Incidence, Disability, and Mortality in Patients With Guillain-Barré Syndrome in Korea: A Nationwide Population-Based Study

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Background and Purpose This study aimed to identify the epidemiological features of Guillain-Barré syndrome (GBS) in the Korean population.

Methods Patients with GBS were defined as those who were hospitalized with a primary diagnostic code of G61.0 on the Korean Classification of Disease in a department of neurology, rehabilitation medicine, or pediatrics. We evaluated the incidence and prevalence of GBS as well as physical disability, mortality, and cause of death in patients with GBS from 2002 to 2018 in the Korean population using the Korean National Health Insurance Service database.

Results We identified 11,146 patients with GBS. The ratio of males to females was 1.48. The age-adjusted incidence rate per 100,000 persons increased steadily from 0.84 in 2002 to 1.68 in 2018, as did the age-adjusted prevalence rate per 100,000 persons, from 0.77 to 15.62. The incidence and prevalence of GBS increased with age, peaking at 70−79 years. Among 10,114 patients without physical disability at the time of GBS being diagnosed, 502 (5.0%) patients had moderate disability and 526 (5.2%) had severe disability by the end of the study period. A total of 1,221 (11.0%) patients with GBS died during the mean follow-up period of 17 years (2002−2019). There were 144 (1.3%) in-hospital deaths.

Conclusions This was the first nationwide epidemiological study of patients with GBS covering the entire population including patients of all ages in the Republic of Korea. We have revealed the seasonality of admissions, disability, and long-term mortality rates in patients with GBS.

Keywords Guillain-Barré syndrome; incidence; disability; mortality; cause of death.

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INTRODUCTION

Guillain-Barré syndrome (GBS) is the most common immune-mediated neuropathy, and is characterized by rapidly evolving muscle weakness, sensory loss, and hyporeflexia. The etiology of GBS remains unclear, but it is considered that an immune-mediated process with molecular mimicry plays an important role in the generation of autoimmune antibodies and the activation of inflammatory cells.[1] The main clinical feature of GBS is progressive symmetric weakness of the limb muscles within 28 days, followed by clinical plateau. Approximately two-thirds of patients have a prodromal illness at from 3 days to 6 weeks before the onset of GBS.[2] The diagnosis of GBS is based on typical clinical features, electrodiagnostic testing, antiganglioside antibodies, and elevated levels of protein in the cerebrospinal fluid. Intravenous immunoglobulin (IVIG) and plasmapheresis have proven to be effective treatments for GBS.

The incidence of GBS has been reported to be between 0.59 and 2.35 per 100,000 persons

worldwide,[3-6] while the reported mortality rate of GBS has ranged from 3% to 13%.[7] The most common causes of death in patients with GBS are respiratory and cardiovascular complications.[7] Although GBS is a common and life-threatening disease, there have been few epidemiological studies of GBS in Republic of Korea.[8,9] Moreover, those studies were restricted to the association of GBS with influenza vaccination and with the elderly in the Korean population.[8,9]

The Republic of Korea has a single public medical insurance system, the National Health Insurance Service (NHIS), which covered approximately 52 million Korean citizens in 2018.[10] All health insurance claims information is integrated into the NHIS database in the Republic of Korea. This claims database includes information on healthcare utilization throughout the country, including demographic characteristics, dates of hospital visits, admissions, and discharges; principal diagnoses based on the Korean Standard Classification of Disease (KCD), which is a modified version of the International Classification of Diseases, 10th edition (ICD-10); diagnostic procedures; medical and surgical procedures; prescriptions filled; and healthcare expenditure.[11] The comprehensive nature of the NHIS database has resulted in it being used to determine the incidence and prevalence of neuromuscular disease in the Korean population.[10,12]

This study performed a nationwide population-based investigation of the incidence, prevalence, physical disability, mortality, and causes of death of GBS in the Korean population using the NHIS database.

METHODS

Developing an operational diagnosis of GBS
An appropriate operational definition for GBS was produced by evaluating the accuracy of various diagnostic criteria, including diagnostic codes, nerve conduction studies (NCSs), hospitalization, and treatment departments. Patients diagnosed with inflammatory polyneuropathy at Gangnam Severance Hospital between January 2018 and December 2019 were selected based on the KCD diagnostic codes for GBS (G61.0), serum neuropathy (G61.1), other inflammatory polyneuropathies (G61.8), and inflammatory polyneuropathy, unspecified (G61.9). Forty-four of the 146 patients identified with these diagnostic codes were identified as having GBS complying with the National Institute of Neurological and Communicative Disorders and Stroke Criteria.[13] Two of these patients had Miller Fisher syndrome, which is cranial-dominant GBS. There were 102 patients with other diseases, comprising 47 with cervical disc disorder with myelopathy, unspecified cervical region (KCD code M50.0); 14 with chronic inflammatory demyelinating polyneuritis (G61.81); 10 with

inflammatory polyneuropathy, unspecified (G61.9); 10 with malingering (Z76.5); 9 with diplopia (H53.2); 4 with multifocal motor neuropathy (G61.82); 4 with hereditary motor and sensory neuropathy (G60.0); and 4 with polyneuropathy, unspecified (G62.9).

