



Factors Associated with Prognosis in Patients with Guillain-Barré Syndrome

Guillain-Barré Sendromlu Hastalarda Prognozla İlişkili Faktörler

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Abstract

Objective: We aimed to evaluate the demographic, clinical, laboratory and electrophysiological findings of patients with inpatient Guillain-Barré syndrome in our clinics and to investigate the effect of these parameters on the prognosis of the disease.

Materials and Methods: Between January 2014 and April 2018, file records of patients admitted to our clinics with the diagnosis of Guillain-Barré syndrome were retrospectively reviewed. Demographic characteristics, clinical, laboratory and electrophysiological findings of the patients at the time of admission were recorded. Patients were clinically graded according to the Hughes classification at the time of admission and on the 3rd month after discharge.

Results: In the study, 25 of the 51 patients were male (49%) and 26 were female (51%) and the mean age was 54.21±17.32 years. According to clinical and electrophysiologic diagnosis, 34 patients (66.7%) had acute inflammatory demyelinating polyradiculoneuropathy, 9 patients (17.6%) had acute motor axonal neuropathy, 6 patients (11.8%) had acute motor sensory axonal neuropathy and 2 patients (3.9%) had Miller Fisher syndrome. According to Hughes scoring on the 3rd month after discharge, 31 patients (60.8%) had in good prognosis (Hughes score ≤2) and 20 patients (39.2%) had in poor prognosis group (Hughes score >2). In the comparison between the two groups according to clinical, demographic, and laboratory parameters, older age (≥50), high Hughes score at admission, weakness in extremities as first complaint, the presence of complications, need for mechanical ventilation and presence of gastroenteritis as a leading infection were evaluated as prognostic factors.

Conclusion: The most common variant of Guillain-Barré syndrome in our study was acute inflammatory demyelinating polyradiculoneuropathy. Older age (≥50), high Hughes score at admission, weakness in extremities as the first symptom, presence of complications, need for mechanical ventilation, and presence of gastroenteritis as a precursor infection were poor prognostic factors.

Keywords: Guillain-Barré syndrome, clinical findings, prognosis

Öz

Amaç: Çalışmamızda, kliniklerimizde yatarak tedavi görmüş Guillain-Barré sendromlu hastaların demografik özelliklerinin, klinik, laboratuvar ve elektrofizyolojik bulgularının değerlendirilmesi ve bu parametrelerin hastalığın prognozuna etkisinin araştırılması amaçlanmıştır.

Gereç ve Yöntem: Ocak 2014 ve Nisan 2018 tarihleri arasında Guillain-Barré sendromu tanısı ile kliniklerimizde yatan hastaların dosya kayıtları retrospektif olarak incelendi. Hastaların başvuru sırasındaki demografik özellikleri, klinik, laboratuvar ve elektrofizyolojik bulguları kayıt edildi. Hastaların yatış esnasında ve taburculuk sonrası 3. ayda Hughes sınıflamasına göre klinik derecelendirmesi yapıldı.

Bulgular: Çalışmaya alınan 51 hastanın 25'i erkek (%49) ve 26'sı kadın (%51) olup yaş ortalamaları 54,21±17,32 yıl idi. Klinik ve elektrofizyolojik verilere göre 34 hasta (%66,7) akut enflamatuvar demiyelinizan poliradikülönöropati, 9 hasta (%17,6) akut motor aksonal nöropati, 6 hasta (%11,8) akut motor duyuşal aksonal nöropati ve 2 hasta (%3,9) Miller Fisher sendromu olarak değerlendirildi. Hastaların taburculuk sonrası 3. ayda Hughes skorlamasına göre yapılan gruplandırmalarında 31 hasta (%60,8) iyi prognozlu (Hughes skoru ≤2) ve 20 hasta (%39,2) kötü prognozlu (Hughes skoru >2) grupta yer aldı. Klinik, demografik ve laboratuvar parametrelerine göre her iki grup arasında yapılan karşılaştırmalarda ileri yaş (≥50), başlangıçta yüksek Hughes skoru, ilk yakınma

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Öz

olarak ekstremitelerde güçsüzlük olması, komplikasyon varlığı, mekanik ventilasyona gereksinim olması ve öncül enfeksiyon olarak gastroenterit varlığı prognoza etkili faktörler olarak değerlendirildi.

