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Original Article

The investigation of guillain-barre syndrome and prognosis

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Abstract

Aim: Guillain-Barre Syndrome (GBS) is an immune-mediated disease of peripheral nervous system. It is important to estimate the prognosis because of disability burden and morbidity. In addition to clinical features and disease severity scales, serum biomarkers were used to estimate prognosis. We aimed to determine the subtypes, demographic and clinical characteristics of GBS patients, and the factors affecting the short-term prognosis.

Material and Methods: The medical files of 94 patients who were followed up with diagnosis of GBS between January 2011 and January 2018 were retrospectively reviewed. Demographic and clinical features, disease severity scores, and neutrophil/lymphocyte (N/L) ratios were determined, and the effects of these parameters on short-term prognosis were investigated.

Results: Most of the patients (60.6%) had acute inflammatory demyelinating polyneuropathy (AIDP) subtype. A majority of the cases were men and were in 5 to 7th decades of age. There was no seasonal relevance with the disease. 77% of the cases had albuminocytologic dissociation. The short-term prognosis was associated with age, respiratory failure, cranial nerve involvement and N/L ratio.

Conclusion: It is important to estimate the prognosis in GBS. In our study, age, respiratory failure, cranial nerve involvement and N/L ratio were found as related factors with short-term prognosis.

Keywords: Guillain-Barré Syndrome; Prognosis; Peripheral Neuropathy.

INTRODUCTION

Guillain Barre Syndrome (GBS) is a syndrome triggered by infectious or non-infectious agents and generally considered as an immune-mediated disorder of the peripheral nervous system (1). GBS usually presents with progressive flask paralysis and reduced reflexes and characterized with widespread sensory, motor and autonomic symptoms (2). In the literature, the incidence was reported between 0.6-4 in 100.000 (3,4). While the frequency of different clinical subtypes of GBS varies according to geographic areas, AIDP is more common in west, while axonal types are seen more frequently in the far east (3,4).

Despite its low incidence, it is a disease with high economic burden due to expensive treatments and need for long-term hospitalization. In 20% of cases, disability and mortality rates were reported 2-10% (3,7). It was shown that prognosis can be determined with serum albumin, glucose, cortisol and sodium levels as well as neutrophil / lymphocyte (N/L) ratio which is reported to be an inflammatory biomarker (6-12). In these studies, the severity of the disease was determined by the Medical Research Council (MRC) and Hughes scores, and it was reported that the severity of the onset of the disease might predict the prognosis (6,8,11). The GBS disability score which named also as the Hughes score and the MRC score, are indicative of the severity of the disease. The GBS disability score is a generally accepted scoring system to assess the functional status of patients with GBS (13).

However, more studies are required in the literature regarding with the clinical features of GBS and severity of disease, the majority of current studies being performed with a small number of patients. In our study, we aimed to evaluate the factors (age, gender, respiratory failure, cranial nerve involvement and N/L ratio) affecting the

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severity of the disease, the demographic and clinical features as well as the relationship between severity of the disease and GBS subtypes.

MATERIAL and METHODS

In this study, we examined the followed patients with GBS diagnosis, who admitted to university hospital which is located in the east of Turkey between January 2011 and January 2018, retrospectively. The demographic and clinical characteristics of all patients (respiratory failure, cranial nerve involvement), and cerebrospinal fluid (CSF) analysis, and the time between the onset of symptoms and the CSF examination were investigated. Disease severity scores (Hughes and MRC total scores) of the patients at admission and discharge were evaluated (11,12). The patients who were diagnosed as AIDP, Acute Motor Axonal Neuropathy (AMAN), Acute Motor-Sensory Axonal Neuropathy (AMSAN) and Miller Fisher syndrome (MFS) according to clinical and electrophysiological examination were included in the study. Patients had no hypertension, anemia, metabolic syndrome or malignancies. The patients diagnosed with another disease at follow-up such as vasculitis, diabetes, toxin exposure and those with missing data were excluded in the study (Figure 1).