Supplementary Table 1 (in the online-only Data Supplement) presented the accuracy of the operational definitions of GBS based on their sensitivity, specificity, positive predictive value, and negative predictive value. We finally decided upon an operational definition of GBS as hospitalized cases with the KCD diagnostic code for GBS (G61.0) treated in a specific department: neurology, pediatrics, or rehabilitation medicine.

Study population
We searched for all patients meeting the final operational definition of GBS in the NHIS database from January 2002 to December 2018. Data collected from patients with GBS included age, sex, medical-visit records, hospital type, income level, physical disability, death information, and the use of specific therapies including IVIG, plasmapheresis, and tracheostomy. Income levels were classified into the following three categories: 1) low (poorest 30% of the population), 2) middle (31%−70% of the population), and 3) high (richest 30% of the population). We defined hospitalization for ≥30 days as a long hospitalization period and hospitalization for <30 days as a short hospitalization period. Hospital type was divided into referral hospitals and nonreferral hospitals.

Incidence and prevalence
The crude incidence rate of GBS was calculated as the number of newly identified patients with GBS at the end of each year (from 2002 to 2018) divided by the total population in that year, as obtained from the Korean Statistical Information Service of Statistics Korea (http://kosis.kr/). The crude prevalence rate was calculated as the total number of patients with GBS at the end of each year divided by the total population in that year. In addition, age-adjusted incidence and prevalence were calculated using the world standard population, as determined by the World Health Organization for 2000−2025.[14]

Long-term physical disability
We evaluated long-term disability in patients with GBS who did not have previous physical disability using the NHIS database. The degree of physical disability was divided into six levels from index 1 (the most-severe disability) to index 6 (less-severe disability). Physical disability levels were reclassified into two categories: 1) moderate physical disability for indexes 4−6 and 2) severe physical disability for indexes 1−3.

We then compared long-term physical disability according to age, sex, income level, hospitalization period, IVIG, hospital type, plasmapheresis, and tracheostomy.

Death information

Participant deaths up to December 31, 2019 were ascertained using the NHIS database based on information derived from the Resident Register of the Republic of Korea. Information on causes of death from January 2002 to December 2018 were obtained from Statistics Korea and based on death certificates, most of which were confirmed by physicians. Causes of death were classified according to the relevant ICD-10 codes, as in a previous study.[10] The standardized mortality ratios (SMRs) for all-cause and cause-specific mortality, along with their 95% confidence intervals (CIs), were determined relative to the general Korean population for 2002−2018. The SMR was calculated as the number of observed deaths in patients with GBS divided by the expected number of deaths in the general population as determined from the data recorded by Statistics Korea. We also analyzed in-hospital deaths, which were defined as death occurring during hospitalization until up to 7 days after discharge.

The survival rate and survival time from the initial diagnosis of patients with GBS were analyzed using the Cox proportional-hazards model.[15] The starting point for these analyses was defined as the date of the initial diagnosis. The end point was defined as either the date of death or December 31, 2019, for those who survived until study termination. We analyzed survival curves affected by factors including age at diagnosis, sex, income level, hospital type, hospitalization period, IVIG, plasmapheresis, and tracheostomy using the Cox proportional-hazards model.

Statistical analysis

All statistical analyses were performed using SAS (version 9.4; SAS Institute, Cary, NC, USA). All p-values were two-sided, and $p<0.05$ was considered statistically significant. Cox regression analysis was used to examine the associations of patient characteristics (age, sex, income level, hospital type, hospitalization period, IVIG, plasmapheresis, and tracheostomy) with physical disability and mortality in patients with GBS.

Ethical considerations

This study was approved by the Institutional Review Board of Gangnam Severance Hospital (approval number: 2020-0438), which waived the requirement to obtain informed consent because all of the data obtained from the NHIS included all personal information anonymized using a strict confidentiality protocol.

Table 1. Annual incidence and prevalence rates of Guillain-Barré syndrome per 100,000 persons at the end of each year in Korea