Sonuç: Çalışmamızda en yaygın Guillain-Barré sendromu varyantı akut enflamatuvar demiyelinizan poliradikülönöropati idi. İleri yaş (≥ 50), başlangıçta yüksek Hughes skoru, ilk yakınma olarak ekstremitelerde güçsüzlük olması, komplikasyon varlığı, mekanik ventilasyona gereksinim olması ve öncül enfeksiyon olarak gastroenterit varlığı kötü prognostik faktörlerdi.

Anahtar Kelimeler: Guillain-Barré sendromu, klinik bulgular, prognoz

Introduction

Guillain-Barré syndrome (GBS) is an acute inflammatory immune-mediated polyradiculoneuropathy that usually presents with ascending paresthesia, progressive weakness, and pain. In one-third of patients, there is severe deterioration that requires long-term follow-up in the intensive care unit or mechanical ventilation. Full recovery is generally achieved (1). Ambulation is recovered in most patients, even in severe cases. Every year, around 100.000 people worldwide are reported to be affected by the disease (2). There is a significant seasonal change in the incidence of GBS and studies reporting increased frequency in the winter months have been published.

The disease is more common in men than in women (3). There are at least four common subtypes, namely acute inflammatory demyelinating polyradiculoneuropathy (AIDP), acute motor axonal neuropathy (AMAN), acute motor and sensory axonal neuropathy (AMSAN), and Miller Fisher syndrome (MFS). The most common type is reported as AIDP (4,5,6). Plasmapheresis and intravenous immunoglobulins (IVIG), which are reported to be equally effective, are the standard treatment for the disease (7,8). Early diagnosis and treatment reduce the risk of disability and mortality in patients with GBS.

The aim of our study was to determine the clinical findings and epidemiologic features in patients with GBS in our clinics, and to investigate the effect of these parameters on prognosis.

Materials and Methods

The records of patients aged over 17 years who were diagnosed as having GBS according to the Brighton criteria (9) and were treated in our neurology clinics between January 2014 and April 2018 were retrospectively reviewed. Age, sex, admission season, preceding infection, initial symptoms, clinical findings, cerebrospinal fluid (CSF) protein concentrations, electrophysiologic findings, treatment approaches, mechanical ventilation requirement during hospitalization, and complications were recorded. According to the clinical and electrophysiologic data, AIDP, AMAN, AMSAN, and MFS subtypes were determined. Disability was graded according to the Hughes disability scale at the time of admission and at the 3rd month after discharge.

The GBS disability scale as recommended by Hughes et al. (10) was as follows: grade 0: healthy; grade 1: minor symptoms and capable of running; grade 2: able to walk 10 meters (m) or more without assistance but unable to run; grade 3: able to walk 10 m with help; grade 4: bedridden or chairbound; grade 5: requiring assisted ventilation, and grade 6: dead. Accordingly, grade 3 and above was evaluated as poor prognosis, and grade 2 and below was accepted as good prognosis. Clinical and epidemiologic data were

compared between the two groups and statistical analysis was performed.

The study was approved by the Ethics Committee of the Kutahya Health Sciences University (Date: 24.10.2018, Protocol number: 2018-13/8). Informed consent was neither required nor obtained due to the retrospective nature of the study.

