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Original Article

Risk factors of disease severity and mechanical ventilation requirement in childhood Guillain-Barré Syndrome

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ABSTRACT

Background. This study aimed to investigate the risk factors associated with the severity of the disease, the need for mechanical ventilation (MV) and poor prognosis in the early stages of Guillain-Barré Syndrome (GBS).

Methods. Data of children who met GBS diagnostic criteria were evaluated retrospectively. The sample was divided into three binary subgroups according to severe GBS (Hughes Functional Grading Scale [HFGS] ≥ 4 at admission), mechanical ventilation (MV) requirement, and poor prognosis (inability to walk independently, HFGS ≥ 3 after six months). Various clinical, laboratory and electrophysiological parameters were compared between these subgroups.

Results. The mean age of 63 children with GBS was 91.55±49.09 months. 13 (20.6%) patients required MV and 4 (6.3%) patients died. Associated risk factors for the need for MV in severe GBS were found to be autonomic dysfunction, bulbar palsy, sensory impairment, lowest total Medical Research Council (MRC) scale for muscle strength score at admission, high modified Erasmus GBS respiratory failure score (mEGRIS), high neutrophil-lymphocyte ratios (NLR) and high systemic immune-inflammation index (SII) values ($p<0.001$, $p=0.003$, $p=0.033$, $p<0.001$, $p<0.001$, $p=0.037$ and $p=0.042$, respectively). The lowest total MRC scale for muscle strength score at admission was a significant indicator of poor prognosis ($p<0.001$).

Conclusions. Autonomic dysfunction, bulbar palsy, sensory impairment, lowest total MRC scale for muscle strength score at admission, high mEGRIS score, high NLR and SII values are potential risk factors for the need for MV in children with severe GBS. The lowest total MRC scale for muscle strength score at admission was associated with poor prognosis.

Key words: Guillain-Barré Syndrome, disease severity, mechanical ventilation, prognosis, risk factors, pediatric.

Guillain-Barré Syndrome (GBS) is an acute immune-mediated peripheral polyradiculoneuropathy and is the leading cause of acute flaccid paralysis in children. The incidence of GBS is 0.62 cases per 100,000 person-years in children aged 0 to 9 years and 0.75 cases per 100,000 person-years in children and adolescents aged 10 to 19 years.[1]

Respiratory failure requiring mechanical ventilation (MV) affects 20–30% of patients with GBS and is the most important prognostic factor for severe GBS.[2] Therefore, early recognition of respiratory failure in patients with GBS is of great importance.[3] Accurately predicting GBS patients who will need MV in the early stages of the disease may improve disease outcomes by allowing clinicians to determine personalized treatments in a timely manner. Previous studies on the predictors for respiratory failure have been reported as shorter time from onset to admission, bulbar

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involvement, total Medical Research Council (MRC) scores for muscle strength score at admission <20/60, higher GBS disability score, lower vital capacity, hypoalbuminemia, neck muscle weakness, inability to raise elbows, inability to stand, inability to cough, dysautonomia, low single breath rate, increased liver enzymes, lower proximal/distal compound muscle action potential ratio, nerve conduction block, longer phrenic nerve latency and acute inflammatory demyelinating polyneuropathy (AIDP) versus acute motor axonal neuropathy (AMAN) or acute motor and sensory axonal neuropathy (AMSAN) in GBS subtypes.[4-16] Modified Erasmus GBS respiratory failure scores (mEGRIS) accurately predict the risk of respiratory failure in the early course of GBS.[3,16] Most of these studies have been conducted in adults with GBS, and significant heterogeneity has been observed between studies. There are however a limited number of studies in the literature on MV risk factors in children with GBS.[17-24]

In this study, we aimed to investigate risk factors associated with the severity of GBS and poor prognostic risk factors and predictors of the need for mechanical ventilation in severe cases of GBS.

Materials and Methods

Study design

The study population consisted of patients younger than 18 years who met the diagnostic criteria for GBS and received sequential treatment during their hospitalization at the İnönü University Faculty of Medicine Hospital Pediatric Neurology Unit between December 2003 and January 2023. Medical records of the patients included in the study were recorded on a predesigned questionnaire. GBS diagnostic classification accuracy levels were defined for each patient.[3] The functional status of the patients was evaluated according to the Guillain-Barré Syndrome Disability Scale (Hughes Functional Rating Scale [HFGS]) at the time of hospital admission and approximately six months after discharge.[25]

Ethics approval

The study was approved by İnönü University Ethics Committee (date: 02.05.2023, number: 2023-4580).

Study inclusion and exclusion criteria

All patients who presented with acute flaccid paralysis and met the diagnostic criteria for GBS, were younger than 18 years of age, and complete medical files were included in the study. Patients diagnosed with acute flaccid paralysis due to other causes, patients diagnosed with diseases such as polio, botulism, toxic neuropathy or diphtheria-related neuropathy, Bickerstaff encephalitis, Miller Fisher syndrome, critical illness polyneuropathy or myopathy, and chronic inflammatory demyelinating polyradiculoneuropathy were excluded from the study.

Data collection

Patients' demographic and clinical characteristics, including age, gender, season of onset, infection history, time from onset of GBS symptoms to hospitalization, length of hospital stay, deep tendon reflex, cranial nerve involvement (facial, glossopharyngeal and vagus nerves), sensory impairment, need for MV, autonomic nerve dysfunction, and therapeutic methods used were recorded and analyzed retrospectively. GBS severity was assessed at admission using HFGS and the lowest total MRC scale for muscle strength score, whereas respiratory failure was predicted with mEGRIS. Patients with HFGS score of ≥ 4 at admission were considered to have severe GBS.[26] Patients with an HFGS score of ≥ 3 (inability to walk independently) within six months after discharge were considered to have poor prognosis.[27] Cerebrospinal fluid (CSF) protein, neutrophil (N), lymphocyte (L), platelet (P), neutrophil-to-lymphocyte ratio (NLR=N/L), platelet-to-lymphocyte ratio (PLR=P/L),

systemic immune-inflammation index (SII = P x [N/L]) values and nerve conduction study (NCS) results were recorded.