Year	General population	Incidence			Prevalence		
		n	Crude rate (95% CI)	Age–adjusted rate* (95% CI)	n	Crude rate (95% CI)	Age–adjusted rate* (95% CI)
2002	48,125,745	391	0.81 (0.73–0.89)	0.84 (0.75–0.92)	370	0.77 (0.69–0.85)	0.77 (0.71–0.87)
2003	48,308,386	410	0.85 (0.77–0.93)	0.84 (0.76–0.93)	760	1.57 (1.46–1.69)	1.59 (1.47–1.70)
2004	48,485,314	392	0.81 (0.73–0.89)	0.81 (0.73–0.89)	1,130	2.33 (2.19–2.47)	2.33 (2.20–2.47)
2005	48,683,040	419	0.86 (0.78–0.94)	0.85 (0.77–0.93)	1,517	3.12 (2.96–3.27)	3.07 (2.92–3.23)
2006	48,887,027	500	1.02 (0.93–1.11)	0.98 (0.89–1.06)	1966	4.02 (3.84–4.20)	3.89 (3.72–4.07)
2007	49,130,354	527	1.07 (0.98–1.16)	1.03 (0.94–1.12)	2,440	4.97 (4.77–5.16)	4.78 (4.59–4.97)
2008	49,404,648	548	1.11 (1.01–1.20)	1.03 (0.94–1.12)	2,941	5.95 (5.74–6.17)	5.64 (5.44–5.85)
2009	49,656,756	630	1.27 (1.17–1.37)	1.21 (1.12–1.31)	3,496	7.04 (6.80–7.27)	6.62 (6.40–6.84)
2010	49,879,812	658	1.32 (1.22–1.42)	1.27 (1.17–1.37)	4,075	8.17 (7.91–8.42)	7.64 (7.40–7.87)
2011	50,111,476	645	1.29 (1.19–1.39)	1.18 (1.09–1.27)	4,627	9.23 (8.97–9.50)	8.51 (8.27–8.76)
2012	50,345,325	669	1.33 (1.23–1.43)	1.20 (1.11–1.29)	5,198	10.32 (10.04–10.61)	9.40 (9.14–9.65)
2013	50,558,952	720	1.42 (1.32–1.53)	1.25 (1.16–1.34)	5,804	11.48 (11.18–11.78)	10.31 (10.04–10.57)
2014	50,763,158	851	1.68 (1.56–1.79)	1.45 (1.36–1.55)	6,560	12.92 (12.61–13.24)	11.42 (11.15–11.70)
2015	50,951,719	849	1.67 (1.55–1.78)	1.42 (1.32–1.52)	7,290	14.31 (13.98–14.64)	12.44 (12.15–12.73)
2016	51,112,972	937	1.83 (1.72–1.95)	1.52 (1.43–1.62)	8,076	15.80 (15.46–16.14)	13.52 (13.23–13.82)
2017	51,230,704	947	1.85 (1.73–1.97)	1.54 (1.44–1.63)	8,886	17.35 (16.98–17.71)	14.60 (14.30–14.91)
2018	51,300,880	1,053	2.05 (1.93–2.18)	1.68 (1.58–1.78)	9,743	18.99 (18.61–19.37)	15.62 (15.31–15.93)

*Age-adjusted rate (per 100,000 persons) using the World Health Organization (2000–2025) world standard population.[14]
CI, confidence interval.

RESULTS

Incidence and clinical characteristics of GBS

We identified 11,146 patients fulfilling the operational definition for GBS during the 17-year study period (2002−2018). The ratio of males to females was 1.48. Table 1 summarizes the incidence and prevalence of GBS. The age-adjusted incidence rate per 100,000 persons increased steadily from 0.84 in 2002 to 1.68 in 2018, as did the age-adjusted prevalence rate per 100,000 persons, from 0.77 to 15.62. The incidence and prevalence of GBS increased with age and peaked at 70−79 years (Figs. 1 and 2). The number of GBS admissions was higher in summer (3,152 cases, 28%) and spring (2,949 cases, 26%) than in winter (2,694 cases, 24%) and autumn (2,351 cases, 21%) (Supplementary Fig. 1 in the online-only Data Supplement). The 11,146 patients comprised 2,955 (27%), 3,354 (30%), and 3,805 (34%) with low, middle, and high incomes, respectively, and 7,032 patients (63%) who were treated at the referral hospitals. A total of 2,190 (20%) patients had a long hospitalization period. During hospitalization, 4,420 (40%) and 165 (1%) patients were treated with IVIG and plasmapheresis, respectively, while 497 patients (4%) underwent tracheostomy.

Long-term physical disability

We evaluated physical disability in 10,114 patients with GBS who did not have a physical disability recorded before the onset of GBS in the NHIS database (Table 2 and Supplementary Table 2 [in the online-only Data Supplement]). A total of 1,028 (10.2%) patients had physical disabilities after their GBS diagnosis. The disability registration occurred at a median of 0.6 years after the GBS diagnosis. There were 502 (5.0%) patients with moderate physical disability and 526 (5.2%) with severe physical disability. Table 2 indicates that increasing age, long hospitalization period, IVIG, plasmapheresis, and tracheostomy were associated with a higher risk of disability in GBS patients.

SMR and causes of death

A total of 1,403 (12.6%) patients with GBS (927 males and 476 females) died during the 17 year study period (2002−2018). The median follow-up duration was 6.2 years (interquartile range: 3.0−10.7 years) after the first diagnosis. There were 144 (1.3%) in-hospital deaths, the main cause of which was GBS (n=86, 60%), followed by acute myocardial infarction (n=6, 4%) and pneumonia (n=3, 2%). Additionally, 552 (5.0%) patients had died within 1 year after being diagnosed with GBS. The SMR decreased as each year passed after the di-