Statistical Analysis

Data are presented as numbers, percent, mean, standard deviation and median, and the data were evaluated for the normality of distribution. Data with normal distribution are expressed as mean \pm standard deviation, and data with non-normal distribution are expressed as median (minimum-maximum). Parametric tests were used for the comparison of normally distributed variables and non-parametric statistical methods were used for the comparison of non-normally distributed variables. The independent samples t-test and Mann-Whitney U test were used where appropriate. The significance of the difference between categorical variables was assessed using the chi-square and Fisher's exact test. Statistical significance level was determined as $p < 0.05$. All statistical analyses were performed using the SPSS 24.0 software package (IBM Corp.; Armonk, NY, USA).

Results

The demographic and clinical characteristics of the patients are presented in Table 1. When the seasonal distribution of the patients was examined, there was no significant difference between the seasons, although the numbers of patients who presented during summer and autumn were higher ($p = 0.65$). There was no seasonal trend regarding sex ($p > 0.05$) (Figure 1).

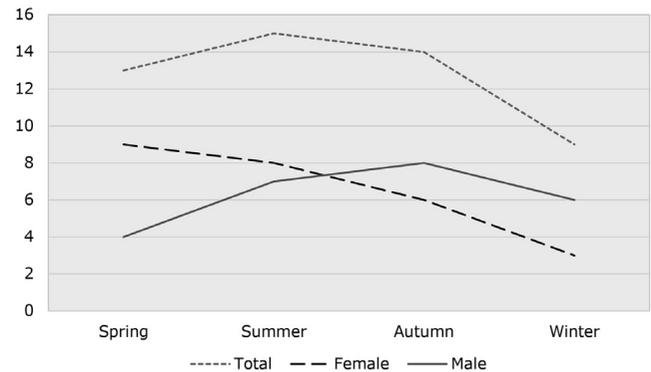


Figure 1. Seasonal distribution of the patients with Guillain-Barré syndrome. The seasonal distribution was not statistically significant in terms of total number and sexes ($p > 0.05$)

Table 1. Demographic, clinical and electrophysiological characteristics of patients (n=51)

Age (years), Mean ± SD	54.21±17.32
Sex, n (%)	
Female	26 (51)
Male	25 (49)
Seasonal distribution, n (%)	
Spring	13 (25.5)
Summer	15 (29.4)
Autumn	14 (27.5)
Winter	9 (17.6)
Preceding infection, n (%)	
URTI	17 (33.3)
Gastroenteritis	8 (15.7)
Pneumonia	1 (2)
Initial symptom, n (%)	
Weakness in the extremities	21 (41.2)
Numbness in hands and feet	19 (37.3)
Lumbar pain and extremity pain	3 (5.9)
Imbalance	3 (5.9)
Difficulty in swallowing	2 (3.9)
Double vision	1 (2)
Facial paralysis	2 (3.9)
GBS subtype, n (%)	
AIDP	34 (66.7)
AMAN	9 (17.6)
AMSAN	6 (11.8)
MFS	2 (3.9)
Treatment, n (%)	
IVIG	44 (86.3)
IVIG + plasmapheresis	6 (11.8)
Untreated	1 (2)
Complication, n (%)	
Pneumonia	6 (11.7)
Deep vein thrombosis	3 (5.9)
Thrombocytopenia	1 (2)
Pneumonia + urinary infection	1 (2)
None	45 (88.2)
Need for mechanical ventilation, n (%)	9 (17.6)
CSF protein level (g/dL), median (minimum-maximum)	88 (27-597)
Symptom-length of hospital stay (days), median (minimum-maximum)	3 (1-15)
Initial Hughes score, median (minimum-maximum)	3 (1-5)
Hughes score at 3 months, n (%)	
≤2	31 (60.8)
>2	20 (39.2)
Mortality, n (%)	
	5 (9.8)

SD: Standard deviation, URTI: Upper respiratory tract infection, GBS: Guillain-Barré syndrome, AIDP: Acute inflammatory demyelinating polyradiculoneuropathy, AMAN: Acute motor axonal neuropathy, AMSAN: Acute motor and sensory axonal neuropathy, MFS: Miller Fisher syndrome, IVIG: Intravenous immunoglobulin, CSF: Cerebrospinal fluid

The most common initial symptom was weakness in the extremities (41.2%) and the least common symptom was double vision (2%).

