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Clinical Features of Guillain-Barre Syndrome in COVID-19 Patients: Aria and Naft Private Hospitals in Ahvaz, Iran

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ABSTRACT

Given the importance of rapid diagnosis and rejection of multiple possible diagnoses and selection of appropriate treatment for Guillain-Barre syndrome in COVID-19 patients, the present descriptive cross-sectional study investigated the clinical features of Guillain-Barre syndrome in COVID-19 patients. The statistical population of the present study was all Guillain-Barre patients with COVID-19 referred to Aria and Naft private hospitals in Ahvaz in 2020 and 2021. The data collection tool was a researcher-made checklist. Paired t-test and Chi-square test were used to determine the relationship between variables. Data was analyzed using SPSS24 software.

The mean age of patients was 47 years. A high percentage of patients had paresthesia (87.5%) lower limb weakness and upper limb weakness was 75%. After hospitalization, 62.5% (5 patients) received IVIg, 12.5% (one patient) received plasmapheresis, and 25% (2 patients) received physiotherapy. Spinal fluid protein was in the range of 45-110 and cell count was in the normal range. IVIg treatment was 0.4 gr / kg / d for 5 days. Based on the results, it is recommended that IVIg treatment is considered along with other COVID-19 specific therapies. In addition, during the COVID-19 pandemic, an increase in GBS was observed in Khuzestan province, indicating the role of COVID-19 in GBS. It is necessary to hold educational courses to enhance information about this disease and its relevant symptoms and conduct studies with a larger sample of patients with COVID-19 at the national and provincial level.

Keywords: Guillain-barre syndrome, COVID-19, Aria, Naft private hospitals.

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INTRODUCTION

Coronaviruses are a large family of viruses ranging from the common cold virus to those that cause serious diseases, such as SARS, MERS, and Covid-19. New coronavirus (SARS - CoV-2) is primarily associated with non-specific symptoms such as nausea, fatigue and body aches, fever, and dry cough. Patients shortly before the onset of fever may initially have symptoms of nausea and diarrhea or headache or vomiting of blood or might be even asymptomatic. Fever, shortness of breath, dry cough, and radiological findings such as lung glassy opacities are common symptoms of this disease [1, 2]. The major cause of Guillain-Barre syndrome is unknown, but the onset of the disease is seemingly associated with the emergence of antibodies against peripheral nerve myelin. The major clinical manifestation

of Guillain-Barre syndrome is weakness, which occurs symmetrically from several days to two weeks. Proximal muscles as distal muscles are involved, and weakness of respiratory muscles might result in death. Other complaints include paresthesia, numbness, and loss of sensation, pain, and muscle discomfort. In this disease, autonomic dysfunction is common but rarely lasts more than one or two weeks [3]. There is no definitive cure for Guillain-Barre, but there are ways to improve symptoms, most of which include IVIG and plasmapheresis [4, 5]. Guillain-Barre syndrome is an autoimmune disorder characterized by a group of different clinical and pathological findings. It is believed that different infections stimulate the immune system and cause a cross-reaction on nerves and demyelination of the myelin membrane. After eradication of polio, Guillain-Barre syndrome is the most common cause of acute flaccid paralysis at all ages, especially in childhood, [6]. The annual rate of this disease around the world is 1 to 4 percent per thousand people and it is higher in males than females, while some reports suggest its prevalence in males and females. The mechanism of this disease has not been understood completely so far, but the involvement of autoimmune processes in it has been proven. In 75% of cases, before paralysis, a history of viral or microbial disease of the respiratory or gastrointestinal tract is seen [7]. Although various clinical events have been reported before Guillain-Barre, infections, and vaccines have received more attention as potential underlying factors. The prevalence of different types of infections reported before the onset of Guillain-Barre syndrome varies in different geographical and social regions. The most common infection reported in some regions with high latitude and countries with better socio-financial status is infection with Campylobacter jejuni with gastrointestinal symptoms [8, 9]. By recognizing the immunological basis of Guillain-Barre Syndrome (GBS), the use of plasmapheresis, Intravenous Immunoglobulin (IVIG) has become more common. The new classification and the use of the mentioned therapeutic methods have caused several studies to be done on the outcome of a disease based on these classifications and therapeutic methods. Some of these studies suggest that the use of intravenous immunoglobulin improves the prognosis of this disease [10, 11]. Campylobacter jejuni is a gram-negative organism that is a common cause of bacterial diarrhea in developed and developing countries and is known as an infectious agent before the onset of neurological symptoms of Guillain-Barre syndrome. It is thought that due to the molecular similarity of the membrane antigens of this bacterium with peripheral nerve gangliosides, antibodies made against the bacterial membrane antigen cause damage to the peripheral nerves [12, 13]. In addition to causing clinical symptoms, Guillain-Barre syndrome may be mistaken with poliomyelitis and since polio is close to eradication, all cases of acute flaccid paralysis, including Guillain-Barre syndrome, are being carefully examined [14]. Rapid diagnosis and rejection of multiple possible diagnoses and the selection of appropriate treatment methods have high importance. After the eradication of polio, it is the most important cause of acute paralysis in most developing countries [15]. Despite several studies on this issue in different parts of the world, no study has been conducted in Iran, especially in the Khuzestan province. Given what was stated above, the present research was conducted to evaluate the clinical features of Guillain-Barre syndrome in patients with COVID-19 in private Aria and Naft hospitals in Ahvaz.

