

Prevalence and Mortality of Pediatrics with Guillain-Barré Syndrome during the COVID-19 Pandemic and Pre-COVID-19 Periods

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ABSTRACT

Objectives

Based on case reports, researchers have observed the incidence and clinical manifestations of Guillain-Barré Syndrome (GBS) following COVID-19 infection. Current hypotheses suggest that the risk of GBS may increase with COVID-19, and worsening GBS could elevate the risk of infection and exposure to the virus. This study aimed to assess the cognitive epidemic and mortality of children under 15 years of age with GBS during the COVID-19 pandemic and to compare them to two years earlier without addressing the etiology.

Materials & Methods

This cross-sectional study was conducted on all children admitted to Iranian hospitals with a diagnosis of GBS and whose clinical information was available in the national flaccid paralysis patient information registration system between April 2018 and April 2021.

Results

The total number of registered cases of GBS in the pre-COVID-19 period and during this period was 778 cases and 504 cases, respectively (total N=1282), indicating a decrease in registered GBS during COVID-19. The mean age of the patients in the pre-COVID-19 period was 9.00 ± 2.78 years, and during the COVID-19, it was 8.99 ± 2.03 years (P-value =0.998). No significant difference was found in gender distribution between the two periods (P-value =0.427). The total number of paralysis cases studied after 60 days was 14.3% before the COVID-19 period and 17.3% during the pandemic (P-value =0.216). The mortality rate in patients with GBS was 0.13% in the pre-COVID-19 period and 0.19% in the COVID-19 period (P-value =0.757).

Conclusion

Despite the decline in the frequency of diagnosis and referrals of patients with GBS during the COVID-19 period, no difference was found in the demographic characteristics and clinical outcomes of children with GBS in the pre-COVID-19 period and during this pandemic.

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Introduction

Guillain-Barré syndrome (GBS) is an inflammatory disease of the peripheral nervous system characterized by rapidly progressive and symmetrical limb weakness accompanied by an absence of deep tendon reflexes, upper and lower limb paresthesia, and impaired sensory symptoms at the onset. In these patients, cranial nerve involvement is occasionally reported, primarily linked to weakness in the fascial and bulbar muscles (1). GBS is divided into clinical subgroups such as classic sensory-motor, paraparetic, motor-only, sensory-only, Miller-Fisher syndrome, pharyngeal-cervical-brachial (PCB) variant, bilateral period facial palsy with paraesthesia, and Bickerstaff brainstem encephalitis (BBE) (2). Another classification of the disease is based on electromyographic findings. The most common form of the disease in this classification is referred to as acute inflammatory demyelinating polyneuropathy or acute inflammatory demyelinating polyneuropathy (AIDP). Other variants are acute axonal motor neuropathy and acute motor and sensory neuropathy (3). Various pathogenic factors have been suggested for GBS, the most common being infections with *Campylobacter jejuni*, cytomegalovirus, hepatitis E virus, *Mycoplasma pneumoniae*, Epstein-Barr virus, and Zika virus (4-7). Furthermore, the relationship between the Mediterranean respiratory distress syndrome or MERS-CoV coronavirus has been noticed and confirmed in recent years (8). Many studies have reported that COVID-19 can affect all vital organs, such as lungs, kidneys, liver, skin, eyes, and the like. Besides, the nervous system is not excluded; therefore, GBS can also be affected (9-13). Based on the reports, mainly case reports, this disease's symptoms and clinical manifestations have also

been reported after contracting COVID-19. Currently, they have put forward the hypothesis that the risk of contracting and aggravating GBS may increase with exposure to COVID-19. At the same time as the onset of COVID-19 in China, the first cases of GBS following infection with COVID-19 were reported (14).

Two questions now arise in this regard: first, whether the epidemic cognitive changes of GBS were visible in all human societies during the COVID-19 pandemic, and second, whether the approach of these epidemic cognitive changes was observed in all age groups, even in affected children. This study compares the epidemiological, laboratory, and clinical outcomes of children with GBS during the COVID-19 pandemic to previous years.