Age	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
0-4	1.57	1.04	1.03	1.07	1.02	1.25	1.00	0.97	1.83	1.20	1.72	1.43	0.78	1.24	1.04	1.11	1.27
5-9	0.68	0.73	0.54	0.43	0.86	0.47	0.53	0.68	1.02	0.72	0.34	0.56	0.78	0.77	0.68	0.72	0.82
10-14	0.45	0.47	0.57	0.67	0.70	0.54	0.73	1.62	0.86	0.61	0.68	0.57	0.64	0.77	0.98	0.81	0.82
15-19	0.54	0.60	0.64	0.57	0.56	0.78	0.41	0.98	0.70	0.87	0.72	0.50	1.20	0.89	0.86	1.05	1.18
20-24	0.49	0.39	0.49	0.54	0.62	0.88	0.63	0.96	0.96	1.09	0.66	0.76	1.66	0.93	1.10	1.18	1.52
25-29	0.56	0.67	0.72	0.74	0.60	0.67	0.62	0.85	1.02	0.85	0.94	1.19	1.20	1.02	1.46	1.38	1.58
30-34	0.37	0.72	0.69	0.46	0.53	0.74	0.77	0.72	0.76	0.52	1.01	0.83	1.05	1.15	1.22	1.42	1.32
35-39	0.67	0.74	0.66	0.76	0.76	0.96	0.53	0.98	0.79	0.69	0.85	0.87	0.98	1.14	1.02	1.11	1.45
40-44	0.65	0.72	0.71	0.72	0.68	0.70	0.86	1.03	0.87	0.89	0.93	1.28	1.33	1.36	1.16	1.39	1.43
45-49	0.67	0.82	0.56	0.76	0.57	1.21	1.37	0.99	1.29	1.21	1.05	1.37	1.29	1.61	1.59	1.50	2.01
50-54	0.87	1.48	1.22	1.22	1.14	1.06	1.32	1.09	1.80	1.62	1.61	1.59	1.85	1.54	1.53	2.12	1.78
55-59	1.33	1.57	1.14	1.43	1.56	1.34	1.99	1.96	1.56	1.84	1.95	1.74	2.42	2.01	2.99	2.70	2.63
60-64	1.69	1.53	1.69	1.66	1.83	1.89	1.96	1.97	2.24	2.16	2.88	2.33	3.12	2.53	3.31	3.05	2.85
65-69	1.99	1.20	1.51	1.65	2.14	2.37	2.34	2.72	3.03	3.00	2.84	3.17	3.37	2.87	2.91	3.28	3.66
70-74	1.90	1.52	0.98	1.33	2.16	3.23	3.47	2.90	2.17	3.41	3.16	3.11	3.33	4.75	5.16	3.35	4.47
75-79	1.74	1.37	1.70	2.67	2.01	2.14	3.81	3.23	2.38	3.01	2.01	4.17	3.72	3.75	4.25	4.48	5.32
80-84	1.11	1.53	0.98	1.17	3.66	1.51	0.82	2.44	2.58	2.43	1.96	2.97	3.00	4.65	3.30	2.89	4.16
≥85	0.47	0.00	1.28	0.40	2.04	2.38	1.24	0.88	1.79	0.53	1.47	1.58	1.45	2.11	2.15	1.65	1.54

Fig. 1. Incidence of Guillain–Barré syndrome per 100,000 persons by age in Korea, 2002–2018.

agnosis (Supplementary Table 3 in the online-only Data Supplement). The SMR was 5.63 (95% CI: 5.17−6.12) within 1 year after the diagnosis, 3.99 (3.70−4.30) within 2 years after the diagnosis, 3.16 (2.93−3.39) within 3 years after the diagnosis, 2.83 (2.63−3.03) within 4 years after the diagnosis, and 2.64 (2.46−2.83) within 5 years after the diagnosis.

Table 3 and Supplementary Table 4 (in the online-only Data Supplement) list the causes of death in patients with GBS. The main cause of death for patients with GBS was neurological diseases (SMR: 19.7, 95% CI: 17.8−21.8). Of 381 patients who died from neurological diseases, 298 (78%) died from inflammatory polyneuropathy including GBS (Supplementary Table 5 in the online-only Data Supplement). Causes of death other than colon cancer and mental disorders were also significantly more common in patients with GBS than in the general population.

Comparing survival times between groups according to age, sex, income level, hospitalization period, hospital type, IVIG, plasmapheresis, and tracheostomy revealed that the mean survival time was significantly shorter among the elderly, males, patients with a low income, patients treated at a nonreferral hospital, patients treated with IVIG and tracheostomy, and patients with a long hospitalization period (all $p<0.001$) (Fig. 3). However, survival time was not significantly

related to plasmapheresis ($p=0.382$). Cox regression analysis showed that increasing age, male sex, low income, admission to a nonreferral hospital, and treatment with IVIG and tracheostomy were associated with increased mortality in GBS patients (Table 2).

DISCUSSION

This study is the first to assess the incidence and prevalence of GBS in the entire Korean population including patients of all ages, as well as the relationships of these metrics with sex, income level, physical disability, mortality, and causes of death. Although there were restrictions in the clinical information regarding GBS in the NHIS database, the accuracy of the operational diagnosis was confirmed as being high since it was based on medical records at a tertiary hospital.

We identified that the age-adjusted incidence and prevalence of GBS in 2018 were 1.68 and 15.62 per 100,000 persons, respectively, in the Korean population. This incidence rate is consistent with those found in other countries (0.59−2.35 per 100,000 persons) (Table 4).[3,4] We found that the incidence of GBS was higher in elderly and male patients, which is also a frequent finding in many countries worldwide; however, the biological reasons are unclear.[6,16-18] The incidence of