Assessment of GBS severity and functional neurological deficit

All patients were evaluated in terms of disease severity and functional neurological deficit using HFGS and MRC. HFGS grades and corresponding functions were as follows: '0': no symptoms; '1': minor symptoms and the ability to run; '2': able to walk 10 meters or more without assistance but unable to run; '3': able to walk 10 meters in an open area with assistance; 'unable to walk unaided' '4': bedridden or wheelchair-bound; '5': requiring ventilation support for at least part of the day; and '6': dead.[23] MRC scores used to evaluate muscle strength were calculated according to the strength of six bilateral muscles in four extremities and ranged between 0 and 60. Accordingly, an MRC score of 0 meant quadriplegic, whereas an MRC score of 60 indicated normal muscle strength.[28] The lowest total MRC and highest HFGS scores were considered to indicate the worst status of GBS.

Grouping of patients with GBS

Patients (n=63) were divided into two subgroups according to disease severity. Accordingly, severe GBS (HFGS score ≥ 4, n=27) and non-severe (HFGS score< 4, n= 36) GBS were included in the subgroups.

Patients with severe GBS were further divided into two subgroups according to whether patients were in need of MV, such that: patients requiring MV (MV subgroup) and patients with normal ventilation (NV subgroup). Intensive care unit (ICU) physicians decided the indication for starting MV based on vital signs and laboratory data (pediatric protocols or standard criteria).[29]

In general, the patients whose conditions had improved or were stable in our neurology service were discharged from the hospital. Patients who could walk independently approximately six months after discharge were considered to have good prognosis (HFGS<3, n=50) and patients who could not walk independently were considered to have poor prognosis (HFGS ≥ 3, n=13).

Respiratory failure prediction

Respiratory failure was predicted based on mEGRIS scores. Accordingly, first, the patients whom the time from the onset of first symptoms to admission was > 7 days, between 4 days and 7 days, and ≤ 3 days were assigned 0 points, 1 point, and 2 points, respectively. Secondly, the patients with and without facial palsy and/or bulbar palsy at admission were assigned 1 point and 0 points, respectively. Thirdly, the patients with a lowest total MRC scale for muscle strength score at admission between 60 and 51, 50 and 41, 40 and 31, 30 and 21, and ≤20 were assigned 0 points, 1 point, 2, 3, and 4 points, respectively. By adding up the three points mentioned above, a total mEGRIS score of 0 to 7 points was obtained. Patients with mEGRIS scores of 0 to 2, 3 to 4, and 5 to 7 were considered to be at low, moderate, and high risk of respiratory failure, respectively.[4]

Statistical analysis

The descriptive statistics obtained from the collected data were expressed as mean ± standard deviation values or median with minimum and maximum values in the case of continuous variables determined to conform and not to conform to the normal distribution, respectively, and as frequency (n) and percentage (%) values in the case of categorical variables. Shapiro- Wilk test was used to analyze the normal distribution characteristics of continuous (numerical) variables. Independent samples t-test and Mann-Whitney U test was used to compare quantitative variables. Yates' chi-square with continuity correction and Fisher's exact tests were used to compare qualitative variables. Probability (p) statistics of ≤ 0.05 were deemed to indicate statistical significance. IBM SPSS Statistics 27.0 (Statistical Product and Service Solutions for Windows,

Version 27.0, IBM Corp., Armonk, NY, U.S., 2020) software package was used to conduct the statistical analyses.

Results

Demographic characteristics of pediatric patients with GBS

The mean age of the 63 children with GBS included in the study sample was 91.55 ± 49.09 (range: 17-180) months at admission. Of these patients, 33 (52.4%) were male. In terms of infection history, 36.5% of the patients had upper respiratory tract infections, 25.4% acute gastroenteritis, and one patient each had hepatitis A, chickenpox and brucellosis. Cranial nerve involvement was present in 31 (49.2%) patients. Of these patients, 15 (23.8%) had bulbar palsy, 13 (20.6%) facial palsy, and 3 (4.8%) both bulbar and facial involvement. Sensory impairment and autonomic dysfunction was present in 28 (44.4%) and 16 (25.4%) patients, respectively. The mean time from the onset of symptoms to hospitalization was 4.31± 2.56 days. The mean length of hospital stay was 9.76±5.67 (range: 4-37) days. There were 27 (42.9%) patients with severe GBS. The lowest total MRC scale for muscle strength in patients with poor prognosis was 36.44 ± 4.10 (median: 38, range: 30 to 42). The mean mEGRIS score of the overall study group was 3.88 ±1.58 (range: 2-7). There were 20 (31.7%) patients in the high-risk group according to the mEGRIS scores. The most common electrophysiological GBS subtype in the overall study group was AMAN, seen in 31 (49.2%) patients, followed by AMSAN, seen in 18 (28.6%) patients, and AIDP, seen in 14 (22.2%) patients. In terms of treatment methods used, the first preferred method was intravenous immunoglobulin (IVIg) administration to 43 (68.3%) patients within 24 hours after admission to the hospital, and plasmapheresis was applied after IVIg to 20 (31.7%) patients who did not show a significant improvement in muscle strength.

During clinical follow-up, 13 (20.6%) patients required MV, 4 (6.3%) died, and 59 (93.7%) were discharged. The common causes of death of the 4 patients monitored on MV were respiratory failure, autonomic dysfunction and cardiac arrest. Penicillin-sensitive *Streptococcus pneumoniae* was detected in the respiratory tract secretion culture of the first patient. Urosepsis (100000 cfu/ml *Escherichia coli* was found in the urine culture) was detected in the second patient. The third patient died due to aspiration pneumonia, pleural effusion, gastrointestinal bleeding and multiorgan failure. The fourth patient had bronchopneumonia (with widespread infiltration on chest radiography) at the time of admission. Echocardiography results of 4 patients were evaluated as normal.

