: Coronavirus Disease of 2019; CT scan: Computed Tomography Scan; PCR: Polymerase Chain Reaction.

Discussion

In this study, there was no significant difference in the proportion of GBS patients during and before the COVID-19 pandemic. Conti et al. [18] showed that COVID-19 is associated with an increased possibility of GBS. There was no significant difference in the distribution of the GBS subtype during and before the COVID-19 pandemic. Caress et al. [25] observed that the subtype of GBS during the COVID-19 pandemic and before the pandemic was not significantly different. These findings are consistent with the results of our study.

In our study, AIDP and AMSAN patients each constituted 35.7% of the GBS patients before the pandemic. Moreover, AMAN accounted for 28.6% of the GBS patients before the pandemic. During the COVID-19 pandemic, AIDP and AMAN constituted 14.3% of the GBS patients. Most GBS patients in the COVID-19 pandemic had AMSAN (71.4%). Although the AMSAN was the most prevalent subtype of GBS during the COVID-19 pandemic period and its distribution was two times higher than that in the pre-pandemic period, the overall distribution difference of the subtypes between the two periods was not statistically significant (P=0.42). Caress et al. [25] reviewed 37 published cases of GBS cases associated with COVID-19 and found that AIDP was the most common subtype (n=24, 64.8%). The number (percentage) of patients with AMSAN, AMAN, and MFS subtypes were 5(13.5%), 1(2.7%), and 5(13.5%), respectively. In this study, the GBS patients received two treatments, including plasmapheresis and IVIG. Most GBS cases (90.5%) received IVIG in the present study. Before the pandemic period, all patients (n=14, 100%) received IVIG treatment. In the COVID-19 pandemic period, 71.4% and 28.2% of the GBS patients were treated with IVIG and plasmapheresis, respectively. In a study by Toscano et al. [26], all patients (n=5) were treated with IVIG. Two patients underwent two periods of IVIG treatment, and 1 patient underwent plasma replacement. In a study by Gutiérrez-Ortiz et al. [27], 2 GBS patients during the COVID-19 pandemic were studied. One of these patients showed improvement with IVIG, as the other did with acetaminophen. During the COVID-19 pandemic, we observed partial and complete recoveries in 42.9% and 26.8% of the GBS patients, respectively. However, before the pandemic, partial and complete recoveries were seen in 42.9% and 42.9% of the GBS patients, respectively. So, during the COVID-19 pandemic period, the rate of full recovery was lower than that before the pandemic period. However, based on statistical analysis, no significant difference was seen.

Conclusion

The present study's findings suggest no difference between the demographic and clinical parameters, type of treatment, and response to therapy in patients with GBS between the COVID-19 pandemic and the pre-pandemic period. AMSAN was the most prevalent subtype of GBS in the COVID-19 pandemic period. The complete recovery rate in the COVID-19 pandemic period was lower than that in the pre-pandemic period.

Ethical Considerations

Compliance with ethical guidelines

All study procedures were done in compliance with the ethical guidelines of the 2013 Declaration of Helsinki. The present study was approved by the Ethics Committee of Guilan University of Medical Sciences (Code: IR.GUMS.REC.1400.030).

Funding

The Clinical Research Development Unit of Poursina Hospital and Guilan University of Medical Sciences supported this study.

Authors contributions

All of the authors helped to shape this collaborative research study and made contributions to the project.

Conflict of interest

The authors declared no conflict of interest.

Acknowledgements

The authors thank the Clinical Research Development Unit of Poursina Hospital, Guilan University of Medical Sciences, Rasht, Iran.

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