	<5	5-10	10-15	15-20	20-25	25-30	30-35	35-40	40-45

Age	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
0-4	1.6	2.4	2.9	3.3	2.8	2.9	2.9	2.9	3.7	3.5	3.9	4.2	3.8	3.2	3.3	2.9	3.2
5-9	0.7	1.6	2.5	3.3	4.8	5.7	6.2	6.8	7.5	7.6	7.3	7.6	8.1	8.7	8.3	8.8	9.0
10-14	0.5	0.9	1.4	2.1	2.6	3.1	4.1	6.2	7.4	8.4	9.5	9.7	10.0	10.5	11.0	10.8	11.3
15-19	0.5	1.2	1.9	2.4	3.0	3.7	4.2	4.9	5.4	6.7	7.3	8.3	10.3	11.1	12.0	13.8	14.2
20-24	0.5	0.9	1.4	1.9	2.6	3.6	4.4	5.5	6.6	7.4	8.0	8.6	9.6	10.5	11.9	12.4	14.0
25-29	0.6	1.1	1.7	2.1	2.4	3.2	3.5	4.2	5.3	6.4	7.5	9.0	10.3	11.5	12.6	13.9	15.6
30-34	0.4	1.2	2.0	2.6	3.6	3.9	4.9	5.5	5.7	6.0	7.2	7.7	8.7	10.2	12.0	13.7	14.9
35-39	0.7	1.3	1.9	2.9	3.2	4.2	4.5	5.2	6.3	7.0	7.4	8.5	9.2	9.7	10.6	12.1	13.7
40-44	0.7	1.4	2.1	2.6	3.1	3.9	4.8	6.0	6.6	7.2	8.0	8.9	10.0	11.6	12.8	13.1	14.8
45-49	0.7	1.4	2.0	2.8	4.0	4.9	6.2	6.7	7.2	7.9	8.8	9.5	10.8	12.3	13.3	14.7	16.1
50-54	0.7	2.2	3.1	3.9	4.8	5.7	6.5	7.6	9.1	10.5	11.4	12.8	13.8	13.7	14.1	16.0	16.7
55-59	1.3	2.5	3.4	4.6	6.9	7.5	9.4	10.2	10.9	11.5	13.8	14.0	16.3	18.0	20.4	21.3	23.2
60-64	1.4	2.6	4.3	5.6	7.1	8.8	10.6	11.6	13.0	15.1	16.7	19.2	21.2	21.2	23.0	26.2	27.0
65-69	1.7	3.1	4.4	5.8	7.7	9.6	11.2	14.2	17.1	18.9	19.8	21.7	23.5	25.7	29.1	30.9	33.9
70-74	1.6	2.7	3.4	5.1	6.9	9.8	12.8	14.7	15.9	19.0	21.6	23.9	27.1	32.4	35.1	35.1	37.8
75-79	1.4	2.7	4.3	5.9	8.2	9.1	12.3	14.7	16.3	18.4	20.5	24.3	27.8	30.6	33.2	37.8	40.3
80-84	1.1	2.6	3.0	4.9	6.6	8.4	9.6	12.4	14.1	17.6	17.6	19.8	22.3	28.9	31.6	35.0	40.1
≥85	0.5	0.9	2.6	2.0	3.4	5.4	7.4	8.5	9.7	10.6	12.7	14.7	18.8	20.4	22.4	25.0	27.8

Fig. 2. Prevalence of Guillain-Barré syndrome per 100,000 persons by age in Korea, 2002–2018.

GBS gradually increased as each year passed during the study period, which is consistent with the results obtained in a Taiwanese population.[18] Additionally, we found that the incidence of GBS was not influenced by influenza or influenza vaccination. The incidence of GBS in 2009, when there was an influenza A (H1N1) outbreak, was similar to that in 2008

**Table 2.** Independent predictors of mortality and disability in patients with Guillain-Barré syndrome

Characteristics	Mortality (*n*=11,146)			Disability* (*n*=10,144)		
	Hazard ratio	95% CI	*p*	Hazard ratio	95% CI	*p*
Age (yr)						
Each 10-year increase	2.02	1.95–2.10	<0.001	1.10	1.04–1.12	<0.001
Sex						
Female	0.55	0.49–0.61	<0.001	0.88	0.78–1.00	0.053
Male	1.00	Reference		1.00	Reference	
Income level†						
Low	1.36	1.21–1.53	<0.001	1.05	0.90–1.22	0.535
Middle	1.11	0.98–1.26	0.103	1.00	0.86–1.16	0.968
High	1.00	Reference		1.00	Reference	
Hospital type						
Referral hospital	0.83	0.75–0.91	<0.001	0.94	0.83–1.06	0.305
Nonreferral hospital	1.00	Reference		1.00	Reference	
Hospitalization period						
≥30 days	0.99	0.88–1.12	0.906	3.36	2.92–3.87	<0.001
<30 days	1.00	Reference		1.00	Reference	
IVIG						
Yes	1.21	1.08–1.34	0.001	1.46	1.28–1.68	<0.001
No	1.00	Reference		1.00	Reference	
Plasmapheresis						
Yes	1.02	0.69–1.50	0.933	1.92	1.46–2.54	<0.001
No	1.00	Reference		1.00	Reference	
Tracheostomy						
Yes	1.92	1.61–2.30	<0.001	2.85	2.41–3.38	<0.001
No	1.00	Reference		1.00	Reference	

*GBS patients who had no physical disability at the time of GBS diagnosis; †Income levels were classified into three categories: 1) low (poorest 30% of the population), 2) middle (31%–70% of the population), and 3) high (richest 30% of the population).
CI, confidence interval; GBS, Guillain-Barré syndrome; IVIG, intravenous immunoglobulin.