The risk factors for severe GBS

No statistically significant difference was observed between severe and non-severe GBS subgroups in terms of age and gender ($p > 0.05$). In the severe GBS subgroup, the time from onset of first symptoms to hospitalization was shorter, albeit not significantly, ($p > 0.05$). There was a statistically significant difference in seasonal morbidity between GBS subgroups. Admission in summer season was significantly higher in the severe GBS subgroup than in the non-severe GBS subgroup ($p = 0.018$). There was a statistically significant difference between GBS subgroups in terms of electrophysiological GBS subtype. In the severe GBS subgroup while AMSAN was most common, AIDP was significantly higher in the non-severe GBS subgroup ($p=0.013$). Cranial nerve involvement, autonomic dysfunction and sensory impairment were observed in significantly more patients in the severe GBS subgroup than in the non-severe GBS subgroup ($p <0.001$ for all cases) (Table I). There was no statistically significant difference between the severe and non-severe GBS subgroups regarding CSF protein, N, L, P, NLR, PLR, and SII values ($p >0.05$) (Table II).

The risk factors for MV need

The mean age of pediatric GBS patients was younger in the MV subgroup, albeit not significantly, than in the NV subgroup

Table I. Comparison of clinical characeristics and presentation of GBS between severe GBS and non-severe GBS groups.

Variables*	Categories	GBS classification		Total	Chi-square statistics	*p*
		Non-severe GBS group (n=36) (HFGS 0,1,2,3)	Severe GBS group (n=27) (HFGS 4,5,6)			
Gender	Girl	16[a] (53.3%)	14[a] (46.7%)	30 (100.0%)	0.107	0.743[2]
	Boy	20[a] (60.6%)	13[a] (39.4%)	33 (100.0%)		
Cranial Nerve	No	26[a] (81.3%)	6[b] (18.8%)	32 (100.0%)	23.452	<0.001[1]
Damage	Facial paralysis	8[a] (61.5%)	5[a] (38.5%)	13 (100.0%)		
	Bulbar palsy	2[a] (13.3%)	13[b] (86.7%)	15 (100.0%)		
	Facial and bulbar palsy	0[a] (0.0%)	3[b] (100.0%)	3 (100.0%)		
Sensory	No	27[a] (77.1%)	8[b] (22.9%)	35 (100.0%)	11.091	<0.001[2]
Disorder	Yes	9[a] (32.1%)	19[b] (67.9%)	28 (100.0%)		
Autonomous	No	36[a] (76.60%)	11[b] (23.4%)	47 (100.0%)	25.554	<0.001[2]
changes	Yes	0[a] (0.00%)	16[b] (100.0%)	16 (100.0%)		
Pain	No	3[a] (100.0%)	0[a] (0.00%)	3 (100.0%)	-	0.253[3]
symptoms	Yes	33[a] (55.0%)	27[a] (45.00%)	60 (100.0%)		
Season at	Spring	7[a] (58.3%)	5[a] (41.7%)	12 (100.0%)	9.821	0.018[1]
admission	Autumn	17[a] (68.0%)	8[a] (32.0%)	25 (100.0%)		
	Summer	7[a] (33.3%)	14[b] (66.7%)	21 (100.0%)		
	Winter	5[a] (100.0%)	0[b] (0.0%)	5 (100.0%)		
EMG	AIDP (myelin)	12[a] (85.7%)	2[b] (14.3%)	14 (100.0%)	8.884	0.013[1]
	AMAN (axonal)	18[a] (58.1%)	13[a] (41.9%)	31 (100.0%)		
	AMSAN (myelin and axonal)	6[a] (33.3%)	12[b] (66.7%)	18 (100.0%)		
Total		36 (57.1%)	27 (42.9%)	63 (100.0%)		

*: Variables are expressed as frequency (percent).
[1]: Pearson chi-square, [2]: Continuity correction [3]: Fisher's exact test.
Each superscript letter denotes a subset of GBS categories whose column proportions do not differ significantly from each other at the 0.05 level. The statistically significant difference is expressed in bold.
AIDP, Acute inflammatory demyelinating polyneuropathy; AMAN, Acute motor axonal neuropathy; AMSAN, Acute motor and sensory axonal neuropathy; EMG, Electromyelography; GBS, Guillain-Barré syndrome; HFGS, Hughes Functional Grading Scale.

Table II. Comparison of laboratory parameters and presentation of GBS between severe GBS and non-severe GBS groups.

Variables*	GBS classification		*p*
	Non-Severe GBS group (n=36) (HFGS 0,1,2,3)	Severe GBS group (n=27) (HFGS 4,5,6)	
Age	95.14 ± 51.01 | 73.5 (25 - 180)	86.78 ± 46.94 | 82 (20 - 180)	0.667
MRC at admission	43.06 ± 3.72 | 44 (34 - 50)	29.19 ± 6.91 | 30 (16 - 42)	<0.001[1]
CSF protein	98.19 ± 49.76 | 81.05 (46 - 257)	98.04 ± 47.32 | 87.4 (45.9 - 230.3)	0.978[2]
Neutrophil	5.1 ± 1.99 | 4.4 (2.6 – 12.3)	5.64 ± 2.62 | 5 (1.79 – 12.2)	0.437[2]
Lymphocyte	2.83 ± 1.13 | 2.54 (1.36 – 6.9)	2.79 ± 1.28 | 2.75 (0.9 – 6.1)	0.802[2]
Platelet	347.75 ± 100.3 | 309 (214 - 681)	343.37 ± 97 | 342 (147 - 556)	0.776[2]
NLR	2.1 ± 1.23 | 1.93 (0.65 – 5.13)	2.68 ± 2.51 | 1.69 (0.57 – 10.17)	0.708[2]
PLR	141.4 ± 74.04 | 126.43 (35.22 – 412.33)	150.73 ± 93.05 | 114.71 (62.18 – 463.33)	0.945[2]
SII	771.52 ± 632.49 | 559.78 (158.48 - 3051.23)	998.62 ± 1220.88 | 560.91 (111.3 – 5652.67)	0.771[2]

*: Variables are expressed as mean ± std. deviation \| median (minimum-maximum).
[1]: Independent samples t-test, [2]: Mann-Whitney U test.
The statistically significant difference is expressed in bold.
CSF, Cerebrospinal fluid; GBS, Guillain-Barré syndrome; HFGS, Hughes Functional Grading Scale; MRC, Medical Research Council; NLR, Neutrophil to lymphocyte ratio; PLR, Platelet to lymphocyte ratio; SII, Systemic immune inflammation index.