MATERIALS AND METHODS

This study is descriptive in terms of the type of study and cross-sectional in terms of time. The statistical population of this study included all patients (8 patients) with COVID-19-induced Guillain-Barre referred to Aria and Naft private hospitals in Ahvaz in 2020 and 2021. Due to the limited population (8 people), no sampling was performed. Inclusion criteria of the study included Guillain-Barre diagnostic criteria based on clinical examination, electrodiagnostic study, and spinal fluid, positive RT-PCR test, and lung CT. Exclusion criteria of the study were negative RT-PCR test, lack of lung CT and Guillain-Barre criteria in the clinical examination, electrodiagnostic study, and unwillingness to participate in the study. All GBS patients were evaluated based on international diagnostic criteria according to electro-diagnostic criteria

and clinical signs, including upper limb weakness, lower limb weakness, dysfunction, and inability to walk within one year. Patients' data was collected from their medical records, which included a medical history based on a standard checklist. The validity of the checklist was examined by 3 relevant experts. The reliability of the checklist was obtained at 0.85. Studied variables included gender, age of onset, duration of hospital stay, patient age, clinical symptoms such as early symptoms and neurological findings during the study period, laboratory findings and other medical conditions, specific therapies such as plasmapheresis and intravenous immunoglobulin. All patients' recorded reports were reviewed and the required data were extracted.

During the research, all ethical principles were observed and the necessary permissions were obtained from the Clinical Research Development Unit of Aria private hospital.

Data was described through charts, tables, and numerical indices. Paired t-test and Chi-square test were used to determine the relationship between variables. Data was analyzed in SPSS24 software.

RESULTS AND DISCUSSION

The average age of the patients was 47 years. Most patients were male (75%). Besides, 75% of patients had a history of hospitalization. The highest percentage of patients (87.5%) had paresthesia and lower and upper limb weakness (75%). The lowest percentage was premature fatigue and weakness with 50%. The results of **Table 1** show it is higher in males than females.

Table 1. Frequency Distribution of Demographic Variables Separately for Different Levels of Variables

Variable	Classes	Frequency	%	p-value
Gender	Male	6	75	<0.01
	Female	2	25	
Hospitalization history	Yes	6	75	0.272
	No	2	25	
Paresthesia	Yes	7	87.5	0.122
	No	1	12.5	
Lower limb weakness	Yes	6	75	0.132
	No	2	25	
Upper limb weakness	Yes	6	75	0.354
	No	2	25	
Dizziness and headache	Yes	5	62.5	0.324
	No	3	37.5	
pPremature fatigue and malaise	Yes	4	50	0.875
	No	4	50	

In the present study, based on the information obtained from patients' medical records, after the diagnosis of the disease, drugs were prescribed and measures were taken to improve the disease. **Table 2** shows the treatment measures after hospitalization of patients with COVID-19-induced Guillain-Barre syndrome.

Table 2. Frequency Distribution of Post-hospital Measures in Patients with COVID-19-induced Guillain-Barre

Variable	Classes	Frequency	%	p-value
IVIg	Yes	5	62.5	0.214
	No	3	37.5	
Plasmapheresis	Yes	1	12.5	0.322
	No	7	87.5	
Physiotherapy	Yes	2	75	0.785
	No	6	25	

The results of **Table 2** show that 62.5% (n = 5) of patients received IVIg, 12.5% (n = 1) received plasmapheresis and 25% (n = 2) received physiotherapy after hospitalization. The results

also indicated that the lowest mean age of the plasmapheresis group was 39 years and the highest mean age of the physiotherapy group was 57 years. Moreover, the relationship between age and any of the variables was not significant (P> 0.05). **Table 3** shows the relationship between gender and symptoms at diagnosis time.

Table 3. The Relationship between Gender and Symptoms at Diagnosis Time in the Subjects

Variable	Classes	Gender		X2	p-value
		Female	Male		
Symptoms at diagnosis time	Lower limb weakness	2	6	6.4	0.923
	Upper limb weakness	1	5		
complications after treatment	Lower limb weakness	1	2	1.2	0.323
	The weakness of 4 limbs	1	1		

The relationship between gender and symptoms at diagnosis time and complications after treatment in the subjects were investigated using the chi-square test. The results showed that the symptoms of the disease at diagnosis time and the complications after treatment were not significantly associated with gender (P> 0.05). Based on the observations, out of 8 patients with COVID-19-induced Guillain-Barre, 1 died, 6 underwent lp, and 2 were not satisfied. Spinal fluid protein was in the range of 45-110 and cells were in the normal range. IVIg treatment was 0.4 gr / kg / d for 5 days.

