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Guillain-Barré syndrome during the COVID-19 era

A nationwide study of hospitalized cases in South Korea

Jin-Mo Park, MD[a,b], Jong-Sup Bae, PhD[a,*]

Abstract

This study aimed to analyze the trends and characteristics of hospitalized Guillain-Barré syndrome (GBS) incidence and management in South Korea before and during the coronavirus disease 2019 pandemic, assessing potential impacts of nonpharmaceutical interventions and shifts in public health dynamics. We conducted a retrospective analysis using data from the Health Insurance Review and Assessment Service database from 2013 to 2021, divided into prepandemic (2013–2019) and pandemic (2020–2021) periods. Incident GBS cases were identified based on the G61.0 code with hospital admissions. A total of 10,596 hospitalized patients with GBS were identified, with 8537 cases in the prepandemic period and 2059 during the pandemic. While the overall GBS incidence did not show a statistically significant change during the pandemic ($P = .056$), the mean age of patients increased. Notably, a significant rise in the proportion of patients receiving intravenous immunoglobulin was observed during the pandemic ($P < .001$), with older patients showing higher mean ages ($P = .007$). However, the proportion of patients requiring mechanical ventilation remained stable ($P = .240$). The findings suggest that while hospitalized GBS incidence remained stable amidst the pandemic and reduced respiratory infection admissions, the increase in intravenous immunoglobulin use points to more severe presentations, particularly among older patients. This highlights the multifactorial nature of GBS triggers and the need for continued investigation into how evolving public health measures and infectious disease patterns influence GBS incidence and management.

Abbreviations: COVID-19 = coronavirus disease 2019, GBS = Guillain-Barré syndrome, HIRA = Health Insurance Review and Assessment Service, IVIG = intravenous immunoglobulin, NPI = nonpharmaceutical intervention, SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.

Keywords: COVID-19, Guillain-Barré syndrome, GBS, HIRA, Korea

1. Introduction

The outbreak of coronavirus disease 2019 (COVID-19), caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus, has had a profound impact on global health since its emergence in late 2019. To mitigate the spread of the virus, many countries implemented stringent nonpharmaceutical interventions (NPIs) such as lockdowns, social distancing, and mandatory mask-wearing. These interventions were introduced to reduce the transmission of SARS-CoV-2, but they also had a broader impact on public health by influencing the spread of other transmissible diseases.

South Korea, however, managed to control the spread of COVID-19 effectively without enforcing extensive lockdowns, thanks to its early and aggressive testing, contact tracing, and public compliance with hygiene practices and mask usage.[1–4] The country's proactive public health strategies not only mitigated the spread of COVID-19 but also indirectly affected the incidence of other infectious diseases.

Amid this global health crisis, there was a notable decrease in hospital admissions for various respiratory diseases in South Korea. A study by Huh et al[2] highlighted a substantial reduction in hospitalizations for pneumonia, influenza, chronic obstructive pulmonary disease, and asthma during the implementation of NPIs. The study found that the cumulative incidence of admissions for chronic obstructive pulmonary disease and asthma dropped to 58% and 48% of the mean incidence during the 4 preceding years, respectively. This reduction was attributed to the enhanced personal hygiene and widespread

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The data that support the findings of this study are available from a third party, but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data are available from the authors upon reasonable request and with permission of the third party.

This study was approved by the Institutional Review Board of Dongguk University, Gyeongju (110757–202201-HR-02-02). Informed consents were waived for this study due to its retrospective design, involving the analysis of anonymized claims data from the Health Insurance Review and Assessment Service.

[a] College of Pharmacy, CMRI, Research Institute of Pharmaceutical Sciences, Kyungpook National University, Daegu, Republic of Korea, [b] Department of Neurology, Dongguk University College of Medicine, Dongguk University Gyeongju Hospital, Gyeongju, Republic of Korea.

** Correspondence: Jong-Sup Bae, College of Pharmacy, CMRI, Research Institute of Pharmaceutical Sciences, Kyungpook National University, 80 Daehak-ro, Buk-gu, Daegu 41566, Republic of Korea (e-mail: baejs@knu.ac.kr).*

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use of masks, which lowered the transmission of common respiratory pathogens. Similarly, another study by Mun et al[1] observed significant changes in the incidence of respiratory diseases in South Korea during the COVID-19 pandemic, further supporting the impact of NPIs on reducing respiratory infections.