($p > 0.05$). The length of hospital stay was significantly longer in the MV subgroup than in the NV subgroup (15 ± 9.8 days vs. 8.4 ± 2.83 days, $p = 0.047$). Of the 13 children who needed invasive MV, 4 died and 9 were discharged with poor functional recovery (negative outcome). The presence of bulbar paralysis, autonomic dysfunction and sensory impairment in children with GBS were identified as significant clinical risk factors for a need for MV ($p < 0.001$) (Table III). The mean mEGRIS score of the pediatric GBS patients was statistically significantly higher in the MV subgroup than in the NV subgroup (6.38 ± 0.51 vs. 3.24 ± 1.02; $p < 0.001$). In parallel, the lowest mean total MRC scale for muscle strength score at admission was statistically significantly lower in the MV subgroup than in the NV subgroup ($p < 0.001$) (Table IV). No statistically significant difference was found between the MV and NV subgroups regarding CSF protein, NLR, PLR and SII values ($p > 0.05$) (Table IV).

The risk factors for MV need in children with severe GBS

The mean age of the 27 pediatric patients with severe GBS at the onset of first symptoms of GBS was 86.08 ± 47.63 months. Of these patients, 13 (48.1%) were male ($p > 0.05$), and 13 needed MV. Comparison of the pediatric severe GBS patients with and without the need for MV is shown in Table V. There was no significant difference between the pediatric severe GBS patients with and without MV need in terms of the season of admission ($p > 0.05$). mEGRIS score was statistically significantly higher in pediatric severe GBS patients with a need for MV than in those without a need for MV ($p < 0.001$). In parallel, the lowest mean total MRC scale for muscle strength score at admission was statistically significantly lower in pediatric severe GBS patients with a need for MV than in those without MV need (23.38 ± 4.72 vs. 34.57 ± 3.18, $p<0.001$). There were significantly more patients with clinical risk factors, like autonomic dysfunction, bulbar palsy, and sensory impairment among pediatric severe GBS patients with a need for MV compared to those without MV need ($p < 0.001$, $p=0.003$, and $p=0.033$, respectively). In terms of anti-inflammatory markers, NLR and SII values calculated at admission were statistically significantly higher among pediatric severe GBS patients with a need for MV compared to those without MV need ($p=0.037$ and $p=0.042$, respectively) (Table VI).

The risk factors for GBS prognosis

No statistically significant difference was observed between GBS subgroups with poor and good prognosis in terms of age and gender ($p > 0.05$). The lowest total MRC scale for muscle strength score at approximately six months after discharge was statistically significantly lower in the GBS subgroup with poor prognosis than in the GBS subgroup with good prognosis [49.84 ± 4.22 (median:50) versus 36.44 ± 4.10 (median:38); $p < 0.001$]

Discussion

We investigated potential risk factors regarding the severity of GBS, the need for MV in the early stages of the disease, and prognosis, using a cohort of children diagnosed with GBS. In 42.8% (27) of the patients with GBS, the disease was severe, 20.6% (13) required MV, and 6.3% (4) died. The potential predictors for severe GBS were found to be summer admission, cranial nerve involvement, autonomic dysfunction, sensory impairment, lowest total MRC scale for muscle strength score at admission, and AMSAN electrophysiological subtype. The predictors of MV requirement in severe GBS patients were found to be bulbar palsy, autonomic dysfunction, sensory impairment, lowest total MRC scale score for muscle strength at admission, high mEGRIS score, high NLR and high SII values. Lowest total MRC scale for muscle strength score at admission was the factor associated with poor prognosis. These results may assist clinicians in accurately predicting the development of respiratory failure in children with GBS using clinical

Table III. Comparison of clinical features and presentation of GBS between MV and NV groups.

Variables*	Categories	Ventilation type		Total	Chi-square statistics	*p*
		Normal ventilation group (n=50)	Mechanical ventilation group (n=13)			
Gender	Girl	24[a] (80.0%)	6[a] (20.0%)	30 (100.0%)	0.000	0.999[2]
	Boy	26[a] (78.8%)	7[a] (21.2%)	33 (100.0%)		
Cranial Nerve Damage	No	32[a] (100.0%)	0[b] (0.0%)	32 (100.0%)	32.939	<0.001[1]
	Facial paralysis	12a (92.3%)	1[a] (7.7%)	13 (100.0%)		
	Bulbar palsy	5[a] (33.3%)	10[b] (66.7%)	15 (100.0%)		
	Facial and bulbar palsy	1[a] (33.3%)	2[b] (66.7%)	3 (100.0%)		
Sensory Disorder	No	34[a] (97.1%)	1[b] (2.9%)	35 (100.0%)	12.853	<0.001[2]
	Yes	16[a] (57.1%)	12[b] (42.9%)	28 (100.0%)		
Autonomous changes	No	47[a] (100.0%)	0[b] (0.0%)	47 (100.0%)	-	<0.001[3]
	Yes	3[a] (18.8%)	13[b] (81.3%)	16 (100.0%)		
Season at admission	Spring	9[a] (75.0%)	3[a] (25.0%)	12 (100.0%)	2.575	0.447[1]
	Autumn	21[a] (84.0%)	4[a] (16.0%)	25 (100.0%)		
	Summer	15[a] (71.4%)	6[a] (28.6%)	21 (100.0%)		
	Winter	5a (100.0%)	0[a] (0.0%)	5 (100.0%)		
Total		50 (79.4%)	13 (20.6%)	63 (100.0%)		

*: Variables are expressed as frequency (percent).
[1]: Pearson chi-square, [2]: Continuity correction [3]: Fisher's exact test.
Each superscript letter denotes a subset of GBS categories whose column proportions do not differ significantly from each other at the 0.05 level. The statistically significant difference is expressed in bold.
GBS, Guillain-Barré syndrome; MV, mechanical ventilation; NV, Normal ventilation.

