

## Original Article



# Comparison of clinical and biochemical parameters of patients with Guillain-Barré syndrome and Myasthenia gravis: A retrospective single center experience

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### Abstract

**Introduction:** Guillain-Barré syndrome (GBS) and myasthenia gravis (MG) are common neurological autoimmune diseases. In this study, we aimed to compare the patients' complaints, clinical course, and laboratory parameters of both diseases.

**Methods:** This study was carried out as a retrospective file scan. The study covers the dates between April 1, 2017, and April 20, 2020. The GBS and MG patients were compared in terms of sociodemographic characteristics, application complaints, clinical course, laboratory findings, treatments, and outcomes.

**Results:** In this study, 51 patients from both groups were included. The mean age of GBS and MG patients was  $52.1 \pm 19.4$  and  $43.6 \pm 15.8$  years, respectively. Respiratory involvement of the patients was 23.5% in GBS and 17.6% in MG. When the treatments of the patients were compared, it was observed that 78.4% of GBS patients and 98% of MG received intravenous immunoglobulin (IVIG) treatments. Only two patients from GBS group were found to be excluded. When the laboratory results were compared, it was found that lactate, vitamin D, transferrin, and total iron binding capacity results were lower in GBS patients, whereas, vitamin B12 and ferritin results were lower in MG patients and this difference was statistically significant ( $P < 0.05$ ).

**Conclusion:** The clinical presentation of GBS and MG is diverse and the prognosis can significantly vary among patients. Within the scope of the data obtained from the study, it was concluded that wide anamnesis and laboratory analyzes are necessary and useful for the differential diagnosis of these two diseases.

### Introduction

Guillain-Barré syndrome (GBS) and myasthenia gravis (MG) disease are the most common autoimmune neuromuscular diseases that may require critical intensive care and mechanical ventilation. Both are the diseases of the peripheral nervous system that goes by the pathology of neurons or neuromuscular junction.<sup>1,2</sup>

GBS is an acute-onset and inflammatory polyneuropathic disease of the peripheral nervous system. GBS symptoms usually appear in 10 to 14 days following upper or lower respiratory disease or acute gastroenteritis.<sup>3,4</sup> It may also occasionally develop after severe surgical operations.<sup>5</sup> MG disease, on the other hand, is a disease in which the neuromuscular transition is blocked by autoimmune antibodies, causing loss of nicotinic acetylcholine receptors. It is mostly associated with thymic tumor, thyrotoxicosis, rheumatoid arthritis, or disseminated lupus erythematosus.<sup>2</sup>

Bilateral, rapid, progressive, and ascending muscle

weakness is typically seen in GBS. In the extremities with muscle weakness, areflexia or decreased tendon reflexes are observed. These symptoms usually start from the lower extremities and progress to the trunk and upper extremity within 2 to 4 weeks.<sup>6</sup> Approximately 50% of GBS patients experience maximum muscle weakness in two weeks, 80% in three weeks and 90% in 4 weeks.<sup>3</sup> During this progressive phase, 20%-30% of patients may develop respiratory failure and/or ventilation needs.<sup>7</sup> Besides, the duration and severity of the disease are quite diverse. While some patients recover spontaneously, some patients may take several months to recover. Some patients may even remain quadriplegic for a long time without signs of recovery and become dependent on the ventilator.<sup>8</sup>

MG disease is characterized by fluctuating weakness, easy fatigue, and inability to perform muscle activities. The involvement of the external eye muscles and other facial, chewing, and swallowing muscles are prioritized.<sup>1,2</sup> Application complaints of MG patients, mostly similar

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to GBS patients, are weakness in the hands and feet and inability to walk. However, proximal muscle weakness is more prominent in MG patients. Electrophysiological examination has an important role in the diagnosis of both diseases and rapid diagnosis should be made.<sup>6,9</sup> In the treatment, intravenous immunoglobulin (IVIG) and plasmapheresis should be started as soon as possible supportive therapy should be applied concomitantly.<sup>2,6,10</sup> The most common cause of mortality in both diseases is respiratory failure.<sup>1</sup> In this study, we aimed to compare the arrival complaints, clinical course, and laboratory parameters of GBS and MG patients.

## Methods

### Study design and adjustment

This study retrospectively analyzed the sociodemographic data, application complaints, laboratory results, clinical course, and treatments of GBS and MG patients from the electronic data system of a university affiliated hospital between April 1, 2017, and April 20, 2020. This study was done in a third level university hospital.