Given the observed decline in respiratory infections, it is plausible to hypothesize that other diseases indirectly related to respiratory infections might also exhibit a similar trend. Guillain-Barré syndrome (GBS), an autoimmune disorder often triggered by infections, could be among these diseases. GBS is known to follow various bacterial and viral infections,[5] including *Campylobacter jejuni* and respiratory infections, which are common triggers. The reduction in these infections, therefore, suggests the possibility of a corresponding decrease in the incidence of GBS during the pandemic, a hypothesis that warrants further investigation.

To explore this hypothesis, data from the Korea National Database were analyzed to investigate the trends in GBS incidence before and during the COVID-19 pandemic. This analysis aims to determine whether the implementation of NPIs and improved personal hygiene during the pandemic had an observable impact on the incidence of GBS in South Korea.

2. Methods

2.1. Data source and study population

This study was performed using data from the Health Insurance Review and Assessment Service (HIRA) research database (M20220115770) established by the HIRA of South Korea and was approved by the Institutional Review Board of Dongguk University Gyeongju Hospital (110757–202201-HR-02-02). The HIRA database contains comprehensive information on diagnoses, procedures, prescription records, demographic details, and direct medical costs. All Korean citizens are required to register for the National Health Insurance System, covering ≈98% of the population.[6]

A retrospective cohort analysis was conducted on patients with the G61.0 code designated for GBS as per the Korean Classification of Diseases (seventh edition, an adaptation of the International Classification of Diseases Tenth Revision for the Korean health system), registered from 2010 to 2021. To ensure diagnostic accuracy, a 3-year "wash-out" period prior to 2013 was implemented to exclude any patients with prior GBS diagnoses. Incident cases were limited to patients with both a G61.0 code for GBS and a confirmed hospital admission during the study period from 2013 to 2021. This approach was chosen to exclude presumptive GBS cases and enhance diagnostic precision, which is crucial for comparing GBS incidence between pre- and post-COVID-19 periods.

2.2. Statistical analysis

Descriptive statistics, including the total number of patients, mean age, and gender distribution, were calculated for each year from 2013 to 2021 and separately for the prepandemic (2013–2019) and pandemic (2020–2021) periods. The Mann-Whitney *U* test was used to assess differences in the distribution of the number of patients with GBS between 2 periods. In addition, the χ^2 tests compared the proportions of patients receiving intravenous immunoglobulin (IVIG) and those requiring mechanical ventilation between 2 periods, assessing differences in GBS case severity. The independent *t* test was used to compare the mean ages of patients with GBS between the 2 periods. All analyses were conducted using the SAS Enterprise Guide (version 7.1, SAS Institute, Inc, Cary, NC), enabling comprehensive data management and statistical testing.

3. Results

3.1. Incidence of GBS hospitalization

A total of 10,596 hospitalized patients with GBS were identified from the HIRA between 2013 and 2021 (Table 1). The data were divided into 2 periods: prepandemic (2013–2019) with 8537 patients and pandemic (2020–2021) with 2059 patients. The mean age of hospitalized patients with GBS increased from 48.06 years in 2013 to 54.69 years in 2021. Gender distribution was consistent across both periods, with males representing ≈60% of the total cases.

The Mann-Whitney *U* test comparing the total number of patients with GBS in the prepandemic and pandemic periods revealed no statistically significant difference in the number of patients with GBS between the 2 periods (U = 14.0; $P = .056$). When analyzed separately, the difference was also not significant for male patients (U = 13.0; $P = .111$; Table 2) and female patients (U = 14.0; $P = .056$; Table 3).

In addition, the age of patients with GBS was analyzed to determine any differences between the prepandemic and pandemic periods. The overall mean age increased from 49.48 years in the prepandemic period to 53.68 years during the pandemic. Although there was an increase in mean age, this difference was not statistically significant (t = –3.73; $P = .100$). For male patients, the mean age increased from 49.5 to 54.2 years (t = –4.21; $P = .072$), and for female patients, the mean age increased from 53.0 to 56.6 years (t = –2.57; $P = .112$). These increases were also not statistically significant.

3.2. Patients with GBS receiving IVIG treatment

Between 2013 and 2019, the number of patients with GBS receiving IVIG treatment, which is typically administered to patients

Table 1

Yearly GBS incidence, age distribution, and proportions of patients receiving IVIG or mechanical ventilation.