Table IV. Comparison of laboratory parameters and presentation of GBS between MV and NV groups.

Variables*	Ventilation type		*p***
	Normal ventilation Group NV (n=50)	Mechanical ventilation Group MV (n=13)	
Age	92.98 ± 49.85 | 74.5 (25 - 180)	86.08 ± 47.63 | 96 (20 - 180)	0.760
MRC at admission	40.68 ± 5.23 | 42 (30 - 50)	23.38 ± 4.72 | 24 (16 - 28)	<0.001
mEGRIS	3.24 ± 1.02 | 3 (2 - 5)	6.38 ± 0.51 | 6 (6 - 7)	<0.001
CSF protein	99.51 ± 49.35 | 81.05 (45.9 - 257)	92.81 ± 45.7 | 92 (53.1 – 230.3)	0.852
Neutrophil	4.99 ± 1.88 | 4.45 (2.4 – 12.3)	6.64 ± 3.16 | 5.4 (1.79 – 12.2)	0.051
Lymphocyte	2.91 ± 1.22 | 2.61 (1.36 – 6.9)	2.43 ± 1 | 2.2 (0.9 – 4.2)	0.262
Platelet	343.22 ± 95.16 | 327 (147 - 681)	356.08 ± 112.4 | 338 (194 - 556)	0.734
NLR	1.99 ± 1.14 | 1.63 (0.65 – 5.13)	3.72 ± 3.27 | 2.17 (0.57 – 10.17)	0.055
PLR	135.72 ± 68.55 | 120.49 (35.22 – 412.33)	182.63 ± 117.38 | 169.09 (62.18 – 463.33)	0.255
SII	707.14 ± 559.27 | 558.48 (158.48 – 3051.23)	1490.83 ± 1630.15 | 762.86 (111.3 - 5652.67)	0.083

*: Variables are expressed as mean ± std. deviation \| median (minimum-maximum).
**: Mann-Whitney U test.
The statistically significant difference is expressed in bold.
CSF, Cerebrospinal fluid; GBS, Guillain-Barré syndrome; mEGRIS, Modified Erasmus GBS Respiratory Insufficiency Score; MRC, Medical Research Council; MV, Mechanical ventilation; NLR, Neutrophil to lymphocyte ratio; NV, Normal ventilation; PLR, Platelet to lymphocyte ratio; SII, Systemic immune inflammation index.

Table V. Comparison of clinical characteristics between MV and NV groups with severe GBS.

Variables*	Categories	Severe GBS patients (n=27)		Total	Chi-square statistics	*p*
		Normal ventilation (n=14)	Mechanical ventilation (n=13)			
Gender	Girl	8[a] (57.1%)	6[a] (42.9%)	14 (100.0%)	0.034	0.853[2]
	Boy	6[a] (46.2%)	7[a] (53.8%)	13 (100.0%)		
Cranial Nerve Damage	No	6[a] (100.0%)	0[b] (0.0%)	6 (100.0%)	11.882	0.003[1]
	Facial paralysis	4[a] (80.0%)	1[a] (20.0%)	5 (100.0%)		
	Bulbar palsy	3[a] (23.1%)	10[b] (76.9%)	13 (100.0%)		
	Facial and bulbar palsy	1[a] (33.3%)	2[a] (66.7%)	3 (100.0%)		
Sensory Disorder	No	7[a] (87.5%)	1[b] (12.5%)	8 (100.0%)	-	0.033[3]
	Yes	7[a] (36.8%)	12[b] (63.2%)	19 (100.0%)		
Autonomous changes	No	11[a] (100.0%)	0[b] (0.0%)	11 (100.0%)	14.136	<0.001[2]
	Yes	3[a] (18.8%)	13[b] (81.3%)	16 (100.0%)		
Season at admission	Spring	2[a] (40.0%)	3[a] (60.0%)	5 (100.0%)	0.449	0.8801
	Autumn	4[a] (50.0%)	4[a] (50.0%)	8 (100.0%)		
	Summer	8[a] (57.1%)	6[a] (42.9%)	14 (100.0%)		
	Winter	0[a] (0.0%)	0[a] (0.0%)	0 (0.00%)		
Total		14 (52.0%)	13 (48.0%)	27 (100.0%)		

*: Variables are expressed as frequency (percent).
[1]: Pearson chi-square, [2]: Continuity correction [3]: Fisher's exact test.
Each superscript letter denotes a subset of GBS categories whose column proportions do not differ significantly from each other at the 0.05 level. The statistically significant difference is expressed in bold.
GBS, Guillain-Barré syndrome; MV, Mechanical ventilation; NV, Normal ventilation.

Table VI. Comparison of laboratory parameters and presentation of GBS between MV and NV groups with severe GBS.

Variables*	Severe GBS patients (n=27)		*p***
	Normal ventilation (n=14)	Mechanical ventilation (n=13)	
Age	87.43 ± 48.09 ǀ 76 (27 - 170)	86.08 ± 47.63 ǀ 96 (20 - 180)	0.884
MRC at admission	34.57 ± 3.18 ǀ 34 (30 - 42)	23.38 ± 4.72 ǀ 24 (16 - 28)	<0.001
mEGRIS	4.14 ± 0.86 ǀ 4 (3 - 5)	6.38 ± 0.51 ǀ 6 (6 - 7)	<0.001
CSF protein	102.9 ± 49.97 ǀ 81.6 (45.9 – 192.7)	92.81 ± 45.7 ǀ 92 (53.1 – 230.3)	0.771
Neutrophil	4.7 ± 1.61 ǀ 4.63 (2.4 – 7.9)	6.64 ± 3.16 ǀ 5.4 (1.79 – 12.2)	0.109
Lymphocyte	3.13 ± 1.45 ǀ 2.83 (1.6 – 6.1)	2.43 ± 1 ǀ 2.2 (0.9 – 4.2)	0.254
Platelet	331.57 ± 82.74 ǀ 342 (147 - 459)	356.08 ± 112.4 ǀ 338 (194 - 556)	0.698
NLR	1.72 ± 0.84 ǀ 1.52 (0.79 – 3.81)	3.72 ± 3.27 ǀ 2.17 (0.57 – 10.17)	0.037
PLR	121.11 ± 51.32 ǀ 97.38 (72.79 – 221.25)	182.63 ± 117.38 ǀ 169.09 (62.18 – 463.33)	0.159
SII	541.58 ± 246.79 ǀ 496.73 (268.71 – 1265.75)	1490.83 ± 1630.15 ǀ 762.86 (111.3 – 5652.67)	0.042