### Patient selection

Patients diagnosed with “Guillain-Barre syndrome (G61.0)” and Myasthenia gravis (G70.0) with International Disease Classification (ICD) diagnostic codes were screened from the hospital electronic data system. In the hospital data system, patients diagnosed with GBS and MG were examined and patients with suspected and undiagnosed definitions were excluded from the study. Patients older than 18 years old and without diabetes were included in the study. Patients under 18 years of age, drug-induced polyneuropathy, radiation, and chemotherapeutic and diabetic polyneuropathy were excluded from the study.

Within the scope of our study, in the last 3 years, newly diagnosed and hospitalized GBS patients in our hospital were screened and 51 patients were identified in accordance with the study criteria. Furthermore, 51 MG patients, whether newly diagnosed or admitted to the hospital for acute flame attack in the last 3 years were included in our study by randomization method. The laboratory findings for all patients were included and analyzed by checking the test results taken bloods in the first hospital visits.

The demographic data of the patients, complaints of application, predisposing factors, physical examination, laboratory and electroneuromyography (EMG) findings, clinical course, treatments, and ventilation needs were evaluated and compared in terms of morbidity and mortality.

### Evaluation of variables

The history of upper and lower respiratory tract infection, acute gastroenteritis, and previous surgery were examined from the electronic files of the patients with GBS diagnosis.

Possible pathogens and biochemical parameters were recorded from patient files. The treatments of the patients were evaluated only for IVIG and plasmapheresis. Other symptomatic and specific treatments were ignored.

EMG studies of the patients were taken according to standard EMG technique with Nihon Kohden Neuropack MEB-9102 and Dantec™ Keypoint® G4 EMG devices. EMG results of the patients were obtained by scanning from the hospital EMG archive. EMG examinations of all patients consisted of four motor nerves (median, ulnar, peroneal, and tibial), two sensory nerves, (ulnar and sural) and two F waves (ulnar and tibial). According to EMG results, GBS subtype definition was made.

### Statistical analysis

In our study, statistical analyses were performed using IBM SPSS 25.0 package program. Kolmogorov-Smirnov test was used for normal distribution assessment. Categorical data were presented as frequency and percentage, mean and standard deviation was given if data is normally distributed, median and interquartile ranges (IQR) if it is not normally distributed.

In the statistical analyses, Student *t* test was used when the two groups are normally distributed, if the distribution is not normal, Mann-Whitney U test was chosen. When the compared group is three or more and it is normally distributed, one way ANOVA variance test was used, whereas, if the distribution is not normal, Kruskal Wallis variance test was used. The statistical significance of the study was taken as  $P < 0.05$ .

## Results

The data of 51 patients from both groups were evaluated for the study. The mean age of the GBS group was  $52.1 \pm 19.4$  years and 56.9% ( $n = 29$ ) of the patients were women. The mean age of the MG group was  $43.6 \pm 15.8$  years and 66.7% ( $n = 34$ ) of the patients were women (Table 1).

While complaints of all GBS patients were progressively progressive, 90.2% ( $n = 46$ ) of patients had symmetrical and 9.8% ( $n = 5$ ) had asymmetrical involvement. Bulbar, respiratory involvements and intubation due to respiratory involvements were presented in 25.5% ( $n = 13$ ); 23.5% ( $n = 12$ ) and in 13.7% ( $n = 7$ ), respectively in GBS patients. Whereas, in MG patients, bulbar and respiratory involvements were presented in 27.5% ( $n = 14$ ) and 17.6% ( $n = 9$ ), respectively, and intubation due to respiratory involvement in only one patient (2%) (Table 1).

Physical examination findings of GBS patients showed that 49% ( $n=25$ ) of the patients had areflexia in the held limb, 29.4% ( $n=15$ ) had hypoactive reflex, and 21.6% ( $n=11$ ) had normal reflex findings. While areflexia was not detected in MG patients, it was found that 5.9% ( $n=3$ ) had hyporeflexia, 90.2% ( $n=46$ ) had normal reflex, and 3.9% ( $n=2$ ) had hyperactive reflex (Table 1).

