Electrophysiological Pattern and Predictors of Functional Outcome of Patients with Guillain Barre Syndrome at a Tertiary Care Hospital in Pakistan

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ABSTRACT

Objective: To determine electrophysiological pattern and predictors of functional outcomes of patients with Gullain Barre Syndrome (GBS) at a tertiary care hospital.

Study Design: Observational study.

Place and Duration of Study: Shifa International Hospital, Islamabad, Pakistan from January 2016 to July 2020.

Methodology: A total of 62 patients with GBS of all age groups, gender, locations and those with no other primary diagnosis such as poliomyelitis, botulism, hysterical paralysis, toxin neuropathy and diabetic neuropathy were included. Functional outcome using modified Rankin Scale (mRS) and HUGHES score were recorded at presentation, on discharge and 6-month follow-up. Results of this study were analyzed using SPSS version 20.

Results: There were 69% males with mean age of 31 ± 21years. The frequency of different GBS variants were 53% acute inflammatory demyelinating polyneuropathy (AIDP), 29% acute motor axonal neuropathy (AMAN), 11% acute motor and sensory axonal neuropathy (AMSAN) and pure sensory and atypical GBS were 2% each. The frequency of various antecedent events was recorded in 33 patients, including respiratory tract infection in 9 (14%) and diarrhea/vomiting in 13 (21%) patients. AIDP and AMSAN had a good prognosis where 31 (77%) patients out of the 40 fully recovered with HUGHES score 0–2 after 6 months. AMAN had poor prognosis as 2 (12%) patients died in the Hospital. Majority (n=32, 52%) of the patients were treated with plasmapheresis.

Conclusion: In this study population, AIDP was the most common variant with good prognosis and AMAN variant had the worst prognosis.

Key Words: *Guillain Barre syndrome (GBS), Acute inflammatory demyelinating polyneuropathy (AIDP), Acute motor axonal neuropathy (AMAN), Peripheral neuropathy, Lower limb weakness, Acute motor and sensory axonal neuropathy (AMSAN), Sensory neuropathy, Autoimmune disease.*

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INTRODUCTION

Guillain-Barre Syndrome (GBS) is a common source of acute severe immune mediated polyradiculoneuropathy. It has various subtypes including acute inflammatory demyelinating neuropathy (AIDP), acute motor axonal neuropathy (AMAN), acute motor sensory axonal neuropathy (AMSAN), Bickerstaff encephalopathy (atypical GBS) and pure sensory GBS.[1-3]

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The annual prevalence of GBS is 0.4 to 2 cases per 100,000 populations,[1] but it can fluctuate in different populations. For instance, a low rate of 0.40 per 100,000 persons–years was reported in Brazil, as compared to extremely high rate of 2.5 per 100,000 persons–years in Curacao and Bangladesh.[4,5] Variants and antecedent events affect its functional outcome.[1]

The diagnosis is usually clinical and requires the presence of progressive motor weakness of more than one limb and areflexia. The tests which support the diagnosis are nerve conduction studies (NCS) and cerebrospinal fluid (CSF) analysis.[6] Children and young adults are less likely to be affected than the elderly: the risk increases by 20% for every decade of life.[7] Despite medical treatment, it is a severe disease with 3%–10% mortality and inability to walk after six months in 20% cases.[8,9]

Viral infections and campylobacter diarrhea are the usual antecedent events; it can be associated with preceding surgery, inocula-

tions, mycoplasma infections, Hodgkin's disease, lymphoma, or lupus erythematous.[10] Similar results were obtained from one of the studies done by Yakoob *et al.*, who reported 64.7% cases with prior history of infection, of which gastrointestinal infections were the most common (54.6%).[11]

This study was conducted to determine the electrophysiological pattern and predictors of functional outcomes of GBS variants, as well as the effects of antecedent events and different treatments such as plasmapheresis and immunoglobulin (IVIG) on the prognosis of patients.

METHODOLOGY

This descriptive study was conducted from January 2016 till July 2020 with 6-month follow- up data. It was approved from the Institutional Review Board (IRB) of Shifa International Hospital, Islamabad, Pakistan. Attrition bias (lost to follow-up) cases were excluded. Patients' charts were reviewed.

Patients of all age groups and gender diagnosed with GBS using Brighton criteria were included.[12] Patients with diabetic neuropathy, Miller Fisher syndrome and patients having any other cause of flaccid paralysis such as poliomyelitis, botulism and toxin neuropathy were excluded.