Materials & Methods

This cross-sectional study was conducted on all children (under 15 years old) admitted to Iranian hospitals with a diagnosis of GBS whose clinical information was available in the "National System for Registration of Information on Flaccid Paralysis Patients" between April 2018 and April 2021, while patients with incomplete information not included in the study. All data examined were extracted from the Hospital Information Registration System (HIS) and contained the following information: 1) demographic characteristics like sex and age; 2) cases of residual paralysis at 60 days; 3) deaths during patient follow-up. Data were presented as mean standard deviation (SD) for quantitative parameters and as counts (%) for categorical parameters. The current study statistically compared the two groups using the t-test or the Mann-Whitney test when the data were not normally distributed. The categorical variables were compared using the chi-square

test. IBM SPSS version 25.0 was also used for statistical analysis. A p-value of less than or equal to 0.05 was assumed as the significance level.

Results

In this study, the number of registered GBS cases was 343 in 2018, 435 in 2019, 257 in 2020, and 247 in 2021, totaling 1,282 cases. One death in the pre-COVID-19 period and COVID-19 period was reported. In addition, 111 cases with residual paralysis after 60 days in the pre-COVID-19 period and 87 cases in the COVID-19 period were recorded. The mean age of the patients in the pre-COVID-19 period was 9.00 ± 2.78 years; in the COVID-19 period, it was 8.99 ± 2.03 years, and no significant difference was observed between these two periods (P-value=0.998). In the pre-COVID-19 period, the proportion of boys was 61.6%, and the proportion of girls was 38.4%, while in the age of COVID-19, they were

57.1% and 42.9%, respectively. This indicates no significant difference in gender distribution between the two study periods (P-value =0.427). The total number of paralysis cases studied after 60 days, before COVID-19 and during this period were 14.3% and 17.3%, respectively, showing no significant difference between the two study periods (P-value =0.216). In males, the analyzed paralysis at 60 days before and during the COVID-19 period was 13.1% and 16.7%, respectively, showing no significant difference (P-value =0.249). In women, the rate of paralysis after 60 days, before COVID-19 and during this period, was 16.1% and 18.1%, respectively, and no significant difference was observed in this case (P-value =0.614). The mortality rate in patients with GBS was 0.13% in the pre-COVID-19 period and 0.19% in the COVID-19 period, and no significant difference was observed between the two periods (P-value =0.757) (Table 1).

Table 1. Descriptive information of GBS in pre-COVID-19 and COVID-19 periods across years

Characteristics	Pre-COVID-19 period		COVID-19 period	
	2018	2019	2020	2021
Total number	343	435	257	247
Mean age, year	8.98±2.32	9.02±3.36	8.26±2.22	9.72±2.46
Number of males<10 years	174	235	105	97
Number of females<10 years	110	134	94	73
Residual paralysis after 60 days, total	52	59	40	47
Residual paralysis after 60 days, males	26	37	21	27
Residual paralysis after 60 days, females	26	22	19	20
Total death	1	0	1	0
Death in males	1	0	1	0
Death in females	0	0	0	0

Generally, males have been infected more than females, and in the pre-COVID-19 period, 479 cases for males and 299 cases for females were recorded, as well as in the COVID-19 period, 288 cases for males and 216 cases for females were recorded (Figure 1). The provincial survey of registered cases in both periods, Tehran, Iran (Total N=217), Khorasan Razavi, Iran (Total N=134), and Isfahan, Iran (Total N=73) accounted for most of the recorded cases, respectively, which can be the effect of the large population of these provinces (Table 2).