	Patients with GBS				GBS + IVIG				GBS + MV			
Year	Number		Mean age, yr (±SD)		Number		Mean age, yr (±SD)		Number		Mean age, yr (±SD)	
2013	1057	U = 14.0	48.06 ± 21.41	t = -3.73	355	$\chi^2 = 127.22$	50.98 ± 22.64	t = -4.41	94	$\chi^2 = 1.38$	56.22 ± 18.38	t = 1.18
2014	1175	$P = .056$	48.12 ± 20.81	$P = .100$	403	$P < .001$	50.88 ± 21.24	$P = .007$	92	$P = .240$	56.11 ± 18.97	$P = .282$
2015	1207		49.43 ± 21.54		408		53.21 ± 22.05		106		60.42 ± 18.64	
2016	1273		49.74 ± 20.92		406		54.29 ± 21.23		92		62.82 ± 13.53	
2017	1237		49.03 ± 20.58		464		52.91 ± 20.52		98		61.22 ± 16.72	
2018	1384		50.35 ± 21.1		560		53.46 ± 22.12		104		60.06 ± 19.17	
2019	1204		51.66 ± 21.68		530		57.29 ± 20.64		92		64.84 ± 15.34	
2020	1039		52.66 ± 21.18		557		57.21 ± 19.1		70		57.76 ± 19.11	
2021	1020		54.69 ± 19.67		476		58.45 ± 19.16		77		59.31 ± 14.05	

GBS = Guillain-Barré syndrome, IVIG = intravenous immunoglobulin, MV = mechanical ventilation, SD = standard deviation.

Table 2

Yearly GBS incidence, age distribution, and proportions of patients receiving IVIG or mechanical ventilation in male patients with GBS.

	Patients with GBS				GBS + IVIG				GBS + MV			
Year	Number		Mean age, yr (±SD)		Number		Mean age, yr (±SD)		Number		Mean age, yr (± SD)	
2013	638	U = 13.0	48.51 ± 19.73	t = -4.21	207	χ^2 = 83.34	51.2 ± 20.25	t = -3.62	60	χ^2 = 1.39	54.22 ± 18.47	t = 0.37
2014	692	*P* = .111	45.89 ± 20.9	*P* = .072	226	*P* < .001	47.41 ± 21.72	*P* = .009	56	*P* = .238	51.91 ± 20.32	*P* = .734
2015	718		47.94 ± 21.2		224		50.69 ± 21.43		65		58.97 ± 18.64	
2016	758		48.75 ± 20.51		236		53.28 ± 20.56		54		61.31 ± 13.87	
2017	750		47.51 ± 20.61		287		50.85 ± 20.82		54		59.78 ± 17.45	
2018	854		49.15 ± 21.06		357		52.2 ± 21.42		62		57.18 ± 19.06	
2019	703		50.73 ± 21.31		283		57.83 ± 19.53		56		61.13 ± 14.91	
2020	642		52.33 ± 20.56		328		56.16 ± 18.78		39		58.38 ± 17.39	
2021	602		54.43 ± 19.34		290		57.32 ± 19.37		47		55.83 ± 14.3	

GBS = Guillain-Barré syndrome, IVIG = intravenous immunoglobulin, MV = mechanical ventilation, SD = standard deviation.

Table 3

Yearly GBS incidence, age distribution, and proportions of patients receiving IVIG or mechanical ventilation in female patients with GBS.

	Patients with GBS				GBS + IVIG				GBS + MV			
Year	Number		Mean age, yr (±SD)		Number		Mean age, yr (±SD)		Number		Mean age, yr (± SD)	
2013	419	U = 14.0	47.38 ± 23.75	t = -2.57	148	χ^2 = 44.04	50.68 ± 25.69	t = -3.93	34	χ^2 = 0.110	59.76 ± 17.95	t = 0.76
2014	483	*P* = .056	51.31 ± 20.28	*P* = .112	177	*P* < .001	55.31 ± 19.8	*P* = .021	36	*P* = .735	62.64 ± 14.65	*P* = .565
2015	489		51.62 ± 21.88		184		56.27 ± 22.46		41		62.73 ± 18.63	
2016	515		51.19 ± 21.44		170		55.69 ± 22.11		38		64.95 ± 12.91	
2017	487		51.36 ± 20.34		177		56.25 ± 19.63		44		63.0 ± 15.8	
2018	530		52.29 ± 21.04		203		55.67 ± 23.2		42		64.31 ± 18.76	
2019	501		52.98 ± 22.14		247		56.67 ± 21.86		36		70.61 ± 14.37	
2020	397		53.19 ± 22.17		229		58.71 ± 19.5		31		56.97 ± 21.34	
2021	418		55.06 ± 20.15		186		60.21 ± 18.75		30		64.77 ± 11.95	

GBS = Guillain-Barré syndrome, IVIG = intravenous immunoglobulin, MV = mechanical ventilation, SD = standard deviation.

with more severe cases of GBS, ranged from 355 to 560 each year. During the pandemic period, 557 patients received IVIG in 2020 and 476 in 2021. The χ^2 tests revealed significant differences in IVIG treatment rates between the prepandemic and pandemic periods. The proportion of patients with GBS requiring IVIG treatment increased notably during the pandemic compared with the prepandemic period (χ^2 = 127.22; *P* < .001). This trend was consistent across both male (χ^2 = 83.34; *P* < .001) and female patients (χ^2 = 44.04; *P* < .001), showing significant increases in the need for IVIG treatment.