When the treatments given to both groups were compared, 78.4% ( $n=40$ ) of GBS patients received IVIG

**Table 1.** General characteristics and comparison of GBS and MG patients

	GBS	MG	P
Age (mean, SD)	52.1±19.4	43.6±15.8	<b>0.017</b>
Sex (Female, %)	56.9	66.7	0.313
Number of days hospitalized (mean, Std. deviation)	19.5±20.2	9.4±10.9	<b>0.002</b>
Respiratory involvement (n, %)	12 (23.5)	9 (17.6)	0.468
Intubation (n, %)	7 (13.7)	1 (2)	<b>0.027</b>
Bulbar involvement (n, %)	13 (25.5)	14 (27.5)	0.825
Normal deep tendon reflex presence (n, %)	11 (21.6)	46 (90.2)*	<b>0.000</b>
Treatment given (IVIg, n, %)	40 (78.4)	50 (98)	<b>0.005</b>
Exitus (n, %)	2 (3.9)	0 (0)	1.000

SD, standard deviation; GBS, Guillain-Barré syndrome; MG, myasthenia gravis.  
\* Hyperreflexia is not included.

therapy, 7.8% (n=4) received plasmapheresis and 13.7% (n=7) received IVIG + plasmapheresis therapy. Of the MG patients, 98% (n=50) received IVIG treatment, while only one (2%) received IVIG + plasmapheresis treatment. 92.2% (n=47) of GBS patients recovered and discharged, 3.9% (n=2) were still in hospital at the time of the study, while 3.9% (n=2) had exitus. All MG patients have recovered and discharged after the treatments (Table 1).

When these data were evaluated, it was found that GBS patients were older, more hospitalized, more intubated, and these conditions were statistically significant compared to MG patients ( $P < 0.05$ ). It was found that female gender, respiratory and bulbar involvement, discharge from hospital and exitus were not statistically significant in both groups ( $P > 0.05$ ).

When predisposing factors are investigated in GBS patients; pre-determined disease rates of patients with upper respiratory tract infection, lower respiratory tract infection, acute gastroenteritis, surgical operation and Hashimoto thyroiditis, were 27.5%; 13.7%; 9.8%; 9.8% and 3.9%, respectively. No predisposing factor was found in 35.3% of the patients (Figure 1).

The diagnoses of GBS patients according to EMG examinations; acute inflammatory demyelinating polyradiculoneuropathy, acute motor and sensory axonal neuropathy, acute motor axonal neuropathy and Miller-Fisher syndrome were found to be 41.2%; 39.2%; 15.7% and 3.9%, respectively (Figure 2).

Hospital admission complaints of both patient groups were examined in Table 2. Accordingly, 80.4% (n=41) of GBS patients had weakness in the feet, 17.7% (n=9) had gait disturbance, and one patient (2%) complained of double vision. MG patients were most frequently referred to the hospital with the complaint of weakness in the arms and legs (56.9%). When comparing the most frequent hospital admission complaints of GBS and MG patients, GBS patients complained of weakness and inability to walk, whereas MG patients presented with complaints of weakness in the eyelid and bulbar complaints, and this was statistically significant ( $P < 0.05$ ).

The comparisons of patients' laboratory test results are given in Table 3. The attained results show that

lactate, vitamin D, transferrin and total iron binding capacity (TIBC) test values were lower in GBS patients; whereas, vitamin B12 and ferritin values were lower in MG patients and these differences were statistically significant ( $P < 0.05$ ). It was determined that there were no statistically significant differences in other tests such as serum electrolytes, CRP, procalcitonin, folate and TSH values ( $P > 0.05$ ).

### Discussion

In this study, general characteristics and the laboratory test results of the patients with GBS and MG diseases were compared. Although their etiology and pathogenesis are different, these diseases should be considered in the differential diagnosis, since patients are presented with similar symptoms. As a result of our study, it was revealed that both diseases show similar features in some aspects and differ in other aspects.

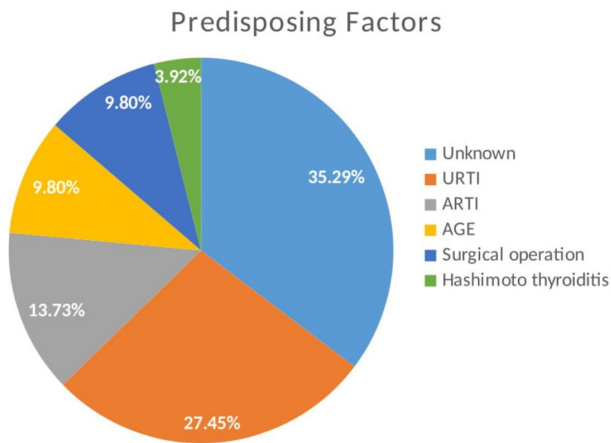
As a result of this study, GBS and MG patients were differed significantly from each other in terms of the patients age, deep tendon reflex, low eyelid complaints, the level of vitamin D, Vitamin B12, lactate, ferritin, and transferrin were significantly differed in assay results ( $P < 0.05$ ).