Discussion

Suffering from neurological disorders, as well as its exacerbation in connection with COVID-19 disease, has been addressed in many reports. Additionally, many discussions have been presented regarding its clinical details and pathophysiological findings (9-13). One of these disorders is GBS and its various types; the increased susceptibility to this disorder in patients with viral diseases, especially COVID-19, has

been fully confirmed (15, 16). In this regard, seemingly, with the beginning and spread of the COVID-19 pandemic, research has seen an increase and aggravation of this disorder in society compared to the pre-COVID-19 period (16). Accordingly, the management and planning for administration and special care for these patients will be completely different. Based on this, it seems necessary to study the changes in the pattern of contracting this disease and the pathophysiological and clinical changes related to it during the COVID-19 period and compare it with the pre-COVID period. What was discussed in this study was the description of the situation of GBS in children during the COVID-19 pandemic and the comparison of it with the pre-COVID-19 period. To achieve the objectives of the study and to collect the required information, the national system for registering the data of patients with GBS has been evaluated retrospectively, and the information on children with GBS in the two periods before the COVID-19 pandemic (2018 and 2019) and also during this pandemic

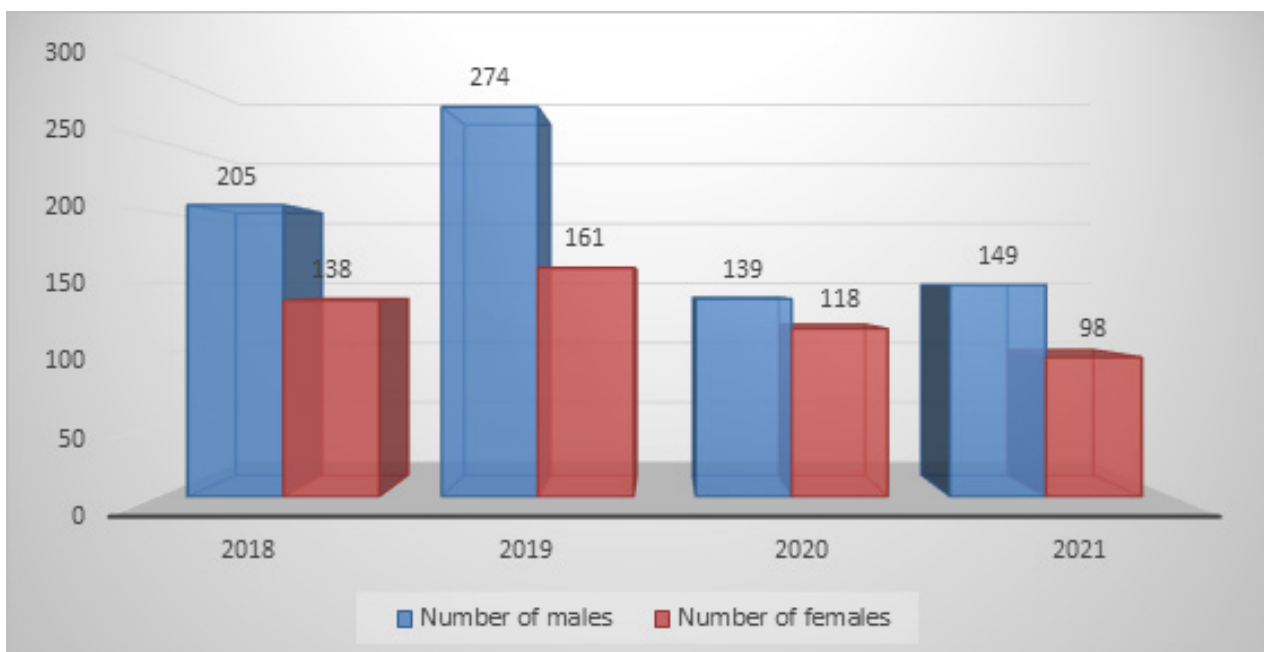


Figure 1. Number of males and females reported across years

Table 2. Frequency of GBS across provinces

Province	Pre-COVID-19 period		COVID-19 period	
	2018	2019	2020	2021
Gilan	1	5	1	1
Mazandaran	7	11	9	3
East Azerbaijan	22	21	7	16
West Azerbaijan	16	18	9	10
Kermanshah	16	15	7	5
Khuzestan	29	22	7	14
Fars	21	38	11	9
Kerman	11	16	14	19
Razavi Khorasan	39	42	26	27
Isfahan	26	27	17	3
Sistan and Baluchestan	12	13	17	3
Kurdistan	5	7	7	4
Chaharmahal and Bakhtiari	4	7	4	2
Lorestan	3	7	6	3
Ilam	6	6	4	2
Kohgiluyeh and Boyer-Ahmad	4	6	7	3
Bushehr	4	5	1	3
Zanjan	10	10	3	3
Semnan	7	8	4	2
Yazd	5	5	3	4
Hormozgan	4	8	6	5
Tehran	60	66	35	44
Ardabil	3	5	4	3
Gom	5	11	5	5
Gazvin	6	7	4	8
Golestan	6	9	7	7
North Khorasan	7	11	7	5
South Khorasan	4	6	5	5
Alborz	4	5	8	7
Markazi	4	0	8	9

(2020 and 2021) was extracted. After analyzing the obtained statistics, a comparison was made between the disease distribution, demographic characteristics, and consequences between the two periods.

What was obtained as the essential results of the study was that, firstly, the number of cases of GBS infection during the COVID-19 period had decreased compared to before, and perhaps the reason for this decrease is the reluctance of patients to go to the centers with the appearance of these symptoms due to the fear of contracting COVID-19 during the pandemic, which resulted in the reduction of GBS diagnoses in clinics and healthcare centers. Secondly, it may have been because of the high sensitivity and fear of getting COVID-19 among people, the cases of underlying infections that can be the cause of GBS decreased significantly, ultimately leading to the reduction of cases of GBS. It is rare to develop GBS following MERS, in which Kim et al. reported only one case of GBS after getting MERS (17).