According to the clinical and electrophysiologic data, 34 patients (66.7%) had AIDP, nine (17.6%) had AMAN, six (11.8%) had AMSAN, and two patients (3.9%) had MFS.

Forty-four patients (86.3%) received IVIG and six patients (11.8%) underwent plasmapheresis and IVIG. No treatment was given to one patient (2%). The patients who underwent plasmapheresis+IVIG were found to quickly deteriorate and needed early intubation.

Complications during hospitalization were pneumonia, deep vein thrombosis (DVT), thrombocytopenia, and pneumonia+urinary tract infection.

During hospitalization, respiratory distress requiring mechanical ventilation was observed in nine patients (17.6%), four of whom could be weaned from the mechanical ventilator during follow-up, but five (9.8%) patients died. Of the five dead patients, three were female and two were male, one patient was aged under 50 years and four were aged over 50 years. Complications in the deceased patients were pneumonia in three patients and DVT in one.

The median initial Hughes score was 3 (range, 1-5) and the median Hughes score at three months was 3 (range, 0-6). The decrease in Hughes scores at three months was significant ($p=0.002$). The median CSF protein concentration of 33 patients with CSF examinations was 88 mg/dL (27-597 mg/dL) and four patients had normal CSF protein concentrations. The median time from symptom onset to hospitalization (symptom-hospital stay) was 3 (range, 1-15) days.

According to Hughes scoring at three months, 33 (60.8%) patients had good prognosis and 20 (39.2%) had poor prognosis. Regarding groups based on clinical and epidemiologic parameters, inter-group comparisons revealed significant correlations between prognosis and initial Hughes score, advanced age, weakness in the extremities as the initial symptom, presence of complications, need for mechanical ventilation, and gastroenteritis as the preceding infection (Table 2).

Discussion

In our study, factors related to poor prognosis in GBS were investigated. In previous studies, advanced age was reported as an indicator of poor prognosis in patients with GBS (7). Contrary to our study, there was no relationship between increased age and disability in the study of Terzi et al. (11). In our study, the number of patients aged 50 years and over was significantly higher in the GBS group.

In previous studies, male sex was more prominent in terms of sex distribution in patients with GBS (6,12,13,14). In the studies reported from our country, it is observed that male patients are in the majority (11,15,16). In our study, the male/female ratio was close to each other and the effect of sex on prognosis was not significant. In the study by Terzi et al. (11) the male/female ratio increased as the degree of disability increased.

Fifty-one percent of our patients had a preceding infection. Of these, approximately 50% were associated with respiratory and gastrointestinal tract infections, and this was consistent

Table 2. Comparison of clinical, laboratory and electrophysiologic parameters of the patients at the end of 3 months

