THE MEDICAL BULLETIN OF
SISLI ETFAL HOSPITAL

DOI: 10.14744/SEMB.2019.82598
Med Bull Sisli Etfal Hosp 2020;54(1):73–77

Original Research

Guillain Barre Syndrome: A Single Center Experience

Onur Akan, Canan Emir, Cihat Örken, Serap Üçler

Department of Neurology, Okmeydanı Training and Research Hospital, Istanbul, Turkey

Abstract

Objectives: To investigate the clinical, electrophysiological and epidemiological features of the patients who were diagnosed as Guillain Barre Syndrome (GBS) in our clinic.

Methods: The clinical and demographical properties of 30 patients with GBS who were hospitalized in our neurology clinic between March 2013 and August 2017 were retrospectively examined in this study. Patients were divided into two groups according to the requirement of stay in the intensive care unit (ICU).

Results: Patients were between 18-71 years range with 46.9 and 19.61 mean age. Seven of 30 patients (23.3%) were female, and 23 of them (76.7%) were male. Males were more dominant in the ICU (-) group (81% and 62%). A recent infection was found in 86.7% of patients. Upper respiratory tract infection (URTI) was more common in ICU (+) group whereas lower respiratory tract infection (LRTI) and acute gastroenteritis (AGE) were more common in the ICU (-) patients (p=0.007). Lower limb weakness was more frequent in the ICU (+) group (p=0.011). ICU (+) patients were lack of diplopia and dysarthria. Ataxia and dysphagia were relatively frequent in the ICU (+) group. Electrophysiological examinations revealed demyelinating polyneuropathy (26.7%), acute axonal polyneuropathy (30.1%) and acute sensorial polyneuropathy (13.3%). Demyelinating polyneuropathy was more common in the ICU (-) group, whereas acute motor and sensorial polyneuropathy (AMSAN) was more frequent in the ICU (+) group. In this study, 26.7 % of study patients required mechanical ventilation, and mortality rate was 6.8 %.

Conclusion: URTI in ICU (+), LRTI and AGE in ICU (-) patients might be major trigger factors of GBS. Ascending weakness, dysphagia and ataxia was more frequent in ICU (+) GBS patients. Demyelinating PNP was predominant in the ICU (-) group, whereas AMSAN was more frequent in the ICU (+) patients. Multicenter randomized studies would be more useful for highlining the epidemiology of GBS.

Keywords: Demographical features; electrophysiology; Guillain Barre Syndrome.

Please cite this article as "Akan O, Emir C, Örken C, Üçler S. Guillain Barre Syndrome: A Single Center Experience. Med Bull Sisli Etfal Hosp 2020;54(1):74–78".

Guillain Barre Syndrome (GBS) is an acute inflammatory immune-mediated polyradiculoneuropathy that typically onsets with tingling, progressive weakness, and pain.[1] The incidence of GBS varies between 0.40-3.25 per 100.000, depending on the geographical location.[1,2] Despite its low incidence, GBS constitutes one of the main components in the differential diagnosis of acute neurological deficits in emergency departments.[2]

Although it exhibits an acute, monophasic, inflammatory, mostly demyelinating polyradiculoneuropathy pathology, there are also axonal onset forms. Before the disease, there is usually a history of predisposing infection. The best known specific causative microorganisms are Campylobacter jejuni, Cytomegalovirus and Epstein-Barr virus.[1,2] In recent years, cases of GBS developing after the Zika virus have been reported.[3,4]

In this study performed to examine whether there is a difference in the epidemiology of GBS with environmental

Address for correspondence: Onur Akan, MD. Okmeydanı Egitim ve Arastirma Hastanesi, Noroloji Klinigi, Istanbul, Turkey
Phone: +90 505 368 28 37 **E-mail:** dronurakan@hotmail.com

Submitted Date: June 10, 2018 **Accepted Date:** April 29, 2019 **Available Online Date:** March 25, 2020

changes in the last decades, we aimed to review the epidemiological, clinical features of patients who were followed up with the diagnosis of GBS in our center and to compare patients with and without intensive care requirement.

Methods

Clinical and demographic data of 30 patients who were hospitalized in our Neurology Clinic between March 2013 and August 2017 with the diagnosis of GBS were retrospectively analyzed in this study. Two patients who were hospitalized with an initial diagnosis of GBS and who were later diagnosed with chronic inflammatory demyelinating polyneuropathy (CIDP) were excluded from this study.