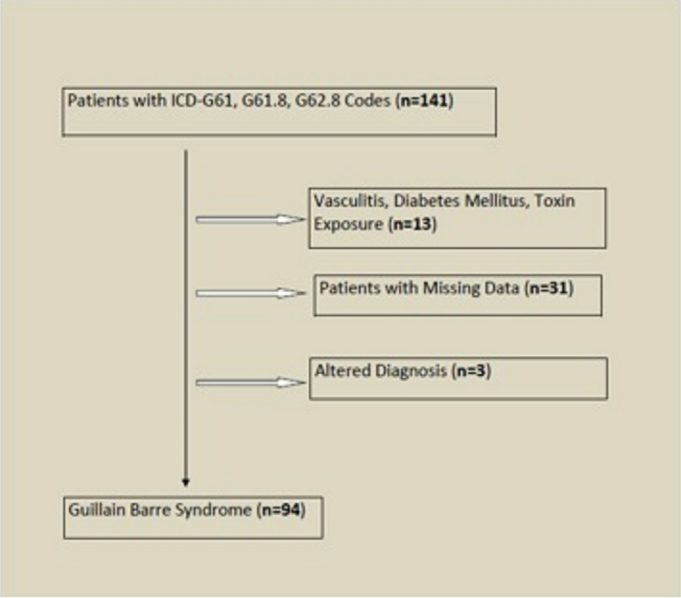

Figure 1. Population of the study (Inclusion and Exclusion Scheme)

The Hughes Score used for GBS disease severity was classified between stages 1-6 (11). In the MRC score determined with six muscle pairs on each side, and each muscle was graded from 0 to 5, with a total MRC score of 0-60 (14). Demographic and clinical characteristics and GBS subtypes of the patients included in the study were examined. The relationship between disease severity and N/L ratio with respiratory failure and cranial nerve involvement were evaluated. In addition, the factors affecting the change in the severity of the disease on arrival and discharge were investigated.

The study was approved by local ethics committee (Protocol No: B.30.2.ATA.0.01.00/280).

Statistical Methods

The data were compared with the D'Agostino-Pearson test to determine whether they have the normal distribution. Nominal variables were compared by chi-square test. The independent samples t-test was used for the normally distributed parameters. ANOVA test was used for the comparison of normally distributed data more than two groups whereas Kruskal-Wallis test was used non-normal distributed data more than two groups. Dependent variables that affect the Hughes and MRC scoring systems were analyzed using multivariate regression model. Two-tail $p<0.05$ was considered as significant. All statistical analyses were performed using the Medcalc program (Medcalc ver 12, Ostend, Belgium).

RESULTS

The medical files of 141 patients aged 18 years and older who were diagnosed between January 2011 and January 2018 with ICD-10 codes G61 (Guillain-Barre Syndrome), G61.8 (polyneuropathies, other inflammatory polyneuropathies) and G62.8 (other specified polyneuropathies) were detected. After the exclusion criteria were approved, 94 patients were included in the study. 60.6% of the patients had AIDP, 14.9% had AMAN, 17% had AMSAN, and 7.4% had MFS. 2 (2.1%) male patients died during hospitalization. The patients were between 18-82 years of age and the mean age was 49.7 ± 16.1 years. 63.8% of cases were in 5-7. decades of age. There were no significant differences between the GBS subtypes and the mean age. 68.1% of the cases were male. Male/Female ratio was determined as 2.1 / 1. 60.6% of the patients had a history of infection before GBS symptoms and the frequency of respiratory tract infection within the infections was more frequent with 36.1% ratio. There was no statistically significant difference between GBS subtypes and infection history. Although there was no significant difference in the distribution of the cases according to seasons, in this study it was found 74.5% of the applicants were in spring and winter seasons. The mean values of MRC were significantly higher in MFS subtype than the others. Hughes scores were significantly lower in AIDP and MFS types. 25.5% of patients had respiratory failure and 55.3% had cranial nerve involvement. Seventy-four patients underwent CSF examination. CSF positivity was detected in 77% of the cases (Table 1). The mean duration between the onset of complaints and the appliance of lumbar punctures was 9.4 ± 3.1 (2-21) days. In terms of the relationship between respiratory failure and cranial nerve involvement, N/L ratios, and MRC and Hughes scores; all three parameters were associated with respiratory distress and cranial nerve involvement (Table 2). In addition, multivariate regression analysis was used for the change in severity scores (MRCd Hughesd scores) and some parameters measured at admitted and discharged (Table 3-4). There

was a significant negative correlation between MRCd and Hughesd scores, age, respiratory failure, cranial nerve involvement and N/L ratio. No significant relationship was found between sex and GBS subtypes. The change in the severity of the onset and discharge severity scales decreased by increasing age, and the same relationship was also detected between respiratory failure, cranial nerve involvement and N/L ratios (Table 3-4).

