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EVALUATION OF POST THERAPY FUNCTIONAL STATUS AND RESIDUAL WEAKNESS OF PATIENTS WITH GUILLAIN-BARRE SYNDROME

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ABSTRACT:
Introduction: The annual global incidence of Guillain-Barre Syndrome is approximately 1–2 per 100,000 person-years. Data on Guillain-Barre Syndrome is very rare from Pakistan, we conducted a retrospective study to assess the clinical presentation, and treatment response of these patients.

METHODOLOGY:
A retrospective observational study was conducted at the Neurology Department, Pakistan Institute of Medical Sciences. A total of 45 patients medical record was reviewed and noted. Administrative permission from head of the Department was taken for using the medical record and study was approved by the hospital ethics committee. Diagnosis was made on the basis of clinical signs and symptoms and the specific laboratory investigations i.e. lumbar puncture for CSF investigation, electromyography and nerve conduction study. Data analysis was conducted in SPSS software.

RESULTS:
Mean age was 38.7 years, with majority 40 years. Females were predominant 31 (68.9%). Most of the patients had AIDP 25 (55.6%) and AMAN 14 (31.1%) variants. There were 25 (55.6%) patients with preceding infections i.e. gastrointestinal tract and upper respiratory tract infection. Most patients presented in Autumn 18 (40.0%) and Summer seasons 14 (31.1%). Plasma exchange treatment was done in 37 (82%), whereas 7 (15.8%) were managed by IV Ig treatment. After treatment fatigue 33(73.2%), and pain 25(55.5%) were frequent symptoms. Majority had improved functional status after treatment, However, 6 (13.3%) patients were able to walk only with help and 5 (11.1%) were bedridden. None of them died. The mean disability rating index was 50.1 ± 15.4.
Conclusion: In conclusion, overall, outcome of Guillain-Barre Syndrome patient is favorable, although fatigue and pain remain the common complaints in sequela. It has affected predominantly female population and most patients were below 40 years of age. Almost one fourth cases had no response to therapy and these patients were bedridden or unable to walk without help.

KEYWORDS; Clinical features, Guillain-Barre Syndrome, Immunotherapy, Plasma exchange, Therapy outcome.

INTRODUCTION:

Guillain–Barré syndrome (GBS) is less common, but a fatal, immune- mediated disease of the peripheral nervous system and the nerve roots.[1]The primary etiology is mostly infection triggered.[2] The annual global incidence of GBS is approximately 1–2 per 100,000 person- years. Data suggests that it occurs more frequently in males and there is a gradual increase in incidence with age, however, it can affect any age group.[3]

Clinically the patients with GBS usually have weakness and sensory signs in the legs that progresses to the arms and cranial nerves, although the clinical presentation of the disease is heterogeneous and several distinct clinical variants exist. About 30% GBS leads to intensive care ventilator dependent due to respiratory muscle weakness, with subsequent increase risk of death.[4] The major clinical manifestation is weakness, mainly symmetrical, that evolves with

time. The average period from onset to Nadir of illness is 8 days.[5]

The overall duration of GBS is < 12 weeks in routine and most of the patients are expected to have complete remission in the severity of illness.[6] Approximately mortality occurs in 10% of GBS patients, usually from respiratory failure, cardiac arrhythmia, or pulmonary embolism, and 20% are left with deficits in ambulation or respiration one year later.[7]

In the US, GBS is a significant contributor to new long-term disability for at least 1,000 persons per year and many more elsewhere. Between 25,000 to 50,000, persons are experiencing at least some residual effects from GBS. However, younger patient has better prognosis with relatively less residual sequele.[8]

Though the primary immunotherapy with either plasma exchange (PE) or immunoglobulin (IVIg) is one of the cornerstone of the treatment.[9,10] At current there is no consensus and no approved treatment for debilitating fatigue and motor weakness in GBS patients who have not fully recovered, leading to significantly reduced functional status and quality of life for many.[11,12,13]

Since GBS is rare condition, the evidence on its complications is not commonly generated. A review by Ahmed SI revealed some observations on GBS over the years from Pakistan. The overall incidence ranges between 1.7/100000/population to 3.8/100000/population in the country.[14] The primary aim of this study was to assess the symptoms and Residual weakness and Functional Status of patient post therapy, secondly to determine seasonal variation of GBS.