Patients' age, gender, application complaints, initial examination findings, cerebrospinal fluid (CSF) analysis results, need for intensive care, clinical and electrophysiological features GBS variants [(acuteinflammatory demyelinating polyneuropathy (AIDP), acute motor axonal neuropathy (AMAN), acute motor and sensorial neuropathy (AMSAN), Miller Fisher syndrome (MFS), and regional forms were recorded from medical files of the cases. The patients were divided into two different groups according to the need of intensive care unit (ICU) and the data of both groups were compared. Approval was received from the Clinical Research Ethics Committee (Dated 05.08. 2018, numbered 48670771-514.10).

Statistical Package for the Social Sciences (SPSS) 18 program was used for statistical evaluation. The fitness of quantitative data to normal distribution was evaluated using the Kolmogorov Smirnov test. Variables with normal distribution were analyzed by parametric methods, and variables that did not comply with normal distribution were analyzed using non-parametric methods. Independent samples- t-test or Mann-Whitney U test was used to compare two independent groups. Categorical data were compared using the Pearson chi-square test. The proportion of variables examined by descriptive statistical tests was specified as numbers and percentages. Quantitative data were expressed as mean±standard deviation (SD) and median (minimum-maximum) values. For all tests, $p<0.05$ was considered statistically significant.

Results

Of the 30 patients diagnosed with GBS, seven (23.3%) were female and 23 (76.7%) were male. The patients were between the ages of 18-71years and the mean age was 46.9±19.61 years. Pre-disease history of upper respiratory tract infection (URTI) revealed in 33% (n=10), acute gastroenteritis in 33% (n=10), lower respiratory tract infection (LRTI) in 10% (n=3), acute gastroenteritis (AGE) with URTI in 6.7% (n=2) and pyoderma in 3.3% (n=1) of the patients. In four patients (13.3%), there was no history of infection (Table 1). When patients were divided into two groups according to the need of ICU, male dominance was much more prominent in the group that was not hospitalized in ICU (p=0.03, 2=8.5). When examined concerning infection, history of URTI revealed in approximately half of the patients who need ICU, whereas the history of LRTI and AGE was more frequently reported by patients who did not need ICU (p=0.007, x^2=22.5), (Table 1).

The age of the patients hospitalized the ICU was 47.5±22.9 years, and the mean age of the patients who did not need ICU was 46.7±18.9 years without any statistically significant difference between the two patient groups (p=0.92).

Admission complaints were weakness in the lower extremities in 14 (46.7%), weakness in the upper extremity in three (10%), weakness in both upper and lower extremities in three (10%), ataxia in three (10%), and dysphagia in four (3.3%) patients. In the examination of reflexes, areflexia (n=14: 46.7%), hyporeflexia (n=10:33.3%), and normoactive deep tendon reflexes (n=6:20%) were detected in respective number of patients.

Lumbar puncture was performed, and protein content of cerebrospinal fluid (CSF) was found to be increased in seven (23.3%) patients while it was within normal limits in six (20%) patients (Table 2).

When the patients with and without ICU need were compared concerning admission complaints, it was observed that the weakness that started only from the lower extremities was more frequent in patients hospitalized in the ICU (p=0.011, r^2=6.53) (Table 2). While diplopia and dysarthria were not observed in the patients hospitalized in the

Table 1. Comparison of the patients who needed and did not need hospitalization in the intensive care unit (ICU) as for age, gender, and history of pre-disease infection

Demographic data	n (%)			p (x^2)
	ICU need (-)	ICU need (+)	Total	
Gender				
Female	4 (18.2)	3 (37.5)	7 (23.3)	0.03 (8.5)
Male	18 (81.8)	5 (62.5)	23 (76.7)	
History of infection				0.007 (22.5)
None	3 (13.6)	1 (12.5)	4 (13.3)	
URTI	6 (27.3)	4 (50)	10 (33.3)	
LRTI	3 (13.6)	0 (0)	3 (10)	
AGE	7 (31.8)	3 (37.5)	10 (33.3)	
URTI+AGE	2 (9.1)	0 (0)	2 (6.7)	
Pyoderma	1 (4.5)	0 (0)	1 (3.3)	

ICU, the rate of ataxia and dysphagia was relatively higher (p=0.001) (Table 2). While most of the patients in the ICU were areflexic, the rates of hyporeflexia and areflexia were found to be close to each other in those who were not hospitalized in the ICU (p=0.01, r^2=6.53), (Table 2). Only one of the eight patients hospitalized in the ICU was examined for CSF protein, and increased CSF protein level was detected in this patient. Normal and increased CSF protein ratios were found close to each other in patients not hospitalized in ICUs (p=0.03, r^2=8.5) (Table 2).