Similar points of both patient groups that we detected in our study were female gender, respiratory and

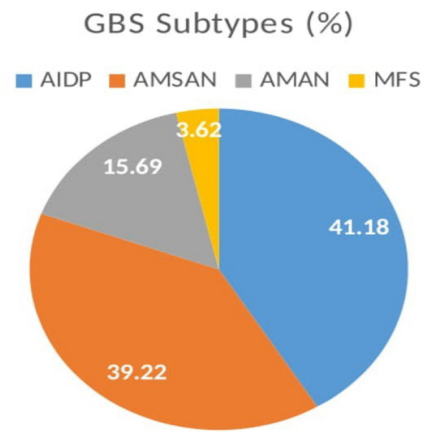
**Table 2.** Hospital arrival complaints of GBS and MG patients

	GBS, No. (%)	MG, No. (%)
Weakness	41 (80.4)	29 (56.9)
Walking disorder	9 (17.7)	1 (2)
Double vision	1 (2)	2 (3.9)
Low eyelid	-	10 (19.6)
Difficulty swallowing	-	4
Shortness of breath	-	2 (3.9)
Low eyelid and difficulty speaking	-	1 (2)
Low eyelid and difficulty swallowing	-	1 (2)
Weakness and double vision	-	1 (2)
<b>Total</b>	51 (100)	51 (100)

GBS, Guillain-Barré syndrome; MG, myasthenia gravis.  
P value = 0.00.



**Figure 1.** Predisposing factors detected in GBS patients. URTI: Upper respiratory tract infection, ARTI: Lower respiratory tract infection, AGE: Acute gastroenteritis



**Figure 2.** Distribution according to GBS subtypes. GBS: Guillain-Barre Syndrome, AIDP: Acute inflammatory demyelinating polyradiculoneuropathy, AMSAN: Acute motor and sensory axonal neuropathy, AMAN: Acute motor axonal neuropathy, MFS: Miller-Fisher Syndrome

bulbar involvement rates, serum electrolyte levels, CRP, procalcitonin, folic acid, homocysteine, and D-dimer assay results ( $P > 0.05$ ).

There are no studies comparing the vitamin B12 levels in GBS and MG patients in the literature. Vitamin B12 deficiency should be kept in mind in differential diagnosis of GBS.<sup>6,11</sup> Muscle weaknesses due to the vitamin B12 deficiency can occur in gastrointestinal system disorders and therefore, it can be confused with both diseases.<sup>12</sup> In our study, although normal levels of the vitamin B12 were determined in both patient groups (the normal level of homocysteine in both groups supports this situation),

it was found that MG patients had a statistically lower vitamin B12 level. This result also reveals the need to investigate the vitamin B12 levels in MG patients.

In our study, vitamin D levels were found at lower rates in both GBS and MG patients. In the literature, a study comparing vitamin D levels of MG patients and healthy control group, a significant decrease in the vitamin D was found in MG patients similar to our study.<sup>13</sup> In a study investigating immune-dependent peripheral neuropathies and vitamin D levels, vitamin D levels were found to be significantly low.<sup>14,15</sup> In an another study comparing vitamin D levels between GBS and MG patients conducted

**Table 3.** Comparison of examined examinations of patients

	GBS			MG			P value
	n	Mean	SD	n	Mean	SD	
Na	51	137.3	4.3	51	138.1	2.5	0.206
K	51	4.03	0.56	51	4.18	0.42	0.136
Mg	51	2.02	0.23	51	2.00	0.21	0.661
Ca	51	9.09	0.82	51	9.22	0.47	0.315
CRP	51	21.4	41.5	51	13.6	37.6	0.322
D-dimer	6	727.3	444.1	11	709.1	1186.6	0.972
Lactate	51	1.33	0.45	42	1.60	0.70	<b>0.037</b>
Folate	51	9.16	5.55	50	10.52	4.23	0.169
Homocysteine	51	12.32	4.29	41	12.92	4.92	0.530
TSH	51	1.56	1.44	51	1.89	2.69	0.435
Procalcitonin	16	6.68	24.9	6	1.28	2.08	0.607
Vitamin D	51	10.9	9.5	51	15.1	10.5	<b>0.038</b>
Vitamin B12	51	448.2	370.7	51	315.9	238.9	<b>0.035</b>
Transferrin	51	2.24	0.76	49	2.63	0.68	<b>0.008</b>
Ferritin	17	266.2	228.3	35	84.1	112.3	<b>0.006</b>
Iron	51	60.3	41.5	50	56.2	29.1	0.567
TIBC	51	218.5	90.6	50	278.3	76.9	<b>0.001</b>