The study's second point was that no significant difference was observed in the comparison between the two periods regarding demographic characteristics such as gender and age of patients with GBS. In other words, the entry into the period of COVID-19 did not cause a noticeable change in the gender distribution or the age of patients with GBS. The third point and finding was that considering that the stability of the symptoms of paralysis caused by GBS in the long term is considered an essential and sometimes life-threatening complication in patients, the frequency of cases with paralysis and long-term disability caused by it during COVID-19 and before that did not show any significant difference. In other words, entering COVID-19 was not associated with the aggravation of the complications of this

disease, specifically the long-term and debilitating paralysis. Furthermore, the obtained results indicated that entering the period of COVID-19 was not accompanied by an increase in the death rate caused by GBS, so the frequency of deaths of patients with GBS in the two periods before and during the COVID-19 pandemic was reported as 0.13% and 0.19%, respectively.

However, in some similar studies, different results were obtained. In the 2022 study by Garg et al. in India, children referred to GBS disease in 2020, the period of COVID-19, had a higher mean age (10.4 years vs. 5 years). Moreover, they had more sensory symptom intensity than in the pre-COVID-19 period (50% vs. 18.2%). However, in their study, the patients referred during COVID-19 had a favorable clinical outcome (8). In addition, in the study of López-Hernández et al. in 2021, compared to the period before COVID-19, the involvement of the cranial nervous system was reported significantly more in GBS sufferers (14). In summarizing the results, it can be said that entering the period of the COVID-19 pandemic was not accompanied by a noticeable change in the clinical characteristics and the outcome of GBS disease in affected children. In other words, the protocols for treating and managing these patients during COVID-19 can continue with the same plan. However, it should be remembered that there is much evidence of a relationship between COVID-19 and an increased risk of GBS (18, 19). In other words, in the case of patients suffering from COVID-19 and GBS simultaneously, the change and correction of treatment and care instructions should be completely changed (19). However, the present study aimed not to evaluate the clinical condition of children with COVID-19 and GBS simultaneously, and only an overview of the condition of GBS and its characteristics

in children in the community before and during COVID-19 was presented.