Electromyographic (EMG) examinations of patients revealed demyelinating polyneuropathy in 14 (26.7%), acute axonal polyneuropathy in nine (30.1%), and acute sensorial axonal polyneuropathy in four (13.3%) patients. While two patients were accepted as having AMAN, two patients as AMSAN, four patients as MFS, and one patient as pharyngeal-cervical-brachial variant. EMG could not be performed in five (16.7%) patients (Table 3). While AMSAN was predominant in the patients hospitalized in the ICU, demyelinating PNP was found more frequently in the patients who did not need ICU (p=0.04, r^2=20.6) (Table 3).

Steroid treatment was administered to all 30 patients included in this study, and one patient received IVIG in addition to steroid therapy. Eight (26.7%) patients needed intensive care. The general condition of two of these eight patients (6.7%) worsened and progressed into multiple organ failure. In our two very old patients who had autonomic involvement exited (Table 4).

Table 2. Comparison of the patients who needed, and did not need hospitalization in intensive care unit (ICU) as for their first admission complaints, the condition of their reflexes during examination, and results of cerebrospinal fluid (CSF) analysis

Parameter	n (%)			p (x^2)
	ICU need (-)	ICU need (-)	Total	
Admission complaint				
Weakness of extremity (ies)				0.011 (6.53)
Upper	2 (9.1)	1 (12.5)	3 (10)	
Lower	8 (36.4)	6 (75)	14 (46.7)	
Upper+Lower	10 (45)	1 (12.5)	11 (36.7)	
Ataxia	2 (9.1)	1 (12.5)	3 (10)	0.001 (22.5)
Diplopia	2 (9.1)	0 (0)	2 (6.7)	0.001 (22.5)
Dysphagia	1 (4.5)	3 (37.5)	4 (13.3)	0.001 (16.1)
Dysarthria	1 (4.5)	0 (0)	1 (3.3)	0.001 (22.5)
Examination of reflexes				0.01 (6.5)
Normal	5 (22.7)	1 (12.5)	6 (20)	
Hyporeflexia	8 (36.4)	2 (12.5)	10 (33.3)	
Areflexia	9 (40.9)	5 (62.5)	14 (46.7)	
CSF protein				0.03 (8.5)
Normal	6 (27.3)	0 (0)	6 (20)	
Increased	6 (27.3)	1 (12.5)	7 (23.3)	
NA	10 (56.7)	7 (87.5)	17 (56.7)	

Discussion

GBS is an acquired inflammatory polyneuropathy that may affect motor, sensorial and autonomic nerve fibers as well as spinal roots. GBS is characterized by ascending flask muscle weakness. GBS is the most common cause of neuromuscular paralysis known worldwide. Contrary to what is expected in autoimmune diseases, it has been reported to be more common in men.[1,2] In this study, 3/1 male dominance was observed. While there was a more moderate male dominance of 3/2 in patients who needed ICU, male dominance exceeding 4/1 was found in patients who did not require ICU.

The incidence of GBS shows bimodal distribution with age.[1,2] In a review of 63 articles, it was reported that the frequency of disease increases over the age of 50 while it

Table 3. Comparison of the patients who needed and did not need hospitalization in the intensive care unit (ICU) as for their electromyographic (EMG) findings

EMG findings	n (%)			p (I^2)
	ICU need (-)	ICU need (+)	Total	
Acute axonal PNP	4 (18.2)	1 (12.5)	5 (16.7)	0.04 (20.6)
Demyelinating PNP	9 (40.9)	2 (25)	11 (36.7)	
AMAN	1 (4.5)	1 (12.5)	2 (6.7)	
AMSAN	0 (0)	2 (25)	2 (6.7)	
AIDP	1 (4.5)	1 (12.5)	2 (6.7)	
Miller Fisher	3 (13.6)	0 (0)	3 (10)	
NA	4 (18.2)	1 (12.5)	5 (16.7)	

Table 4. Comparison of the patients who needed and did not need hospitalization in the intensive care unit (ICU) as for drugs used in their treatments and their survival rates

	n (%)			p (I^2)
	ICU need (-)	ICU need (+)	Total	
Treatment				0.001(48.6)
IVIG	20 (91)	8 (100)	28 (93.3)	
IVIG+Steroid	1 (4.5)	0 (0)	1 (3.3)	
Untreated	1 (4.5)	0 (0)	1 (3.3)	
Final condition				0.001(22.5)
Survived	22 (100)	6 (75)	28 (93.3)	
Exited	0 (0)	2 (25)	2 (6.7)	

tends to decrease over the age of 80.[3] In our study, the mean age of the patients was found to be 50. Any statistically significant difference was not found between the patients who needed and did not need ICU.