METHODOLOGY:

This retrospective study was carried out at the Neurology Department, Pakistan Institute of Medical Sciences, Islamabad in a period of 2 years from 1st July 2018 to 30th June 2020 A total of 45 cases of GBS presented during this period whose medical record was available for analysis. Administrative permission from head of the Department was taken for using the medical record and study was approved by the hospital ethics committee.

The diagnosis of GBS was made on the basis of clinical signs and symptoms symmetrical and the specific laboratory investigations i.e. lumbar puncture for CSF investigation to demonstrate cytological-albumin dissociation. The subtypes of GBS was classified on the basis electromyography and nerve conduction study (axonal motor, axonal motor and sensory or demyelinating).

Patient included in this study was 13 to 60 years, with history of less than 4 weeks of progressive, symmetrical weakness with areflexia or hyporeflexia. Weakness supported with cranial nerve involvement or sensory symptoms Patient was recruited during all seasons with or without history of preceding illness. Patient who were less than 13 and above 60 years of age excluded. Patient already diagnosed and taking treatment for neuropathy secondary to metabolic disease (Diabetes, Hypothyroidism, Chronic kidney disease, Vitamin B12 deficient, Toxins) were excluded.

Table 1: Demographic features of study patients (n=45)

	No. of cases	%age
Age (years)		
13 to 20	6	13.3%
21 to 30	16	35.6%
31 to 40	6	13.3%
41 to 50	3	6.6%
51 to 60	8	17.7%
61 or above	6	13.3%
Mean ± SD	38.7 ± 19.1	
Gender		
Male	14	31.1%
Female	31	68.9%

The study information included demographic (age, gender), clinical (variants, preceding infection, type of infection, autonomic dysfunction, ventilator support and seasonal presentation), treatment status (type of treatment, post treatment symptoms, functional status and residual weakness).

The primary outcome was to quantify the clinical presentation of patients with GBS and to see the outcome after treatment. Secondly, the seasonal variation of GBS was also measured.
Data was analyzed in SPSS version 20.0. The categorical variables like clinical presentation, treatment, type of infection and post treatment symptoms were measured as frequency and percentages. The continuous numerical variables like age and disability rating index (residual weakness) were measured as mean and standard deviations.

RESULTS:

There were 45 cases of GBS in this study. The mean age of patients was 38.7 years, majority of them were

below 40 years. Females were predominant, n=31 (68.9%). Most of the patients had AIDP, n=25 (55.6%) and AMAN, n=14 (31.1%) variants. There were 25 (55.6%) patients with preceding infections; gastrointestinal tract and upper respiratory tract infection were the infection types. Three (6.6%) patients each had autonomic dysfunction and required ventilator support.

The presentation of GBS was assessed according to seasonal variation. Most of the patients presented in (September, October, November) Autumn, n=18 (40.0%) and (June, July, August) Summer seasons, n=14 (31.1%). In this study most of the patients were treated using PLEX treatment (5, sessions 200-250 ml of plasma per Kg weight) n=37 (82%), whereas n=7 (15.8%) were managed by IV Ig treatment (0.4mg/Kg in divided doses). (Figure I) and (Figure II)

Majority of patient was falling in HUGES Grade 3-5 in pre-treatment group and at discharge patient improvement after immunotherapy. We evaluated the condition of patients after 3 months interval post therapy. The common symptoms after the treatment were fatigue, n-=33 (73.2%), pain, n=25 (55.5%), depression, n=17 (37.7%) and muscle wasting, n=16 (35.5%). The other frequent symptoms were tremors, dysaesthesia and ataxia. The majority of the patients had improved functional status after the treatment. There were 26 (57.7%) patients with minor sign symptoms (tremor, dysasthesia, and ataxia). Moreover, 8 (17.7%) patients were able to walk 5 meters without help, whereas 6 (13.3%) patients were able to walk five meters only with help and 5 (11.1%) of the patients were bedridden, unable to walk. None of the current study patients died, albeit 3 (6.6%) required mechanical ventilation. The mean disability rating index was 50.1 ± 15.4 and ranging from 30 to 60. (Table 3)

Table 1: Demographic features of study patients (n=45)