As mentioned, according to the available evidence, infection with COVID-19 could be associated with an increased risk of occurrence and exacerbation of neurological disorders such as GBS, which was evident in the published reports (18). In the study of Pimentel et al. (5), the occurrence of GBS symptoms during an aging period of 19 days after the infection of COVID-19 was fully shown. A study by Pourbakhtyaran et al. (7), among 37 patients with GBS, SARS-CoV-2 IgG-positive cases were reported in seven patients. However, a positive test for COVID-19 was reported in only one patient. In patients with GBS, co-infection with COVID-19 was associated with worse outcomes, such as higher GBS disability scores and more extended hospital stays. In a 2021 systematic review by Sansone et al. (15), in patients with GBS co-infected with COVID-19, the course of the disease was often more severe, with one-third requiring mechanical ventilation. Mortality in these patients was reported as 10.8%. Besides, Zahed et al. reported 0.3% Guillain-Barre syndrome among 375 patients (16). Therefore, having two diseases can simultaneously have far more severe consequences than cases of GBS without being infected with COVID-19, and therefore, they should be evaluated and managed more carefully. A comparison of the COVID-19 pandemic with the pre-COVID-19 period is of great importance in this study. This study is one of the largest in the Guillain-Barré syndrome and COVID-19 field, but it did not evaluate the paraclinical data.

In Conclusion

In summary, while this study showed a decrease in the diagnosis and referral rates of patients with

GBS during the COVID-19 period, we did not see any difference in the demographics, mortality, and paralysis of children with GBS between the pre- and during-period COVID-19 disease. Hence, this pandemic and these patients' treatment and care plans during the COVID-19 period can continue as in previous years.

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Authors' Contribution

Study concept and design: Sami Akbari, and Farzad Ahmadabadi. Acquisition of data: Sami Akbari, Mohammad Mehdi Taghdiri, Mohammad Mehdi Nasehi. Analysis and interpretation of data: Elaheh Khanipour. Drafting of the manuscript: Sami Akbari, and Farzad Ahmadabadi. Critical revision of the manuscript for important intellectual content: Sami Akbari, and Farzad Ahmadabadi, Elaheh Khanipour, Mohammad Mehdi Taghdiri, Mohammad Mehdi Nasehi.

Conflict of Interest

The authors declare no conflicts of interest.

References

1. Orlikowski D, Porcher R, Sivadon-Tardy V, et al. Guillain-barré syndrome following primary cytomegalovirus infection: a prospective cohort study. *Clin Infect Dis*. 2011;52:837–44. <https://doi.org/10.1093/cid/cir074>
2. Counotte MJ, Meili KW, Taghavi K, Calvet G, Sejvar J, Low N. Zika virus infection as a cause of congenital brain abnormalities and Guillain-Barré syndrome: a living