Table 1. The distribution of demographical and clinical features and the mean severity scores of subtypes of GBS and the relationship between them

	AIDP n=57	AMAN n=14	AMSAN n=16	MFS n=7	Total n=94 (%)	p
Mean age, age ± SD	49.7±16.8	45.8±16.2	57.5±12.1	39.8±10.1	49.7±16.1	0.064
2. decade	2	0	0	0	2 (2.1)	
3. decade	8	2	0	0	10 (10.6)	
4. decade	8	3	2	2	15 (16)	
5. decade	7	4	3	3	17 (18.1)	
6. decade	11	0	5	1	17 (18.1)	
7. decade	17	4	4	1	25 (26.6)	
8. decade	4	1	1	0	6 (6.4)	
9. decade	0	0	1	0	1 (1.1)	
Sex, male n (%)	40 (70.2)	9 (64.3)	11 (68.8)	4 (57.2)	64 (68.1)	0.897
History of an infection	34 (59.6)	9 (64.3)	10 (62.5)	4 (57.1)	57 (60.6)	0.903
Gastrointestinal system	15	3	4	1	23 (24.5)	
Respiratory system	19	6	6	3	34 (36.1)	
Season						0.081
Spring	14	7	8	4	33 (35.1)	
Summer	11	2	3	0	16 (17.0)	
Autumn	4	0	2	2	8 (8.5)	
Winter	28	5	3	1	37 (39.4)	
Albuminocytologic Dissociation						0.132
Positive	33	9	10	5	57 (77.0)	
None	8	3	6	0	17 (23)	
Cranial nerve involvement	25	11	9	7 ***	52 (55.3)	0.008
Respiratory failure	13	5	4	2	24 (25.5)	0.795
MRC at onset, mean	37.6	32.6	30.8	46.1*	36.32	0.020
Hughes at onset, mean	2**	4	4	2**	3	0.001

* Significantly higher than the other groups
** Significant difference to the other groups
*** Significantly higher than the other groups

Table 2. The relationship between N/L ratio of respiratory insufficiency. cranial nerve involvement and severity of the disease

	Respiratory failure		P	Cranial nerve involvement		P
	Positive	Negative		Positive	Negative	
N/L ratio, mean*	2.4	1.8	0.001	2.2	1.6	0.001
MRC, mean**	31.9	37.5	0.043	34.1	39.0	0.021
Huges, median***	4	3	0.029	4	2	0.001

Mean and min max of N/L of total population = 1.9 (1.3-3.34)
Mean and min max of MRC of total population = 36.3 (18-60)
Median and min max of Hughes of total population = 3 (0-5)

Table 3. Multivariable regression analysis between MRC_d index and dependent variables

	Constant	Standard deviation	p value
Age	-0.138	0.046	0.003
Sex	-0.120	1.551	0.938
GBS subtypes	-1.077	0.712	0.133
Respiratory failure	-3.671	1.750	0.013
Cranial nerve involvement	-4.671	1.595	0.004
N/L Ratio	-5.801	1.258	<0.001

MRC_d: Difference between MRC scores at the times of application and discharged

Table 4. Multivariable regression analysis between $Hughes_d$ index and dependent variables

	Constant	Standard deviation	p value
Age	-0.011	0.006	0.021
Sex	-0.021	0.203	0.914
GBS subtypes	-0.078	0.093	0.400
Respiratory failure	-0.362	0.229	0.018
Cranial nerve involvement	-0.486	0.209	0.023
N/L Ratio	-0.685	0.165	0.001

$Hughes_d$: Difference between Hughes scores at the times of application and discharge

DISCUSSION

In this study, it was obtained novel findings in addition to previous researches. GBS is more frequently seen in the fifth and sixth decades and is more common in men. AIDP subtype is more common and there is no seasonal relevance with the incidence of the disease. Age, respiratory failure, cranial nerve involvement and N/L ratio are effective on prognosis.

GBS is an immune-mediated disease. It was reported that 3-10% of cases died and 20% could not been mobilized in the first 6 months (2). According to literature, GBS subtypes are determined at different rates in different geographic areas, in the United States, Canada, Western Europe and Australia, AIDP accounts for 80-90% of all GBS cases, while in Asian countries this is under 25% (2-4,5,15). In a recent study in South America, 65.9% of GBS cases were reported to be AIDP and 26.8% were axonal subtypes (16). MFS was reported as high as 19% in Asia, but this rate was reported lower in the west with the ratio 2-7% (17,18). Turkey is located in a geography where the connection of Asian and European continents is. In the studies which were performed in Turkey, 61.1-70.3% of the GBS cases were reported to be AIDP, 25% to 33.3% axonal types (AMAN-AMSAN) and 4.7-5.6% to MFS (19,20). The current study, we found that 2.1% of the patients died during hospitalization. We found axonal forms were seen in 31.9% our patients and MFP in 7.4% while the most common type was AIDP (60.6%). Our AIDP ratio was found considerably higher than studies which reported on Asian continents, while lower than quite a few researches that reported in Europe and America, also our results were compatible previous studies conducted on in Turkey. Studies demonstrated increasing incidence of GBS, which was considered to be directly proportional to age, and this was associated with decreased immunosuppressive mechanisms in the elderly and increased susceptibility to autoimmune diseases (18,21). In one study which was carried out in Europe and North America, cases were reported to be more frequent in the fifth and more decades of age (17). In another study, 60.1% of the cases were reported to be in the 36-65 age range (16). In our study, in accordance with the literature, 63.8% of the cases were between 40 and 70 age (4). In the literature, it is reported that GBS is more common in males than females and this rate varies between 1.6-2.7 / 1 (16,19). In our study, we found male / female ratio to be 2.1 / 1.