Approximately two-thirds of GBS patients have a history of infection 3-4 weeks before the onset of neurological symptoms.[3,4] The rate of precursor infections is even higher in children compared to adults (67-85%).[3] In our study, a history of infection history was reported by the majority (86%) of patients. In the literature, it has been reported that infections in adults are most commonly respiratory (67-85%) and gastrointestinal system (22-53%) infections.[3]

In IGOS consortium, which was a large cohort study involving 1000 GBS patients living in different geographical regions of the world, it was observed that gastroenteritis was more prevalent in Bangladesh, while respiratory tract infections were higher in Europe and America.[4] In our study, rates of infections involving GIS or respiratory tract were found close to each other. This lack of difference in infection rates can be explained by the region where our patients live and socioeconomic variables. On the other hand, while half of our patients with ICU needs were found to have a history of URTI, it was observed that those who did not need ICU had a history of LRTI and AGE. In addition, the onset of GBS after surgery and vaccination has not been reported in the literature

GBS patients classically refer to the clinic with weakness.[1] In our study, the disease started with weakness in two-thirds of the cases, and in half of them, weakness was observed in the lower extremities. Especially in patients hospitalized in the ICU, it was found that the weakness that started only from the lower extremity was higher than those who did not need ICU. Other cardinal findings known in GBS are hyporeflexia or areflexia.[1,2] In this study, almost half of the patients had hyporeflexia, and one-third of them had areflexia. While diplopia and dysarthria were not observed in our patients hospitalized in ICU, the rate of ataxia and dysphagia was relatively higher.

Hearing loss, cranial nerve involvement and respiratory distress can be seen with decreasing frequency in GBS.[1,2] While sensorial disorders are more prominent in Europe and the USA, cranial nerve involvement and oculomotor weakness have been reported to be common in Asia.[4] In our study, while bulbar and oculomotor nerve involvement were observed in 13%, and 6.7% of the cases, respectively, respiratory distress was not encountered at the first admission of the patients. These variable results may be related to the genetic, phenotypic and environmental differences of our patient population living in the transition zone between Asia and Europe.

Increased cell-free protein, also known as albumin-cytological dissociation in the cerebrospinal fluid, is one of the main diagnostic findings. In the first few weeks, when neurological symptoms appear, the CSF protein level is normal but increases later on. In approximately 10% of cases, the CSF protein level remains within normal limits throughout the course of the disease.[2] In our study, only 25% of the patients had high CSF protein.

Compared to conventional knowledge, this low rate may be related to early CSF analysis. In addition, since some of the patients' general condition was impaired, and some of them were definitely received the diagnosis of GBS based on clinical and electrophysiological examinations, CSF analysis was not performed.

Electrophysiological studies are very useful in making a diagnosis of GBS and they help determine the subtypes and prognosis of the disease, and indicate the degree of axonal loss. Early EMG anomalies occur in more than 80% of GBS patients. Needle EMG is recommended to detect fibrillation and positive wave potentials within the first two weeks of disease onset.[5] In our study, the electrophysiological disorder was found in almost all of the patients who underwent EMG, and the most common demyelinating polyneuropathy was found with a rate of 36.7%.

In the literature, the most common electrophysiological abnormality in GBS has been reported to be demyelinating polyneuropathy.[3] While this rate was 55% in Europe and the USA, in IGNOS consortium, it was found to be 45% in Asia. Axonal GBS has been reported with a rate of 3-17% in Europe and 23-65% in Asia. While the frequency of the Miller Fischer variant is 3% in Europe, this rate increases to 34% in Far East Asia.[4] In our study, axonal GBS was found as 16.7% similarly in European data. Miller Fisher variant was seen in 13.8% of our cases. Among other GBS subgroups, AMAN and AMSAN were found at a rate of 6.7%. On the other hand, while AMSAN is at the forefront of those hospitalized in ICU, demyelinating PNP was found more frequently found in the patients who did not need ICU. These rates that we found in the clinical and electrophysiological subgroups of GBS can be explained in part by local differences in exposure to infections and other environmental factors.