*: Variables are expressed as mean ± std. deviation ǀ median (minimum-maximum).
**: Mann-Whitney U test.
The statistically significant difference is expressed in bold.
CSF, Cerebrospinal fluid; GBS, Guillain-Barré syndrome; mEGRIS, modified Erasmus GBS Respiratory Insufficiency Score; MRC, Medical Research Council; NLR, Neutrophil to lymphocyte ratio; PLR, Platelet to lymphocyte ratio; SII, Systemic immune inflammation index.

features available at the time of admission, making clinical decisions regarding patient transfer to the ICU, and providing counseling for prognosis.

Early detection of patients with severe GBS may reduce residual sequelae and mortality. However, few studies have evaluated the severity of GBS.[27] In the current study, summer admission was among the factors predicting severe GBS. This finding may be associated with the increase in gastrointestinal infections in spring and summer.[1] Additionally, AMSAN variant, cranial nerve involvement, autonomic dysfunction, and the lowest total MRC scale score for muscle strength at admission were found to be associated with GBS severity. These results were consistent with previous studies.[3,19,27] In the current study, the time from symptom onset to hospital admission was not associated with disease severity. This may be attributed to differences between studies on whether it is the time from the onset of symptoms to hospitalization or the time of peak functional neurological deficit, and the difficulties in determining the exact time of peak functional neurological deficit in children with GBS.[4,23,24]

In the current study, 20.6% (13) of the patients required MV. Our MV rate was consistent with previous studies (20–30%).[2,3] The potential predictors of MV requirement in patients with severe GBS were found to be autonomic dysfunction, presence of bulbar palsy, lowest total MRC scale for muscle strength score at admission, and high mEGRIS scores.[3,9,10,16,27,30-32] It is of great importance to predict the need for MV early, as 60% of these patients may experience many complications that increase the risk of mortality, therefore early recognition and intervention can improve the prognosis.[33,34] It has been reported that severe muscle weakness (MRC <20) is more likely to progress to MV.[32] It has been shown that the NSB score model (Neck muscle weakness, Single breath count, Bulbar palsy) developed in patients with GBS can accurately predict MV requirement.[8] Single breath count (SBC) < 20 (inability to count 1 to 20 out loud in a single breath) is a useful bedside tool that can assess the need for MV, but may be an indicator rather than a predictor.[3] The current study showed that high NLR and SII values may be potential predictors of MV requirement in children with severe GBS. Inflammatory markers may reflect an underlying proinflammatory state and immunological dysfunction in patients with GBS.[35] A relative decrease in adaptive immunity, reflected by an elevated NLR value, may lead to dysregulated proinflammatory responses that contribute to the development of GBS.[36] High NLR may be useful in the evaluation of diagnosis, prognosis and treatment response in patients with GBS and may also predict the need for MV.[36] SII can predict disease severity and short-term prognosis, and is even more valuable than NLR in predicting the need for MV.[37]

In the current study, 4 patients (6.3%) died. A large series of 527 adult patients with GBS reported a mortality rate of 2.8%.[38] Mortality rates reported in the pediatric age group vary between 6.5-12.7%.[19,39,40] Two of the patients who died were the youngest patients in our cohort. The presence of bulbar palsy, respiratory failure and autonomic dysfunction were common features of all of them. The time from onset of muscle weakness to admission was between 1 and 5 days, and the disease appeared to progress rapidly. Three patients required MV on the first day of admission. Duration of stay in the ICU was between 3-10 days. In the literature, the most frequently identified causes of death in GBS are respiratory failure, pneumonia, cardiovascular complications and autonomic dysfunction.[38,39] Risk factors for mortality have been reported to be associated with older age, more severe weakness at admission, need for ventilation and pre-existing comorbidity, and a longer delay between the onset of weakness and presentation.[38] The mortality rate in GBS can be reduced by more intensive management of respiratory failure and dysautonomia, early treatment of infections, and greater attention to patients with cardiovascular risk factors.[38]

GBS has a variable clinical course and outcome, but patients are treated with a standard approach. Patients with a poor prognosis may benefit from treatment as long as nerve degeneration can be detected early when it is potentially reversible and treatment is most effective. GBS guidelines recommend that the risk of poor prognosis be assessed at the early stage of the disease.[3] Predicting both short-term prognosis (likelihood of needing MV) and long-term prognosis (likelihood of being able to walk unaided after six months) is important for treatment goals and counseling. The predictors for poor prognosis in GBS (with a large amount of evidence) have been reported to be older age, prior history of gastroenteritis, higher GBS disability score at presentation, lower MRC total scores at admission, and reduced compound muscle action potential amplitude on NCS.[3] The current study found that a lower MRC scale score at admission may predict poor prognosis for the patient. A study conducted in Turkey has shown that the duration of weakness, length of hospital stay and need for ventilation may negatively affect prognosis.[41]

The research has some limitations. First, the single-center retrospective design of the study allowed only a limited number of clinical features to be analyzed. Therefore, data such as functional vital capacity, which are quantitative indicators of the likelihood of need for ventilation, could not be collected. Second, the relatively small number of our participants (given the rarity of GBS in children) limited our ability to identify underlying risk factors for GBS (such as associated sources of infection, electrophysiological subtypes, or autoantibodies) as prognostic predictors.