	No. of cases	%age
Age (years)		
13 to 20	6	13.3%
21 to 30	16	35.6%
31 to 40	6	13.3%
41 to 50	3	6.6%
51 to 60	8	17.7%
61 or above	6	13.3%
Mean ± SD	38.7 ± 19.1	
Gender		
Male	14	31.1%
Female	31	68.9%

Table 2: Electrophysiological presentation of GBS patients (n=45)

	No. of cases	%age
Variants		
AIDP	25	55.6%
AMAN	14	31.1%
AMSAN	4	8.9%
MFS	1	2.2%
PHARYNGEL-CERVICAL-BULBAR (PCB)	1	2.2%
Preceding infections		
Yes	25	55.6%
No	20	44.4%
Infection type		
GI	15	33.3%
URTI	10	22.2%
Autonomic dysfunction	3	6.6%
Ventilator support	3	6.6%

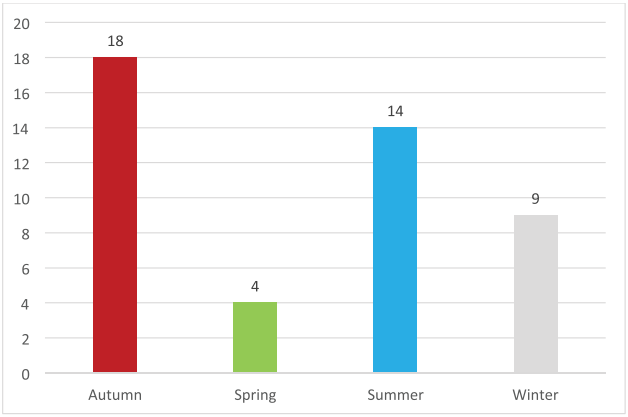

Figure I: Seasonal presentation of GBS in the study (n=45)

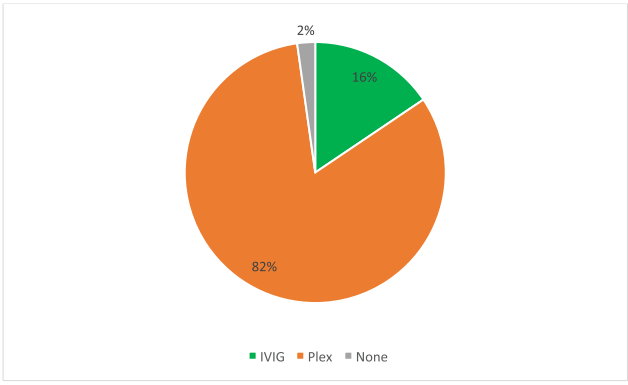

Figure II: Treatment given to patients (n=45)

Table 3: Post treatment status of GBS patients (n=45)

	No. of cases	%age
Post treatment symptoms		
Ataxia	5	11.0%
Depression	17	37.7%
Dyaesthesia	9	20.0%
Fatigue	33	73.3%
Pain	25	55.5%
Tremors	9	20.0%
Wasting	16	35.5%
Functional status of GBS		
No or Minor signs & symptoms, able to run	26	57.7%
Able to walk five meters without help	8	17.7%
Able to walk five meters only with help	6	13.3%
Bedridden; unable to walk	5	11.1%
Needs mechanical ventilation	3	6.6%
Death	0	0.0%
Residual weakness (Disability rating index)		
Mean ± SD	50.1 ± 15.4	
Range	30 - 60	

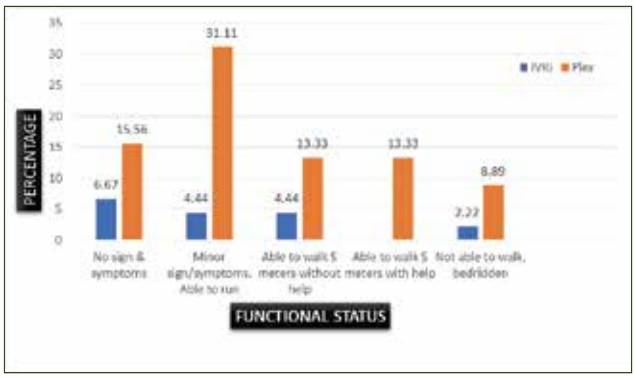

Figure III: Comparison of functional status between treatment modalities (n=45)