Table 3. Causes of death among patients with Guillain-Barré syndrome in Korea, 2002–2018

Diseases	Observed deaths			Expected deaths			SMR (95% CI)		
	Total	Male	Female	Total	Male	Female	Total	Male	Female
Total	1,403	927	476	710.5	458.8	251.8	1.97 (1.87–2.08)	2.02 (1.89–2.15)	1.89 (1.72–2.07)
Neoplasms (C00–D48)	302	225	77	210.9	151.5	59.3	1.43 (1.28–1.60)	1.48 (1.30–1.69)	1.30 (1.02–1.62)
Endocrine, nutritional, and metabolic diseases (E00–E90)	59	30	29	33.9	19.8	14.1	1.74 (1.33–2.25)	1.52 (1.02–2.17)	2.05 (1.37–2.95)
Diseases of the nervous system (G00–G99)	381	226	155	19.3	10.4	8.9	19.75 (17.8–21.8)	21.77 (19.0–24.8)	17.39 (14.8–20.4)
Diseases of the circulatory system (I00–I99)	198	121	77	165.4	94.9	70.5	1.20 (1.04–1.38)	1.27 (1.06–1.52)	1.09 (0.86–1.37)
Diseases of the respiratory system (J00–J99)	111	74	37	64.3	44.3	20.0	1.73 (1.42–2.08)	1.67 (1.31–2.10)	1.85 (1.30–2.55)
External causes of morbidity and mortality (V01–Y98)	90	70	20	67.1	50.3	16.9	1.34 (1.08–1.65)	1.39 (1.09–1.76)	1.19 (0.72–1.83)
Others (A00–B99, D50–89, F00–F99, H00–H95, K00–K93, L00–L99, M00–M99, N00–N99, O00–O99, P00–P96, Q00–Q99, R00–R99)	262	181	81	149.7	87.6	62.1	1.75 (1.54–1.98)	2.07 (1.78–2.39)	1.31 (1.04–1.62)

CI, confidence interval; SMR, standardized mortality ratio.
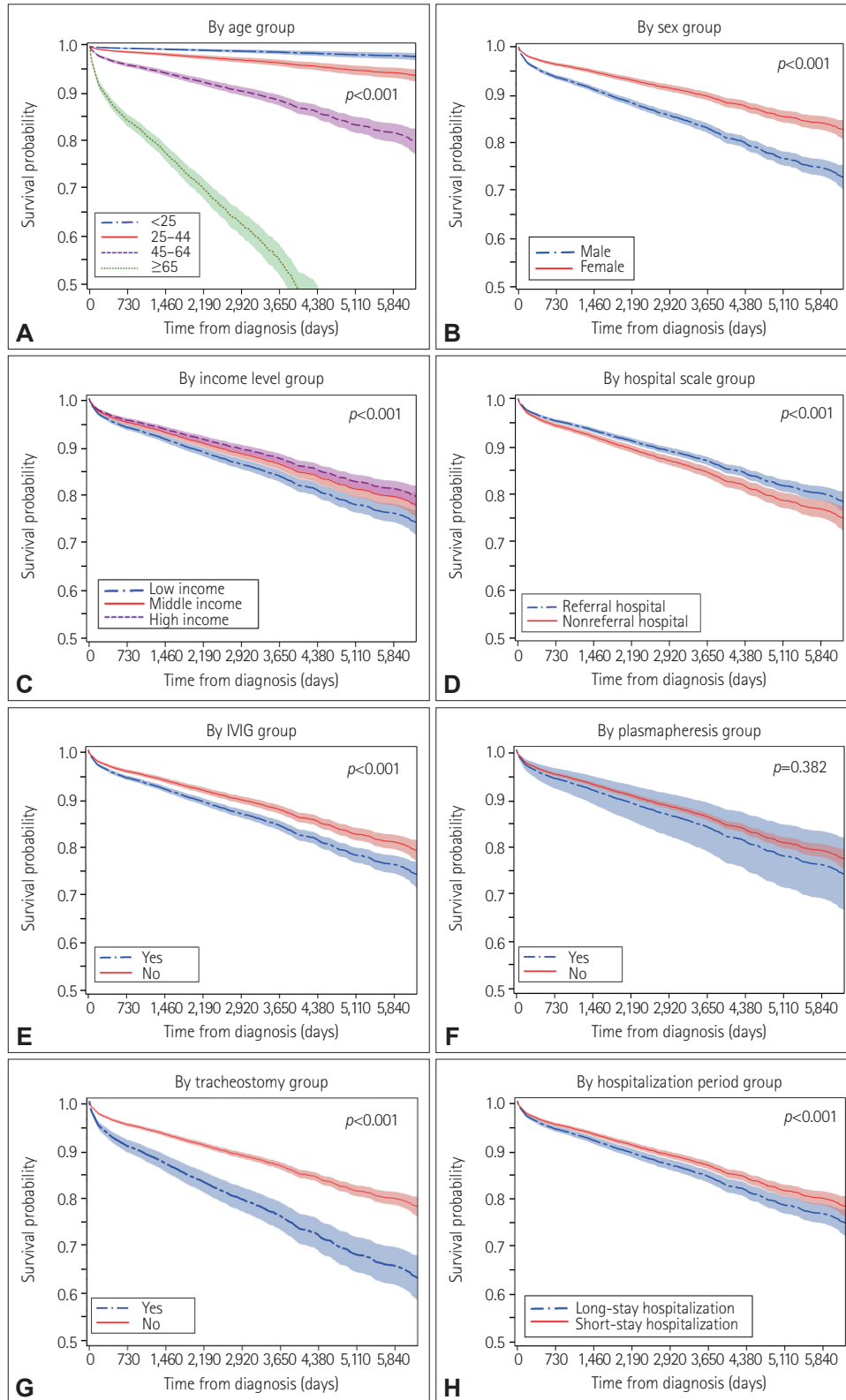
Fig. 3. Comparison of survival curves from the time of diagnosis to the time of death in patients with Guillain-Barré syndrome reveals significant differences among groups defined by age at diagnosis (A), sex (B), income level (C), hospital type (D), IVIG (E), plasmapheresis (F), tracheostomy (G), and hospitalization period (H) (2002–2018). The mean survival time was significantly shorter in the elderly, males, patients with a low income, patients treated at a nonreferral hospital, patients treated with IVIG and tracheostomy, and patients with a long hospitalization period (log-rank test, $p < 0.05$). IVIG, intravenous immunoglobulin.