The study proforma reflected information on age, gender, symptom, duration before presentation, antecedent events, symptomatic presentation on arrival, nerve conduction study (NCS), CSF findings, treatment methods opted (plasmapheresis or IVIG), Hughes score (Grade 0–6) and mRS (modified Ranking Scale 0–6) were included at admission, discharge, one month and six months follow-up after treatment to assess the functional outcome. Patients with Hughes Grade 0-3 were classified as improved outcome while more than 3 as poor outcomes. Predictors of poor outcome were also taken into account during the study (autonomic dysfunction, neck flexor weakness, ventilator assistance, *etc*.).

Data gathered in the study were subjected to statistical analysis with Statistical Package for Social Sciences (SPSS) version 20. For ease of understanding, categorical variables were summarized as counts (percentage) and continuous variables as means or medians. Bivariate analysis of the data was done using the Chi-square test. A two-tailed probability value of <0.05 was considered significant.

RESULTS

The mean age of the 62 patients included in the study was 31 ± 21years ranging from <1– 70 years. Most of the patients 38 (61%) were <40 years of age with 20 (53%) in the pediatric age group of 0-18 years; only 8 patients of older age group of 61-80 years. Male majority 42 (68%) was seen with male-to-female ratio of 2:1. Out of 62 patients, 32 (52%) patients belonged to Punjab, 10 (16%) to Khyber Pakhtunkhwa and 8 (13%) to Islamabad. Patients from other areas included 4 (7%) each from Azad Jammu Kashmir and Afghanistan and 1 (2%), from Gilgit-Baltistan. Antecedent events were recorded in 33 patients mostly 1–2 weeks before the onset of GBS. The most common antecedent events recorded were diarrhea/vomiting 13/62 (21%) followed by respiratory tract and other infections including measles, meningitis, typhoid, pyrexia of unknown origin 9/62 (14.5% each). Two patients underwent surgery for atrial septal defect and sleeve gastrectomy.

Most of the patients 44 (71%) presented within one week of the onset of symptoms and 17 (27%) came within 2–3 weeks. Of the total, 58 (93%) patients came with symmetric limb weakness with 56 (90%) having areflexia, 3 (5%) with asymmetrical limb weakness, and 2 (3%) with nonspecific symptoms of irritability and unresponsiveness that was diagnosed as Bickerstaff encephalopathy (atypical GBS). Pure motor weakness seen in 44 (71%), respiratory illness in 14 (22%) and cranial nerve involvement in 16 (26%). Only two patients had numbness of both limbs diagnosed as pure sensory variant of GBS. Table I summaries the clinical manifestations of the main subtypes of GBS (AIDP and Axonal Variant). Some patients developed autonomic and respiratory manifestations during their illness. Lumbar puncture was done in 42 patients, out of which 27 (64%) had CSF cytoalbuminological dissociation according to Brighton criteria. Out of 27, 8 (30%) had CSF proteins more than 100mg/dl. According to the nerve conduction study, different variants were found to be 33 (53%) AIDP variant, 18 (29%) AMAN variant, 7 (11%) AMSAN, variant, while 1 (2%) each had pure sensory and Bickerstaff encephalopathy (atypical GBS). Two patients had no NCS changes.

Table I: Clinical features in 2 broad subcategories of GBS (demyelinating and axonal variants).

Clinical features	Demyelinating variant n=33	Axonal variant (AMAN and AMSAN) n=25	p-value
Motor weakness	(33; 100%)	(24; 96%)	.44
Sensory disturbances	(4; 14.2%)	(5; 18%)	.450
Bulbar weakness	(3:10.7)	(6; 18%)	.13
Facial weakness	(5; 15%)	(4; 15%)	1
Autonomic dysfunction	(2;6%)	(3; 4%)	0.6
Respiratory distress	(6; 18%)	(6; 23%)	0.74
Neck Flexor weakness	(2; 6%)	(2; 8%)	1
The result is not significant at p <0.05.			

In this study, most of the patients 32 (52%) received plasmapheresis while 20 (32%) received IVIg. Only two (3.2%) patients received IVIg post-plasmapheresis, while 8 (13%) of the patients did not receive any treatment. No statistical significance ($p>0.05$) was found in the outcome of patients in the two treatment groups. There was no significant difference in the need for assisted ventilation in the two groups. Out of total patients, 87% were admitted with mRS Score >3, while 85% patients improved within six months' follow-up with mRS grade ≤3. Three (5%) patients died. Both Hughes and mRS GBS disability scores depicted the same ratios as shown in Table II. A statistically significant relationship ($p=0.003$) was seen between patients with mechanical ventilation and poor prognosis compared to the group with no respiratory failure.