DISCUSSION:

The Guillain-Barre syndrome patients in the current study presented with AIDP and AMAN variants and majority having preceding infections like upper respiratory tract infection and gastrointestinal infections. After treatment with intravenous Immunoglobulin and Plasma exchange the majority of patients recovered and were found with minor signs or symptoms and were able to run or walk without help. However, few cases were still bedridden and few others were not able to move without aid. Fatigue and pain were the two most frequent symptoms post therapy. The evidence regarding epidemiology and management of GBS is common but results on sequel is limited. This study was planned keeping in view the local context where scientific base on GBS is limited specially, the outcome of therapies such as IVIG and Plasma exchange.

As witnessed the variants of GBS were AMAN and AMSAN in majority of the current study patients, however, AIDP presented as the most frequent. This fact has been proven by many previous studies as well.[15] AMAN and AMSAN are two frequent variants characterized by an immune system attack mainly focused at the axons rather than Schwann cells and myelin.[16, 17] Ho et al, revealed that patients could be categorized into AIDP (86.3%), AMAN (7.8%), and AMSAN (5.9%) according to electrophysiological findings of GBS.[18]

The findings of the current study are comparable with many previous studies on the topic from different parts of the world. A previous local study by Yaqoob et al reviewed 125 34 cases between 1995 to 2003. The investigators reported that male gender was more likely to have GBS, however, it occurred in all age groups. Before GBS their patients had GI and URTI infections. Moreover, their patients were managed with IVIG and Plasma exchange and no significant difference in the outcome of two treatments was observed.[19] In the present study though we witnessed more females to be affected by GBS, however, age distribution was similar to that of Yaqoob et al study. The preceding infections were also GI and URTI in the current study. Moreover, in the current study we also noticed similar outcome with IVIG and plasma exchange.

Another local study by Wali M and colleagues compared the outcome of Plasmapheresis and Immunoglobulin treatment in GBS patients and reported that there is no difference in the therapeutic effect of both treatment regimens.[20] These findings are similar to our results where we also witnessed that both plasma exchange or IVIG treatment are similar in treating GBS. Other investigators have also witnessed that outcome is good in almost 80-90% patients with Guillain-Barre syndrome (GBS) in terms of motor recovery and functional outcome, [21] However, in the long run about 20% patients still face severe motor disability.[22] This was comparable to the current results as well, it was noticed that around 25% of patients had still poor functional ability in terms of walk with aid only and bedridden state despite being treated for a long period. The patients with severe GBS condition do not fully recover with IVIg or plasma exchange, There is scientific base suggesting that in critical conditions of GBS the

non-responsive patients could be given a second dose of IVIg after a gap and recovery is certain.[23] However, our patient only received treatment from either PLEX or IVIG's. Though immunotherapy could be used in critical conditions, they must be opted taking into consideration the cost factors and the clinical status (staging, complications, and other comorbid conditions) of individual patients.[24]

The current study has many advantages; firstly this was a rare data on GBS patients from a large tertiary care hospital. Secondly, though retrospective in design the study collected detailed information regarding patients clinical course, seasonal variation and management outcome.

The limitations of the study lie in its retrospective observational design, where lack of control and randomization could lead to selection and personal bias. Moreover, a large number of patients were found without response to therapy, how these patients were managed and no data on further intervention was available.

CONCLUSION:

In this study most of the patients presented with AIDP and AMAN variants. More than half had history of preceding infections of URTI and GI. Most of the patients were below 40 years of age and females were predominantly effected by GBS. Majority of cases of GBS were found in autumn season. The patients were managed with IVIg and plasma exchange therapies and most of them responded to it. Fatigue and pain were the most frequent symptoms after therapy. There were almost one fourth cases with no response to therapy and these patients were bedridden or unable to walk without help.

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Iqra Ather; concept, data collection, data analysis, manuscript writing, manuscript review
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Mansoor Iqbal; concept, data collection, data analysis, manuscript writing, manuscript review
Sumaira Nabi; data collection, data analysis, manuscript writing, manuscript review
Mazhar Badshah; concept, data collection, data analysis, manuscript writing, manuscript review
Syeda Rida; data collection, data analysis, manuscript writing, manuscript review