Table 4. Comparison of the incidence rates of GBS in various countries

Study location	Data source	Diagnostic criteria	Period	Age (yr)	Cases	Incidence per 100,000	Reference
Victoria, Australia	Medical record systems at teaching hospitals	Not reported	1980–1984	≥15	110	0.90	Storey et al.[39]
Western Australia	Case record search for GBS, polyneuritis, or polyneuropathy codes	Asbury criteria	1980–1985	All	109	1.35	Hankey[40]
UK	Population-based study using a general-practice research database	Codes for GBS or infective neuritis	1992–2000	All	228	1.33	Hughes et al.[41]
Southeast England	A voluntary reporting scheme, hospital activity analysis, a contemporary research database, and death certificates	Asbury and Cornblath criteria	1993 & 1994	All	79	1.20	Rees et al.[32]
Denmark	Danish national patient registry	ICD-8 code for polyradiculitis acuta and ICD-10 code for GBS	1987–2016	≥16	2,319	1.77	Levison et al.[42]
Germany	Nationwide administrative database from reimbursement scheme implementation	ICD-10 code G61.0	2003–2005	All	4,349	1.60–1.89	Lehmann et al.[43]
Southwest Greece	Medical records at two referral hospitals	NINCDS	1989–2001	All	105	0.99	Chroni et al.[29]
USA	Nationwide inpatient sample database	ICD-9-CM code for GBS (357.0)	2000–2004	≥18	4,954	1.65–1.79	Alshekhlee et al.[36]
USA	Vaccine Safety Datalink	ICD-9 code for GBS (357.0)	2000–2009	All	1,619	1.72	Shui et al.[16]
Finland	Hospital discharge database	Asbury criteria and Poser criteria	1981–1986	All	247	0.84	Kinnunen et al.[44]
Finland	Finnish Care Register for Health Care	ICD-10 code G61.0	2004–2014	All	989	1.70	Sipilä et al.[45]
Italy	Italian network for the study of GBS	Asbury criteria	2010 & 2011	≥18	365	1.84	Benedetti et al.[46]
Lombardy, Italy	Prospective hospital-based survey, in which patients were interviewed and atypical cases were discussed	NINCDS	1994 & 1995	All	109	0.92	Beghi et al.[47]
Piemonte and Valle d'Aosta, Italy	Piemonte and Valle d'Aosta Register for Guillain–Barré Syndrome	ICD-9 codes 357.0, 357.8, and 357.9	1995 & 1996	All	120	1.36	Chiò et al.[48]
Taiwan	National Health Insurance Research Database	ICD-9-CM code for GBS (357.0)	1997–2011	All	5,998	1.52–2.31	Huang et al.[18]
Jiangsu province, China	Survey	NINCDS	2008–2010	All	441	0.59	Chen et al.[5]
Western Norway	Hospital records	NINCDS	1957–1982	All	109	1.19	Larsen et al.[49]
Serbia	Medical records at five tertiary healthcare centers in Serbia	Brighton criteria	2009–2018	≥18	640	1.07	Stojanov et al.[38]
Spain	Retrospective review of national health service	NINCDS	1985–1997	>19	337	0.86	Cuadrado et al.[50]
Sweden	Hospital Inpatient Register of the National Board of Health and Welfare in Sweden	ICD-9 code for GBS (357A)	1978–1993	All	2,257	1.77	Jiang et al.[28]
Quebec and Ontario, Canada	Hospital discharge databases	ICD-9 codes 357.0, 357.8, 357.9, and 375.0	1983–1989	All	2,333	1.51–1.78	McLean et al.[51]
Chile	Department of Statistics and Health Information of the Chilean Ministry of Health for all public and private health providers in Chile	ICD-10 code for GBS (G61.0)	2001–2012	All	4,158	1.61–2.35	Rivera-Lillo et al.[6]
Korea	Medical records at 28 randomly selected hospitals	Brighton criteria	2008–2010	All	245	0.63–0.87	Kim et al.[9]
Korea	Korean National Health Insurance Service claims data	Hospitalized cases with ICD-10 code for GBS (G61.0)	2014–2016	≥65	320	4.14–4.16	Lee et al.[8]