In many studies related to GBS, it was reported that 40-70% of cases had an infection history 2 to 4 week before the onset of the symptoms (4,22). Respiratory system infection was reported in terms of frequency as 22-53% and gastrointestinal tract infection was seen as 6-26% (22,23). In our study, 60.6% of patients had a history of previous infection and the history of respiratory infection was more frequent. In one study, it was reported that GBS did not differ seasonally and was sporadically (4). Although there were no seasonal differences in disease development in many studies (24,25), in some studies were reported to cluster in autumn and winter months (26,27) and some in the spring (28,29). In our study, we did not find a seasonal relationship with the disease, but 74.5% of the cases were observed in spring and winter. Most of the cases can be related with the spring and winter season due to the frequency of respiratory infections during this season.

CSF examination is an important diagnostic test in the diagnosis of GBS. In CSF examination, approximately 80% of cases were reported to have albuminocytologic dissociation (11,15). In one study, while the CSF positivity was 49% on the first day, it was reported that the rate

increased to 88% after two weeks (30). In our study, 74 patients received a CSF examination at an average of 9.4 days after the onset of complaints and 77% of them had an albuminocytologic dissociation.

Cranial nerve involvement is common in GBS and ratio in the literature were reported as 50-62.5% (31,32). Respiratory failure is a life-threatening manifestation of Guillain-Barré syndrome (GBS), which occurs in 20-30% of patients and is associated with a functionally poor outcome (33,34). In addition, it has been reported that there was a relation between respiratory problem and the need of ventilator, in the patients with cranial nerve involvement. In one study, it was reported that 32.5% of patients needed mechanical ventilator (32). In our study, we found that 55.3% of the patients had cranial nerve involvement and 25.5% of them had respiratory failure.

Some clinical findings and severity scales have been reported in the literature to detect disease prognosis early, and respiratory failure and cranial nerve involvement have been reported to be poor prognosis indicators (35). Cranial and bulbar involvement, autonomic system disorder, MRC score, Hughes score and areflexia were reported to relation with respiratory failure in GBS (15,35). In many studies, the Hughes score and the MRC score were reported to be related to the prognosis of the disease and in the same studies it was reported that the age also to be effective in the prognosis (36,37). In a different study investigating prognostic factors in GBS, it was reported that age and prognosis were related but there was no relation between gender and prognosis (13). It was also reported that the axonal involvement had a poor relation with prognosis (10). Serum albumin levels, glucose levels, folate, sodium and cortisol levels and N/L ratio were also used as biomarkers to monitor prognosis and response to treatment except for clinical findings or severity scales which could be used to estimate prognosis (6-11.38). N/L ratio was reported to may be important to prognosis in various neurological diseases (39,40). In some studies, it was reported that GBS prognosis could be estimated with N/L ratio (8.39). In our study, we found a significant statistical relation between MRC and Hughes scores with respiratory failure and cranial nerve involvement. In addition, N/L ratio was significantly higher in patients with respiratory failure and cranial nerve involvement. Hughes scores and N/L ratios were higher and MRC scores were lower in patients with respiratory failure and cranial involvement. We found a significant relationship between age, respiratory failure, cranial nerve involvement, and N/L ratios with changes in MRC and Hughes scores of the patients at the time of application and discharge. Advanced age, presence of respiratory failure, cranial involvement and high N/L ratios and severity scores at the time of application and discharge were inversely proportional. Again, gender was not effective on changes in severity of disease, similarly GBS subtypes are also determined as not effective. It was similar to other studies in the literature to comment on prognosis with advance age and expected immune system weakness and change in severity of the disease. In addition, the inverse correlation of N/L ratio, which is an indicator of inflammation, with prognosis was consistent with similar methodological studies in the literature.

CONCLUSION

Although GBS has a low incidence, it is a disease with high cost burden, therefore it is important to predict the prognosis of the disease. Age, disease severity and N/L ratio are effective on prognosis and may help to predict short-term prognosis.

Competing interests: The authors declare that they have no competing interest.
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Ethical approval: The study was approved by local ethics committee (Protocol No: B.30.2.ATA.0.01.00/280).

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