	Hughes score ≤2 n=31	Hughes score >2 n=20	p
Age (years), mean ± SD	48.54±16.20	63.00±15.55	0.003
≥50	16 (51.6)	16 (80)	0.041
Sex, n (%)			
Female	16 (51.6)	10 (50)	0.91
Male	15 (48.4)	10 (50)	-
Seasonal distribution, n (%)			
Spring	9 (29)	4 (20)	-
Summer	9 (29)	6 (30)	0.75
Autumn	7 (22.6)	7 (35)	-
Winter	6 (19.4)	3 (15)	-
Preceding infection, n (%)			
URTI	15 (50)	11 (55)	0.64
URTI	13 (41.9)	4 (20)	0.1
Gastroenteritis	2 (6.5)	6 (30)	0.045*
Pneumonia	-	1 (5)	-
Initial complaint, n (%)			
Weakness in the extremities	9 (29)	12 (60)	0.02
Numbness in hands and feet	14 (45.2)	5 (25)	0.14
Lumbar pain and extremity pain	2 (6.5)	1 (5)	0.83
Imbalance	3 (9.7)	-	-
Difficulty in swallowing	-	2 (10)	-
Double vision	1 (3.2)	-	-
Facial paralysis	2 (6.5)	-	-
GBS subtype, n (%)			
AIDP	20 (64.5)	14 (70)	0.68
AMAN	6 (19.4)	3 (15)	0.69*
AMSAN	3 (9.7)	3 (15)	0.66*
MFS	2 (6.5)	-	-
Treatment, n (%)			
IVIG	27 (87.1)	17 (85)	0.83
IVIG + plasmapheresis	3 (9.7)	3 (15)	0.66*
Untreated	1 (3.2)	-	-
Complication, n (%)			
Pneumonia	-	6 (30)	-
Pneumonia	-	3 (15)	-
Deep vein thrombosis	-	1 (5)	0.02*
Thrombocytopenia	-	1 (5)	-
Pneumonia + urinary infection	-	1 (5)	-
None	31 (100)	14 (70)	-
Need for mechanical ventilation, n (%)			
Need for mechanical ventilation, n (%)	2 (6.7)	7 (35)	0.02*
CSF protein level (g/dL), median (minimum-maximum)			
CSF protein level (g/dL), median (minimum-maximum)	84.5 (33-346)	98 (27-597)	0.6
Symptom - length of hospital stay (days), median (minimum-maximum)			
Symptom - length of hospital stay (days), median (minimum-maximum)	4 (1-15)	3 (1-10)	0.14
Initial Hughes score, median (minimum-maximum)			
Initial Hughes score, median (minimum-maximum)	3 (1-4)	4 (2-5)	<0.001

*Fisher's exact test, SD: Standard deviation, URTI: Upper respiratory tract infection, GBS: Guillain-Barré syndrome, AIDP: Acute inflammatory demyelinating polyradiculoneuropathy, AMAN: Acute motor axonal neuropathy, AMSAN: Acute motor and sensory axonal neuropathy, MFS: Miller Fisher syndrome, IVIG: Intravenous immunoglobulin, CSF: Cerebrospinal fluid

with the literature. In large-scale studies, respiratory infections and gastrointestinal tract infections have been reported as the most common preceding infections with a rate of 37.8-80% (6,12,14,15,17). In accordance with the literature, the presence of gastroenteritis as a preceding infection was considered as a poor prognostic factor (7,18).

Although the number of patients in our patient group was high in summer and autumn, it was not significant. There are studies emphasizing that GBS frequency is highest in the spring and summer months (6), and there are also studies reporting higher incidences in the winter months (3). In the study by Gazioglu et al. (15) no significant seasonal tendency was observed, although there was an increase in the frequency of GBS in spring and summer seasons. Seasonal changes can cause sudden temperature differences. This causes more frequent gastrointestinal and respiratory infections in certain months, which are important preceding factors for GBS (6).

In our patient group, the most common GBS variant was AIDP, followed by AMAN, AMSAN, and MFS, and this is consistent with the literature. The most common form in Western societies is AIDP, and the most common form in Asia and Japan is AMAN (19). In our country, AIDP has been reported as the most common form (11,15,16). In the study of Gazioglu et al. (15) it was reported that axonal forms of GBS subtypes had a worse prognosis. In our study, no relation was found between GBS variants and prognosis.

Electrophysiologic examinations and CSF examinations are important diagnostic tests in the diagnosis of GBS (20). Increased CSF protein has been reported as an indicator of poor prognosis (21). In our study, the effect of CSF protein concentration on prognosis was not significant. In another study, no significant relationship was found between CSF protein concentrations and prognosis, as in our study (15).