In conclusion, the potential predictors of MV requirement in severe GBS patients were found to be bulbar palsy, dysautonomia, sensory impairment, lowest total MRC scale for muscle strength score at admission, high mEGRIS score, high NLR and high SII values. The lowest total MRC scale for muscle strength score at admission was shown to be associated with poor prognosis. Multicenter prospective studies for early prediction of outcome in GBS are needed to develop clinical prognostic prediction models valid for clinical practice and future therapeutic trials.

Ethical approval

The study was approved by İnönü University Ethics Committee (date: 02.05.2023, number: 2023-4580).

Author contribution

The authors confirm contribution to the paper as follows: Study conception and design: GY, AKA; data collection: GY; analysis and interpretation of results: GY, AKA, BÖ, SG; draft manuscript preparation: GY, AKA. All authors reviewed the results and approved the final version of the article.

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Conflict of interest

The authors declare that there is no conflict of interest.

REFERENCES

1. Sejvar JJ, Baughman AL, Wise M, Morgan OW. Population incidence of Guillain-Barré syndrome: a systematic review and meta-analysis. Neuroepidemiology 2011; 36: 123-133. https://doi.org/10.1159/000324710
2. Willison HJ, Jacobs BC, van Doorn PA. Guillain-Barré syndrome. Lancet 2016; 388: 717-727. https://doi.org/10.1016/S0140-6736(16)00339-1
3. van Doorn PA, Van den Bergh PYK, Hadden RDM, et al. European Academy of Neurology/Peripheral Nerve Society Guideline on diagnosis and treatment of Guillain-Barré syndrome. J Peripher Nerv Syst 2023; 28: 535-563. https://doi.org/10.1111/jns.12594
4. Walgaard C, Lingsma HF, Ruts L, et al. Prediction of respiratory insufficiency in Guillain-Barré syndrome. Ann Neurol 2010; 67: 781-787. https://doi.org/10.1002/ana.21976

5. Orlikowski D, Porcher R, Sivadon-Tardy V, et al. Guillain-Barré syndrome following primary cytomegalovirus infection: a prospective cohort study. Clin Infect Dis 2011; 52: 837-844. https://doi.org/10.1093/cid/cir074

6. Sharshar T, Chevret S, Bourdain F, Raphaël JC; French Cooperative Group on Plasma Exchange in Guillain-Barré Syndrome. Early predictors of mechanical ventilation in Guillain-Barré syndrome. Crit Care Med 2003; 31: 278-283. https://doi.org/10.1097/00003246-200301000-00044

7. Islam Z, Jacobs BC, van Belkum A, et al. Axonal variant of Guillain-Barre syndrome associated with Campylobacter infection in Bangladesh. Neurology 2010; 74: 581-587. https://doi.org/10.1212/WNL.0b013e3181cff735

8. Kannan Kanikannan MA, Durga P, Venigalla NK, Kandadai RM, Jabeen SA, Borgohain R. Simple bedside predictors of mechanical ventilation in patients with Guillain-Barre syndrome. J Crit Care 2014; 29: 219-223. https://doi.org/10.1016/j.jcrc.2013.10.026

9. Tan CY, Razali SNO, Goh KJ, Shahrizaila N. The utility of Guillain-Barré syndrome prognostic models in Malaysian patients. J Peripher Nerv Syst 2019; 24: 168-173. https://doi.org/10.1111/jns.12320

10. Barzegar M, Toopchizadeh V, Maher MHK, Sadeghi P, Jahanjoo F, Pishgahi A. Predictive factors for achieving independent walking in children with Guillain-Barre syndrome. Pediatr Res 2017; 82: 333-339. https://doi.org/10.1038/pr.2017.67

11. Witsch J, Galldiks N, Bender A, et al. Long-term outcome in patients with Guillain-Barré syndrome requiring mechanical ventilation. J Neurol 2013; 260: 1367-1374. https://doi.org/10.1007/s00415-012-6806-x

12. Ning P, Yang B, Yang X, et al. A nomogram to predict mechanical ventilation in Guillain-Barré syndrome patients. Acta Neurol Scand 2020; 142: 466-474. https://doi.org/10.1111/ane.13294

13. Durand MC, Porcher R, Orlikowski D, et al. Clinical and electrophysiological predictors of respiratory failure in Guillain-Barré syndrome: a prospective study. Lancet Neurol 2006; 5: 1021-1028. https://doi.org/10.1016/S1474-4422(06)70603-2

14. Fokkink WR, Walgaard C, Kuitwaard K, Tio-Gillen AP, van Doorn PA, Jacobs BC. Association of Albumin Levels With Outcome in Intravenous Immunoglobulin-Treated Guillain-Barré Syndrome. JAMA Neurol 2017; 74: 189-196. https://doi.org/10.1001/jamaneurol.2016.4480

15. Durand MC, Lofaso F, Lefaucheur JP, et al. Electrophysiology to predict mechanical ventilation in Guillain-Barré syndrome. Eur J Neurol 2003; 10: 39-44. https://doi.org/10.1046/j.1468-1331.2003.00505.x

16. Luijten LWG, Doets AY, Arends S, et al. Modified Erasmus GBS Respiratory Insufficiency Score: a simplified clinical tool to predict the risk of mechanical ventilation in Guillain-Barré syndrome. J Neurol Neurosurg Psychiatry 2023; 94: 300-308. https://doi.org/10.1136/jnnp-2022-329937

17. Hu MH, Chen CM, Lin KL, et al. Risk factors of respiratory failure in children with Guillain-Barré syndrome. Pediatr Neonatol 2012; 53: 295-299. https://doi.org/10.1016/j.pedneo.2012.07.003

18. Luo H, Hong S, Li M, Wang L, Jiang L. Risk factors for mechanical ventilation in children with Guillain-Barré syndrome. Muscle Nerve 2020; 62: 214-218. https://doi.org/10.1002/mus.26905

19. Tiwari I, Alam A, Kanta C, et al. Clinical profile and predictors of mechanical ventilation in Guillain-Barre syndrome in North Indian children. J Child Neurol 2021; 36: 453-460. https://doi.org/10.1177/0883073820978020