The mean age of patients with COVID-19-induced Guillain-Barre was 47 years. Most patients were male (75%). The highest prevalence of patients was in the age group of 40 to 50 years. In a study conducted by Huda *et al.* on all age groups with Guillain-Barre, 27% of patients were in the age group of 41-50 years [16]. The mean age of Guillain-Barre patients in China was reported to be 46.37 and the highest frequency in this study was seen in people over 60 years of age [17]. Rocha *et al*., in Brazil observed a significant increase in the incidence of this disease between the ages of 15 and 40 years [18]. All three studies are in line with the present study. Unlike the present study, in the study conducted by Barzegar *et al.*, Karalok *et al.*, there was a slight difference between males and females in terms of the prevalence of this disease [19, 20]. Climatic factors and the prevalence of seasonal infections seem to be involved in changing the pattern of disease-related factors in various parts of the world. However, there are worries that vaccination may be one of the underlying causes of Guillain-Barre disease [21]. The present study showed that the highest manifestation of this disease in the onset of the disease was paresthesia with 87.5% and lower limb and upper limb weakness with 75%. In most studies, lower limb weakness has been reported as the most common symptom. In the study conducted by Rahimi Jaberi *et al.* to examine the epidemiology and clinical and laboratory findings of patients with Guillain-Barre in the south of Iran during 2007-2012, the results showed that the highest manifestation of this disease was related to lower limb weakness with 69% [22].

In the study conducted by Fredmal *et al.* to examine the demographic and clinical features of Guillain-Barre syndrome in patients referred to Farshchian Hospital in Hamadan province, the highest manifestation of the disease was related to lower limb weakness (95%) [23]. Paralysis or weakness of the eye muscles (ophthalmoplegia), balance and coordination problems (ataxia), and lack of reflexes were also reported for this disease. People with this disorder can have common signs and symptoms of Guillain-Barre syndrome, including muscle weakness [24]. Fever occurs with the onset of symptoms of muscle weakness is not recognized as a common symptom of Guillain-Barre syndrome, but in the present study and some other studies, slightly less than half of the patients had a fever in the course of their recent disease [25]. The prevalence of fever has been reported in other studies from 3 to 42% [26, 27]. Myalgia or muscle pain has been reported in many studies simultaneously with the onset of disease. In the present study, like the study conducted by Naini *et al.*, this symptom was found in about 20-25% of patients [26].

Results of the present study show that 62.5% (5 patients) received IVIg, 12.5% (1 patient) received plasmapheresis and 25% (2 patients) received physiotherapy after hospitalization. Most patients with COVID-19 (with Guillain-

Barre syndrome) were treated with IVIG. In the study conducted by Chaudhuri, although the efficacy of plasmapheresis therapy was almost similar to that of IVIG, there was not agreement on the combined use of them. Also, the length of hospital stay in plasmapheresis was longer than IVIG and the use of IVIG was more expensive than plasmapheresis [28]. Clinical and laboratory findings of patients with Guillain-Barre disease in the south of Iran showed that there was a difference between the patterns of this disease in Iran and other countries [29]. In one study conducted in the Netherlands and another study conducted in Iran, 7% and 9% of patients, respectively, did not receive specific treatment for mild Guillain-Barre syndrome [30]. The repeated dose of IVIG has also been used in some treatment-resistant cases with or without other drugs and plasmapheresis [31]. Due to the ease of performing plasmapheresis in adults compared to children and the costs of IVIG, the tendency to use plasma replacement techniques in adults is higher in comparison to children, although the effectiveness of this method alone still needs further investigations [32]. Although mortality in this disease can be due to complications of autonomic or infectious system disorders, it is often due to complications of respiratory failure, related treatment measures, and mechanical ventilation. In Iran, deaths of patients with this syndrome have been reported to be about 2.8% to 7.5% and slightly higher than that in developed countries [22, 33]. The present study suffered some limitations. The small size of the statistical population and the unwillingness of patients with COVID-19-induced Guillain-Barre syndrome to participate in the study were among the limitations of this study.

CONCLUSION

According to the results of the research, the prevalence of this disease was higher in males. Thus, it is necessary to pay more attention to the factors affecting the incidence of this disease in males and to effective treatment methods and measures. Based on the results, it is recommended to consider IVIg therapy along with other COVID-19 therapies. In addition, during the COVID-19 pandemic, an increase in GBS was observed in Khuzestan province, indicating the role of COVID-19 in the GBS, and training classes are needed to enhance the level of awareness about this disease and its relevant symptoms. It is also necessary to conduct studies with a larger statistical population of patients with COVID-19 at the national and provincial levels.

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