SD, standard deviation; GBS, Guillain-Barré syndrome; MG, myasthenia gravis; Na, sodium; K, potassium; Mg, magnesium; Ca, calcium; CRP, C-reactive protein; TSH, Thyroid stimulating hormone; TIBC, Total iron binding capacity.

on a small number of patients, it was found that a lower vitamin D was found in GBS patients, which was similar to our results.<sup>16</sup> However, interestingly, they found that there were high vitamin D levels in MG patients compared to the healthy group. Vitamin D levels in our study were found to be quite low in both GBS and MG patients compared to this study.

In our study, ferritin, transferrin, and TIBC assays of GBS and MG patients were compared for the first time in the literature. Ferritin levels were higher in patients with GBS, while transferrin and TIBC tests were lower than the MG patients. Since ferritin is a positive acute phase reactant and GBS has an acute inflammatory pathogenesis, it was evaluated that ferritin was found to be meaningfully higher. However, since the CRP and procalcitonin assays are both acute markers of infection but they were not statistically differed between these groups, the usability of the ferritin test in the differential diagnosis of GBS becomes more apparent.

Mortality in neuromuscular diseases generally depends on the respiratory involvements. Respiratory and blood gas parameters should be closely monitored in these patients.<sup>2</sup> In respiratory involvements, blood lactate level due to hypoxia increases.<sup>17</sup> In our study, the lactate levels of GBS and MG patients were compared for the first time in the literature, and it was found that MG patients had statistically higher blood lactate levels. Although respiratory involvement and intubation rates were lower in MG patients, it was concluded that respiratory functions should be closely monitored in the follow-up of MG patients, due to the relationship of blood lactate levels with body oxygenation.

In a study by Vellipuram et al, it was found that there was a higher need for intubation in MG patients.<sup>2</sup> However, in our study, it was found that the need for intubation was higher in GBS patients than MG, which was an interesting result and should be linked with the timing of the treatments.

Studies have shown that IVIG follows plasmapheresis treatment has no advantage over IVIG alone or plasmapheresis only.<sup>18</sup> In the treatments, IVIG and plasmapheresis and supportive treatment should be started as soon as possible before irreversible nerve damage occurs. Although plasmapheresis is cheaper, IVIG treatment is preferred by most centers because it is more accessible, easier to apply and has fewer side effects.<sup>6,18,19</sup> In our study, it was observed that the majority of patients were given IVIG treatment.

### Limitations

Our study had some limitations. First of all, our study was a retrospective study and patients in the last 3 years were included in the study using ICD codes. Since 51 GBS patients were detected in the last 3 years, 51 MG patients were selected by a randomization method. Therefore, the number of patients included in the study was partially

## Study Highlights

### What is current knowledge?

- Although the etiology and pathogenesis of GBS and NG are different, these diseases should be considered in the differential diagnosis, since patients are presented with similar symptoms.

### What is new here?

- GBS and MG patients were differed significantly from each other in terms of the patients age, deep tendon reflex and low eyelid complaints, and vitamin D, Vitamin B12, lactate, ferritin, transferrin were significantly differed in assay results.

small. The second limitation was that patients' treatments were compared only in terms of IVIG and plasmapheresis. Other treatments were not included in the study because they differed between the groups. Another point is that since the study is retrospective, not all assay results were available in all patients, and some comparative assay data have been made in relatively few patients, since these missing assays cannot be compensated.

## Conclusion

The clinical presentation of GBS and MG patients are heterogeneous and the prognosis can vary significantly among patients. In differential diagnosis, both diseases can be confused with each other. In scope of this, the general features and laboratory findings of GBS and MG patients were compared, and similar and different aspects of these two patient groups were revealed in our study. It was concluded that detailed anamnesis and laboratory analyzes are necessary and useful for the differential diagnosis of these two diseases.

## Conflict of Interest

The authors have no conflict of interest to declare.

## Ethical Approval

The study protocol was approved by the Ethical Committee of the Ataturk University, Medical Faculty (Number: B.30.2.ATA.0.01.00/198, date: 07.05.2020). Since this study is a retrospective study, patient consent was not obtained.

## Author's Contributions

The authors contributed equally to the study.

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