GBS, Guillain–Barré syndrome; ICD, International Classification of Diseases; NINCDS, National Institute of Neurological and Communicative Disorders and Stroke Criteria.

and 2010, which was also consistent with previous results.[9,19] Our results showed that the incidence of GBS peaked in late spring and summer, which is similar to results obtained in northern China.[20-22] This may be due to the high proportion of acute motor axonal neuropathies in the Korean and Chinese populations, which is caused by prodromal infection (including *Campylobacter jejuni* infection) in the summer. However, studies of the seasonality of GBS have produced highly heterogeneous results, especially in Western countries, with some studies showing a winter peak,[23-25] others showing a peak in late summer and autumn,[26,27] and still others not finding any seasonal variation.[5,28,29]

Our study found that 40% of patients received IVIG, whereas only 1% received plasmapheresis. We believe that the proportion of patients treated with IVIG is much higher than 40%, since patients with mild muscle weakness can be treated with IVIG via prescriptions that are not claimed from the NHIS. The use of IVIG can only be claimed in patients with GBS with the following conditions: 1) when walking is difficult without the help of others due to at least moderate muscle weakness in both legs or arms (Medical Research Council scale grades 0−3) or 2) having difficulties in respiration or swallowing related to aspiration. The proportion of patients receiving plasmapheresis was tiny since this is usually only applied to hemodynamically stable patients at major referral hospitals with the requisite equipment and trained medical staff.[30] These findings are consistent with a previous report that IVIG is usually the treatment of choice in GBS due to its high availability and convenience.[31]

Few studies have investigated disabilities in patients with GBS. Our study found that about 10% of people had moderate-to-severe physical disabilities, and 90% had a good functional outcome during the long-term follow-up. The disability registration occurred at a median of 0.6 years after the GBS diagnosis, which was due to disability being recorded no earlier than 0.6 years after the onset of a disease. The rate of good functional outcomes found here is similar to previous results from southeast England (88%), northern Italy (91%), and Nepal (93%),[32-34] but higher than those found in southwest Greece (75%) and Taiwan (80%).[29,35]

Our study revealed both short- and long-term mortality rates. The in-hospital mortality rate was 1.3% in the present study, which is lower than those found in the USA and Taiwan.[18,36] The 1-year mortality rate was 5.0% in the present study, which is similar to previous results in southeast England (8%), Asian countries (6%), Taiwan (4%), and the Netherlands (3.9%),[7,32,35,37] and better than the 6-month mortality rate of 9.7% found in Serbia.[38] Our study also revealed the mortality rate over a very long mean observation period of 9.0 years after the diagnosis. Finally, the SMR of patients with

GBS had decreased year by year after the diagnosis, but remained significantly high until 5 years after the diagnosis in the Korean population.

The rates of death in all categories were significantly higher in patients with GBS than in the general population, which means overall health was worse for patients with GBS. Among the causes of death, diseases of the nervous system (including GBS) were the most common underlying cause in the Republic of Korea, while other studies have often found immediate causes of death such as pneumonia in patients with GBS.[7] This is due to causes of death frequently being recorded as underlying conditions in the Republic of Korea and many of the deaths due to conditions of the nervous system being ascribed to GBS in the Republic of Korea.

This study has identified that the independent predictors of physical disability are age, hospitalization period, IVIG, plasmapheresis, and tracheostomy in Korean patients with GBS. In contrast, the independent predictors of mortality are age, sex, income level, hospital type, the use of IVIG, and tracheostomy. These differences are probably due to mortality being associated with both the severity of GBS and the general factors contributing to mortality in the Korean population, which are being older, male sex, and lower income level (https://kosis.kr/eng/). The poor prognosis associated with treatment was probably due to the severity of GBS in the treated group. For example, the NHIS database contains only claimed prescriptions related to the use of IVIG in patients with severe GBS. Many patients with mild disability—both those treated with IVIG as an unclaimed prescription and those who were not treated—were included in the untreated group in our study. Therefore, the poor prognosis may be due to the disease severity rather than the use of IVIG.

Our study had critical limitations. First, the NHIS database does not provide detailed clinical information, such as on the presence of prodromal infection, NCS results, antiganglioside antibody profiles, or clinical severity. Therefore, we could not determine the subtype of GBS according to NCS results or antiganglioside antibody profiles. Second, considering our use of hospital data, the analyzed sample would have included a small number of patients with cranial-dominant GBS. Third, the proportion of patients treated with IVIG was probably underestimated due to the exclusion of prescriptions that were not claimed from the NHIS.

In summary, the incidence of GBS in Korean patients was 1.7 per 100,000 persons, with a higher incidence in the elderly, male individuals, and during the summer. Approximately 11% of the patients had physical disabilities after the diagnosis of GBS. The in-hospital and long-term (mean: 9 years) mortality rates were 1.3% and 11.0%, respectively.

In conclusion, this first nationwide epidemiological study of

patients with GBS covering the entire population of all ages in the Republic of Korea has revealed the seasonality of admissions, disability, and long-term mortality of patients with GBS.

Supplementary Materials

The online-only Data Supplement is available with this article at https://doi.org/10.3988/jcn.2022.18.1.48.

Availability of Data and Material

All data generated or analyzed during the study are included in this published article (and its supplementary information files).

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Conflicts of Interest

The authors have no potential conflicts of interest to disclose.

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