- systematic review [version 1; peer review: 2 approved]. *F1000Research*. 2019;8. <https://doi.org/10.1371/journal.pmed.1002203>
3. Kim JE, Heo JH, Kim HO, et al. Neurological complications during treatment of middle east respiratory syndrome. *J Clin Neurol*. 2017;13:227–33. <https://doi.org/10.3988/jcn.2017.13.3.227>
 4. Zhao H, Shen D, Zhou H, Liu J, Chen S. Guillain-Barré syndrome associated with SARS-CoV-2 infection: causality or coincidence? *Lancet Neurol*. 2020;19:383–84. [https://doi.org/10.1016/S1474-4422\(20\)30109-5](https://doi.org/10.1016/S1474-4422(20)30109-5)
 5. Pimentel V, Wallau Luchsinger V, Carvalho GL, Marinho Alcará A, Bianchini Esper N, Marinowic D, Zanirati G, Costa da Costa J. Guillain-Barré syndrome associated with COVID-19: A systematic review. *Brain Behav Immun Health*. 2023;28:100578. <https://doi.org/10.1016/j.bbih.2022.100578>
 6. Abbati G, Attaianese F, Rosati A, Indolfi G. Neurological Involvement in Children with COVID-19 and MIS-C: A Retrospective Study Conducted for More than Two Years in a Pediatric Hospital. *Children (Basel)*. 2022 Nov 24;9:1809. <https://doi.org/10.3390/children9121809>
 7. Pourbakhtyaran E, Heidari M, Ghahvechi Akbari M. Childhood Guillain-Barre syndrome in the SARS-CoV-2 period: Is there any causative relation? *Clin Case Rep*. 2022 Dec 20;10:e6772. <https://doi.org/10.1002/ccr3.6772>
 8. Garg D, Dhamija RK, Choudhary A. Impact of the COVID-19 Pandemic on the Frequency, Clinical Spectrum and Outcomes of Pediatric Guillain-Barré Syndrome in India: A Multicentric Ambispective Cohort Study. *Ann Indian Acad Neurol*. Jan-Feb 2022;25:60-67. https://doi.org/10.4103/aian.aian_392_21
 9. Tabatabaie SA, Soltani P, Khanbabaee G, Sharma D, Valizadeh R, et al. SARS Coronavirus 2, Severe Acute Respiratory Syndrome, and Middle East Respiratory Syndrome in Children: A Review on Epidemiology, Clinical Presentation, and Diagnosis. *Arch Pediatr Infect Dis*. 2020;8: e104860. <https://doi.org/10.5812/apid.104860>
 10. Besharat S, Alamda NM, Dadashzadeh N, Talaie R, Mousavi SS, Barzegar A, et al. Clinical and Demographic Characteristics of Patients with COVID-19 Who Died in Modarres Hospital. *Open Access Maced J Med Sci*. 2020;8:144-9. <https://doi.org/10.3889/oamjms.2020.5013>
 11. Rahimi MM, Jahantabi E, Lotfi B, Forouzes M, Farshid S. Renal and liver injury following the treatment of COVID-19 by remdesivir. *J Nephropathol*. 2021;10: e10. <https://doi.org/10.34172/jnp.2021.10>
 12. Dadashzadeh N, Farshid S, Nanbakhsh M, Rahimi MM. Acute respiratory distress syndrome in COVID-19 disease. *Immunopathol Persa*. 2020;6:e16. <https://doi.org/10.34172/ipp.2020.16>
 13. Lotfi B, Farshid S, Dadashzadeh N, Valizadeh R, Rahimi M M. Is Coronavirus Disease 2019 (COVID-19) Associated with Renal Involvement? A Review of Century Infection. *Jundishapur J Microbiol*. 2020;13:e102899. <https://doi.org/10.5812/jjm.102899>
 14. López-Hernández JC, Pérez-Valdez EY, León-Manríquez E. Guillain-Barre syndrome during COVID-19 pandemic: experience from a referral healthcare center in Mexico. *Rev Neurol*. 2021 Nov 1;73(9):315-320. <https://doi.org/10.33588/rn.7309.2021364>
 15. Sansone P, Gregorio Giaccari L, Aurilio C,

- Coppolino F, Esposito V, et al. Post-Infectious Guillain-Barré Syndrome Related to SARS-CoV-2 Infection: A Systematic Review. *Life* (Basel). 2021 Feb 21;11(2):167. <https://doi.org/10.3390/life11020167>
16. Zahed G, Karimzadeh P, Wissow L S, Arman S, Babaee M, et al. Neuropsychiatric Manifestations of COVID-19 in Hospitalized Pediatrics: A Multicenter Cross-sectional Study. *Arch Pediatr Infect Dis*. 2023;11(1):e131511. <https://doi.org/10.5812/apid-131511>
17. Kim JE, Heo JH, Kim HO, Song SH, Park SS, Park TH, Ahn JY, Kim MK, Choi JP. Neurological Complications during Treatment of Middle East Respiratory Syndrome. *J Clin Neurol*. 2017 Jul;13(3):227-233. <https://doi.org/10.3988/jcn.2017.13.3.227>.
18. Abolmaali M, Heidari M, Zeinali M, Moghaddam P, Ghamsari MR, Makiani MJ, Mirzaasgari Z. Guillain-Barré syndrome as a parainfectious manifestation of SARS-CoV-2 infection: a case series. *J Clin Neurosci*. 2021 Jan 1;83:119-22.
19. Shoraka S, Ferreira ML, Mohebbi SR, Ghaemi A. SARS-CoV-2 infection and Guillain-Barré syndrome: a review on potential pathogenic mechanisms. *Frontiers Immunol*. 2021 May 10;12:674922.