The overall mean age of IVIG-treated patients increased significantly from 53.29 years in the prepandemic years to 57.83 years during the pandemic (t = –4.41; *P* = .007). The mean age of IVIG-treated male patients increased significantly from 52.2 years in the prepandemic period to 56.16 years during the pandemic (t = –3.62; *P* = .009). For female patients, the mean age rose from 55.67 to 58.71 years, with a significant difference between the 2 periods (t = –3.93; *P* = .021).

3.3. Patients with GBS requiring mechanical ventilation

The number of patients with GBS requiring mechanical ventilation remained relatively low throughout the study period. The highest number was observed in 2015 with 106 patients. During the pandemic, 70 patients required mechanical ventilation in 2020 and 77 in 2021. The χ^2 test indicated no significant difference in the proportion of patients requiring mechanical ventilation between the 2 periods for overall patients (χ^2 = 1.38; *P* = .240), male patients (χ^2 = 1.39; *P* = .238), and female patients (χ^2 = 0.11; *P* = .735).

The mean age of patients requiring mechanical ventilation ranged from 56.22 years in 2013 to 64.84 years in 2019. During the pandemic, the mean ages were 57.76 years in 2020 and 59.31 years in 2021. However, the *t* test showed no significant differences in mean age between the prepandemic and pandemic periods for overall patients (t = 1.18; *P* = .282), male patients (t = 0.37; *P* = .734), and female patients (t = 0.76; *P* = .565).

4. Discussion

This study provides an in-depth analysis of the incidence and clinical characteristics of GBS in South Korea before and during the COVID-19 pandemic. The analysis focused on various indicators such as hospital admissions, the use of IVIG, and mechanical ventilation. While the number of GBS cases did not show a statistically significant change during the pandemic (U = 14.0; *P* = .056), shifts in patient demographics and clinical management were observed.

The finding that the overall number of GBS cases remained stable during the pandemic is consistent with other studies. For instance, Gigli et al[7] found no significant increase in the incidence of GBS during the COVID-19 outbreak in northern Italy, suggesting that the pandemic did not directly influence the occurrence of GBS despite initial concerns about potential post-infectious neurological complications related to SARS-CoV-2 infection. Similarly, Sriwastava et al[8] reported stable GBS rates during the pandemic in the United States, further supporting the notion that the incidence of GBS was not significantly affected by COVID-19. However, unlike these studies, which primarily focused on regions with high COVID-19 infection rates and

aimed to assess the direct association between COVID-19 and GBS, our study sought to understand the broader effects of infection control measures, including COVID-19 management, on GBS incidence in a setting where overall infection control was highly effective. Although South Korea effectively reduced the spread of COVID-19 and lowered admissions of respiratory infections through NPIs, our study did not observe a corresponding decrease in GBS cases.

Several potential explanations exist for why GBS incidence did not decrease despite a reduction in hospital admissions for respiratory infections during the pandemic. One reason is the diversity of pathogens: GBS can be triggered by various pathogens, not limited to respiratory infections. While NPIs may have reduced common respiratory infections such as influenza and pneumonia, they might not have impacted other pathogens such as *C. jejuni*, which is associated with gastrointestinal infections. Therefore, other triggering factors for GBS might have remained stable. Another reason could be asymptomatic or mild infections: Some infections that can lead to GBS may be asymptomatic or mild and, thus, not captured in hospital admission data. Although NPIs might have reduced the severity of respiratory infections, they did not completely eliminate the circulation of pathogens. As a result, individuals could still contract mild infections that went undetected but were sufficient to trigger GBS. In addition, delayed healthcare utilization during the pandemic may have contributed to the observed trends. Concerns about COVID-19 exposure in medical settings could have led individuals to avoid or delay seeking care for mild symptoms or early-stage infections.[9] As a result, there may have been a decrease in reported respiratory infection admissions, reflecting an underestimation of the true burden of infections. This reduction in admissions, however, would not necessarily have prevented the occurrence of GBS, as some undetected or untreated infections could still have triggered the condition. To confirm these potential explanations, detailed assessments of preceding infections in individual GBS cases would be required. Such investigations could help clarify the relationship between NPIs, reduced respiratory infections, and GBS incidence. Future studies incorporating these additional data are warranted to better understand the multifactorial triggers of GBS.