GBS progresses over days, often starting with numbness and weakness in the lower extremities. The progression of symptoms, especially weakness, may be rapid and may result in quadriplegia within a few days. Approximately 50% of patients reach maximum weakness in two weeks, 80% in three weeks, and 90% in four weeks (4). In our study, the most common initial symptom was weakness and numbness in the extremities. In our study, a significant relationship was found between the initial symptom and poor prognosis. Our results are consistent with previous reports (15,22).

Severe disability during hospital admission was reported to be one of the poor prognostic factors (7,15). In our study, a significant relationship was found between the two groups in terms of initial Hughes scores. Patients with poor prognosis had high Hughes scores at admission.

Plasmapheresis and IVIG are equally effective treatments in GBS (7). The combination of IVIG+methylprednisolone is not more effective than IVIG. Administration of IVIG following plasmapheresis has no superiority to plasmapheresis or IVIG administration. There is no study showing that a second IVIG application is effective when deterioration continues in GBS (2). It has been reported in the literature that treatment options in GBS prognosis are not effective and that recovery may be due to self-limitation of the disease (23). In our study, 44 patients (86.3%) received IVIG and six patients (11.8%) underwent plasmapheresis+IVIG.

Approximately 30% of patients with GBS require intubation and ventilation due to respiratory failure (4). This rate was found to be less (17.6%) in our study. The need for intubation and ventilator support predicts poor prognosis (2,7). In our study, the rate of patients who required mechanical ventilation in the group with poor prognosis was found to be significantly higher. Five (9.8%) of nine patients who needed mechanical ventilation died in our study. The respiratory distress of the remaining four patients completely resolved.

Despite current treatments, GBS is still an important cause of mortality and morbidity. The main causes of death are reported as infections, pulmonary emboli, and cardiac rhythm disorders. Autonomic symptoms such as tachycardia, hypertension, and sinus arrhythmia are common (24). Even in developed countries, 5% of patients with GBS die of sepsis, pulmonary embolism or dysautonomia. Therefore, early detection of such complications is necessary (25). In patients undergoing long-term mechanical ventilation, mortality can be doubled and it may approach 10% to 20% in patients with severe comorbidity (1). Three out of the five deceased patients had sepsis due to pneumonia. The other two patients died of arrhythmia.

Eighty percent of the patients can walk independently in six months. This rate increases to 84% in one year. In total, 14% of patients may have a severe disability (7). Significant functional improvements have been reported with early rehabilitation in patients with GBS (26). In our study, Hughes scoring of patients was performed at three months after discharge. Accordingly, 30 patients (60.8%) were able to walk independently. We can foresee that this rate may be much higher in the following months with rehabilitation programs.

Study Limitations

Although the retrospective nature of our study and the limited number of patients were the main limitations of our study, we can say that our results are consistent with the literature.

Conclusion

In conclusion, the seasonal features and the presence of preceding infection in our study are consistent with the literature in terms of clinical and demographic characteristics of GBS cases. High initial Hughes score, advanced age (≥ 50 years), initial symptom as weakness in extremities, presence of complications, need for mechanical ventilation, and presence of gastroenteritis as preceding infection were associated with poor prognosis. No sex differences were found in our study. The most common form was AIDP. Early recognition of GBS in the emergency department and early treatment and follow-up in centers with appropriate intensive care conditions provide positive support for prognosis.

Ethics

Ethics Committee Approval: The study was approved by the Ethics Committee of the Kutahya Health Sciences University (Date: 24.10.2018, Protocol number: 2018-13/8).

Informed Consent: Informed consent was neither required nor obtained due to the retrospective nature of the study.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: M.Ç., G.A., Ö.T., H.D., Concept: M.Ç., G.A., Ö.T., M.S., Design: M.Ç., S.C.K., H.D., Data Collection or Processing: M.S., M.Ç., H.D., Analysis or Interpretation: S.C.K., G.A., Literature Search: M.Ç., S.C.K., M.S., Writing: M.Ç.

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