Immunotherapy is recommended as soon as the diagnosis is made in GBS patients.[2] Evidence-based studies have demonstrated that IVIG and plasmapheresis are equally effective in the treatment of GBS.[6] In our patients, almost all patients were given IVIG and plasmapheresis was not preferred due to its invasiveness. The general opinion in the literature is that steroid does not have a place alone or in combination in the treatment of GBS.[1,2] On the contrary,

one of our patients who did not respond to IVIG achieved clinical remission after steroids therapy. This experience supports the argument that the IVIG + steroid combination stated in the 2006 Cochrane database[7] will accelerate recovery in GBS but will not affect long-term outcome.

GBS patients develop respiratory failure requiring mechanical ventilation in up to 30% of the patients associated with phrenic nerve involvement and 2-5% of patients are lost due to complications.[8-10] In this study, 26.7% of the cases required hospitalization in the intensive care unit due to the need for mechanical ventilation, and the mortality rate was found to be 6.8%. While the mortality rate of GBS decreases to 2% in Asia, it rises to 5% in the USA and Europe.[4] The relatively higher mortality rate determined in our study may be associated with the patients' clinic, response to treatment, and admission conditions.

Conclusion

In conclusion, UTI can be seen as the main triggering factor in GBS patients requiring ICU and AGE and ARTI in the patients who do not. The rate of ascending weakness, dysphagia and ataxia is relatively more common in GBS patients who need ICU. Demyelinating PNP is more frequently seen in the patients who do not need ICU, and AMSAN is the priority in the patients who are hospitalized in ICU. Steroids may be considered in treatment-resistant GBS cases. This study reflects the experience of a single center with a limited number of patients. Multi-centered studies conducted with a greater number of patients in our country will be more informative about the epidemiology of GBS.

Disclosures

Ethics Committee Approval: Approval was received from the Clinical Research Ethics Committee (Dated 05.08. 2018, numbered 48670771-514.10).

Peer-review: Externally peer-reviewed.

Conflict of Interest: None declared.

Authorship Contributions: Concept – O.A.; Design – O.A.; Supervision – C.E.; Materials – O.A., C.E., C.O., S.U.; Data collection &/or processing – O.A.; Analysis and/or interpretation – O.A.; Literature search – O.A., C.E.; Writing – O.A.; Critical review – O.A., C.E., C.O., S.U.

References

1. Wijdicks EF, Klein CJ. Guillain-Barré Syndrome. Mayo Clin Proc 2017;92:467–79.
2. Chad DA. Disorders of nerve roots and plexuses. In: Bradley WG, Daroff RB, Fenichel GM, Mardsen CD, editors. Neurology in Clinical practice principles of diagnosis and management. 3rd ed. Boston: Butterworth Heinemann; 2000. p. 2019–130.
3. McGrogan A, Madle GC, Seaman HE, de Vries CS. The epidemiology of Guillain-Barré syndrome worldwide. A systematic literature review. Neuroepidemiology 2009;32:150–63.
4. Doets AY, Verboon C, van den Berg B, Harbo T, Cornblath DR, Willison HJ, et al. Regional variation of Guillain-Barré syndrome. Brain 2018;141:2866–77.
5. Arcila-Londono X, Lewis RA. Guillain-Barré syndrome. Semin Neurol 2012;32:179–86.
6. Donofrio PD. Guillain-Barre syndrome. Continuum (Minnep Minn) 2017;23:1295-9.
7. Hughes RA, Swan AV, van Koningsveld R, van Doorn PA. Corticosteroids for Guillain-Barré syndrome. Cochrane Database Syst Rev 2006:CD001446.
8. Alshekhlee A, Hussain Z, Sultan B, Katirji B. Guillain-Barré syndrome: incidence and mortality rates in US hospitals. Neurology 2008;70:1608–13.
9. Netto AB, Taly AB, Kulkarni GB, Uma Maheshwara Rao GS, Rao S. Complications in mechanically ventilated patients of Guillain-Barre syndrome and their prognostic value. J Neurosci Rural Pract 2017;8:68–73.
10. van den Berg B, Bunschoten C, van Doorn PA, Jacobs BC. Mortality in Guillain-Barre syndrome. Neurology 2013;80:1650–4.