The significant increase in IVIG treatment rates during the pandemic ($P < .001$) reflects a shift toward more severe presentations of GBS, particularly in older patients, as indicated by their significantly higher mean age ($t = -4.41$; $P = .007$). IVIG is a standard treatment for GBS, especially in patients with significant weakness that impairs their ability to walk independently.[5] While GBS incidence remained stable, the rise in IVIG use suggests that these patients experienced more pronounced motor weakness, necessitating earlier and more aggressive treatment. This observed increase in the mean age of patients with GBS may reflect the general aging trend in South Korea over the study period. In addition, this trend of rising average age among patients with GBS was evident even before the pandemic, suggesting that it may not be solely attributable to pandemic-specific factors.[10] In contrast, the proportion of patients with GBS requiring mechanical ventilation ($P = .240$) did not change, indicating that the most critical cases involving respiratory failure remained consistent. This suggests that while more patients required IVIG for severe limb weakness, the progression to respiratory compromise was not more frequent. These findings highlight that the increased IVIG use could partly be due to the gradual aging of patients with GBS over time, and the observed trend during the pandemic may simply reflect its timing in the later years of this study. The increased use of IVIG during the pandemic might also be influenced by external factors, such as changes in IVIG availability due to reduced demand in other conditions, though this hypothesis could not be examined within the scope of this study. Further research is warranted to investigate both these possibilities and determine whether the observed trends in IVIG use reflect a longer-term shift in GBS presentations.

The findings of this study have important implications for public health strategies and the clinical management of GBS. The stability in GBS incidence despite the pandemic suggests that NPIs and public health measures aimed at controlling COVID-19 may not have adversely affected the incidence of certain autoimmune disorders. However, the observed changes in patient demographics and treatment patterns underscore the importance of continuous monitoring and adapting clinical guidelines to ensure optimal care for patients with GBS. The shifts in GBS presentation are likely influenced by multifactorial causes rather than simply by a reduction in respiratory infection admissions, pointing to the need for a more comprehensive understanding of GBS triggers during this period.

An important aspect of this study is our focus on how well-controlled infection states during the pandemic impacted GBS incidence in South Korea. Notably, the study was conducted before the spread of the Omicron variant, which significantly increased infection rates in the country despite NPIs.[3,4] As the Omicron variant and subsequent vaccination efforts reshaped the public health landscape, it is important to consider that multifactorial influences could have affected GBS incidence in more complex ways, making it difficult to isolate the impact of any one factor. Future studies will be needed to assess the long-term effects of these factors on GBS incidence.

One limitation of this study is the exclusion of presumptive GBS cases, as we focused solely on hospital admissions with a confirmed G61.0 code. While this approach ensured diagnostic precision, it may have led to an underestimation of true GBS incidence. However, for the purposes of comparing GBS incidence between pre- and post-COVID-19 periods, diagnostic accuracy was prioritized over inclusiveness. In addition, the lack of data on GBS subtypes in the HIRA dataset is a limitation, as we were unable to examine potential changes in the distribution of GBS subtypes during the study period.

5. Conclusion

This study provides valuable insights into the trends and characteristics of hospitalized GBS incidence and management in South Korea before and during the COVID-19 pandemic. While the incidence of hospitalized GBS did not show a significant change during the pandemic, an increase in the mean age and a higher proportion of patients receiving IVIG were observed, suggesting more severe presentations among older patients. These findings indicate that the stability in GBS incidence amidst reduced respiratory infection admissions underscores the multifactorial nature of GBS triggers. Future studies that observe changes in GBS incidence as infectious disease patterns evolve could help clarify the factors influencing GBS presentation. Such research would enhance understanding of how GBS trends respond to shifts in public health measures and the broader epidemiological landscape.

Author contributions

Conceptualization: Jin-Mo Park, Jong-Sup Bae.
Data curation: Jin-Mo Park.
Formal analysis: Jin-Mo Park.
Funding acquisition: Jin-Mo Park.
Software: Jin-Mo Park.
Writing – original draft: Jin-Mo Park.
Supervision: Jong-Sup Bae.
Validation: Jong-Sup Bae.
Writing – review & editing: Jong-Sup Bae.

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