20. Roodbol J, Korinthenberg R, Venema E, et al. Predicting respiratory failure and outcome in pediatric Guillain-Barré syndrome. Eur J Paediatr Neurol 2023; 44: 18-24. https://doi.org/10.1016/j.ejpn.2023.02.007

21. Qinrong H, Yuxia C, Ling L, et al. Reliability and validity of prognostic indicators for Guillain-Barré syndrome in children. Dev Med Child Neurol 2023; 65: 563-570. https://doi.org/10.1111/dmcn.15418

22. Korinthenberg R, Schessl J, Kirschner J. Clinical presentation and course of childhood Guillain-Barré syndrome: a prospective multicentre study. Neuropediatrics 2007; 38: 10-17. https://doi.org/10.1055/s-2007-981686

23. Wu X, Li C, Zhang B, et al. Predictors for mechanical ventilation and short-term prognosis in patients with Guillain-Barré syndrome. Crit Care 2015; 19: 310. https://doi.org/10.1186/s13054-015-1037-z

24. Green C, Baker T, Subramaniam A. Predictors of respiratory failure in patients with Guillain-Barré syndrome: a systematic review and meta-analysis. Med J Aust 2018; 208: 181-188. https://doi.org/10.5694/mja17.00552

25. Hughes RA, Newsom-Davis JM, Perkin GD, Pierce JM. Controlled trial prednisolone in acute polyneuropathy. Lancet 1978; 2: 750-753. https://doi.org/10.1016/s0140-6736(78)92644-2

26. Reisin RC, Pociecha J, Rodriguez E, Massaro ME, Arroyo HA, Fejerman N. Severe Guillain-Barré syndrome in childhood treated with human immune globulin. Pediatr Neurol 1996; 14: 308-312. https://doi.org/10.1016/0887-8994(96)00050-1

27. Wen P, Wang L, Liu H, et al. Risk factors for the severity of Guillain-Barré syndrome and predictors of short-term prognosis of severe Guillain-Barré syndrome. Sci Rep 2021; 11: 11578. https://doi.org/10.1038/s41598-021-91132-3

28. Kleyweg RP, van der Meché FG, Schmitz PI. Interobserver agreement in the assessment of muscle strength and functional abilities in Guillain-Barré syndrome. Muscle Nerve 1991; 14: 1103-1109. https://doi.org/10.1002/mus.880141111

29. Sarnaik AP, Clark JA, Sarnaik AA. Respiratory distress and failure. In: Kliegman RM, Stanton BF, St Geme III JW, Schor NF, Behrman RE, editors. Nelson Textbook of Pediatrics. 20th ed. Philadelphia: Elsevier; 2016: 528-536.

30. Lawn ND, Fletcher DD, Henderson RD, Wolter TD, Wijdicks EF. Anticipating mechanical ventilation in Guillain-Barré syndrome. Arch Neurol 2001; 58: 893-898. https://doi.org/10.1001/archneur.58.6.893

31. Wang Y, Shang P, Xin M, Bai J, Zhou C, Zhang HL. The usefulness of chief complaints to predict severity, ventilator dependence, treatment option, and short-term outcome of patients with Guillain-Barré syndrome: a retrospective study. BMC Neurol 2017; 17: 200. https://doi.org/10.1186/s12883-017-0982-3

32. Islam Z, Papri N, Ara G, et al. Risk factors for respiratory failure in Guillain-Barré syndrome in Bangladesh: a prospective study. Ann Clin Transl Neurol 2019; 6: 324-332. https://doi.org/10.1002/acn3.706

33. Henderson RD, Lawn ND, Fletcher DD, McClelland RL, Wijdicks EF. The morbidity of Guillain-Barré syndrome admitted to the intensive care unit. Neurology 2003; 60: 17-21. https://doi.org/10.1212/01.wnl.0000035640.84053.5b

34. Orlikowski D, Sharshar T, Porcher R, Annane D, Raphael JC, Clair B. Prognosis and risk factors of early onset pneumonia in ventilated patients with Guillain-Barré syndrome. Intensive Care Med 2006; 32: 1962-1969. https://doi.org/10.1007/s00134-006-0332-1

35. Zahorec R. Neutrophil-to-lymphocyte ratio, past, present and future perspectives. Bratisl Lek Listy 2021; 122: 474-488. https://doi.org/10.4149/BLL_2021_078

36. Sarejloo S, Khanzadeh S, Hosseini S, et al. Role of the neutrophil to lymphocyte ratio in Guillain Barré syndrome: a systematic review and meta-analysis. Mediators Inflamm 2022; 2022: 3390831. https://doi.org/10.1155/2022/3390831

37. Wu X, Wang H, Xie G, Lin S, Ji C. Increased systemic immune-inflammation index can predict respiratory failure in patients with Guillain-Barré syndrome. Neurol Sci 2022; 43: 1223-1231. https://doi.org/10.1007/s10072-021-05420-x

38. van den Berg B, Bunschoten C, van Doorn PA, Jacobs BC. Mortality in Guillain-Barre syndrome. Neurology 2013; 80: 1650-1654. https://doi.org/10.1212/WNL.0b013e3182904fcc

39. Rangan RS, Tullu MS, Deshmukh CT, Mondkar SA, Agrawal M. Clinical profile and outcome of Guillain-Barre syndrome in pediatric patients admitted to a tertiary care centre: a retrospective study. Neurol India 2021; 69: 81-84. https://doi.org/10.4103/0028-3886.310112

40. Shibeshi MS, Mengesha AA, Gari KT. Pediatric Guillain-Barré syndrome in a resource limited setting: clinical features, diagnostic and management challenges, and hospital outcome. Pediatric Health Med Ther 2023; 14: 107-115. https://doi.org/10.2147/PHMT.S401461

41. Konuşkan B, Okuyaz Ç, Taşdelen B, Kurul SH, Anlar B; Turkish Childhood Guillan-Barre Syndrome Study Group. Electrophysiological subtypes and prognostic factors of childhood Guillain-Barré syndrome. Noro Psikiyatr Ars 2018; 55: 199-204. https://doi.org/10.5152/npa.2017.16996