Table II: GBS disability scores (HUGHES and mRS) at arrival and at 6 months' follow-up.

HUGHES disability score		
Hughes Grading Scale	**At arrival n = 62**	**At 6 months follow-up n=62**
No signs and symptoms (Grade 0)	0	17 (27%)
Minor Signs and symptoms, able to run (Grade 1)	0	15 (24%)
Able to walk 5 meters, Independently (Grade 2)	5 (8%)	17 (27%)
Able to walk 5 meters with a walker/support (Grade 3)	10 (16%)	8 (13%)
Bed or chair bound (Grade 4)	42 (66%)	2 (3.2%)
Requiring Assisted Ventilation (Grade 5)	5 (8%)	0
Death	0	3 (5%)
mRS Grading Scale		
No signs and symptoms (Grade 0)	0	18 (29%)
No significant disability despite symptoms (Grade 1)	0	17 (27%)
Unable to carry out all previous activities but able to walk without support (Grade 2)	3 (5%)	12 (19%)
Moderate disability, requiring some help but able to walk without support (Grade 3)	5 (8%)	6 (10%)
Moderately Severe disability, need assistance for their own body needs (Grade 4)	37 (60%)	6 (10%)
Severe disability, bed ridden (Grade 5)	17 (27%)	0
Death (Grade 6)	0	3 (5%)
Missing	0	0
Total	62	62

Outcome of patients among GBS variants is shown in Figure 1. Most of the patients treated with either plasmapheresis or IVIG improved with one death reported in each plasmapheresis and IVIG group. There was no statistical significance in mean improvement of the two. The recurrence rate was 3.5%, two patients with AIDP and one with AMAN that had recurrence within 2 years of previous attack.

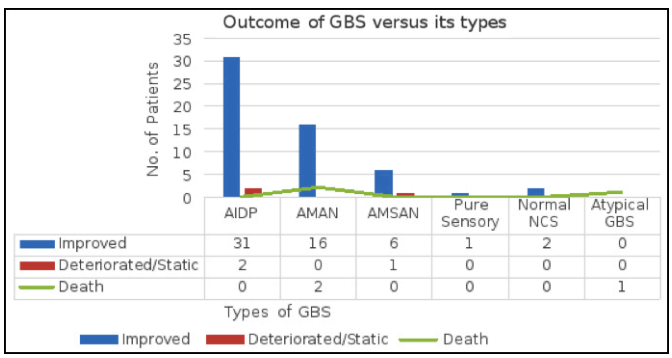

Figure 1: Types of GBS and their outcome.

DISCUSSION

In this study of 62 patients, male to female ratio was 2:1 with male majority as shown by many studies.[4,7,11,13] The mean age was 31 ± 21 years comparable to most of the other studies done in Western and Asian countries. [4,13,14] The incidence of GBS increases with age as shown by Van Doorn.[8] However, in this study, the majority 38 (61%) of the patients were younger than 40 years, among which 20 (53%) were in the pediatric age group. Similar patterns were also observed by Lyu *et al* and Bhagat *et al*.[15,16]

Symmetrical limb weakness was the most common sign in patients of this study (98%) like other studies, [9,11,13,14] followed by respiratory distress 14 (22%) out of which 8 (57%) required invasive ventilation. Willison described respiratory failure as the most severe, generalized manifestation of GBS accounting for 20%-30% of cases, similar to this study.[17]

This study showed autonomic nervous system (ANS) dysfunction in 6 (9%) of patients like the incidence reported by others.[14,18,19] It was manifested in the form of blood pressure instability, sinus tachycardia and pupillary or sweating abnormality.

Neurological deficits included sensory loss and cranial nerve involvement as facial palsy and bulbar palsy in 16% each, with neck flexor weakness in 6.45%. Sensory dysfunction in this study showed the same results as done by Meganathan *et al*.,[19] however studies by Sandhya *et al.,* and Areeyapinan *et al*. showed 75%-80% sensory dysfunction.[13,14] A significant relationship was found between facial and bulbar palsy with the need of mechanical ventilation with similar results shown by Hughes.[20]

AIDP was the most common variant found in this study 33 (53%) comparable to other studies done in Asian countries that have similar prevalence.[11,13,14] However, meta-analysis from Europe and United States showed 60%-80% of people with GBS had demyelinating subtype (AIDP). Similarly, in Western studies prevalence of axonal variants *i.e*., AMAN and AMSAN, is only 6%-7%,[9] which is in marked contrast to this study, which showed a much higher prevalence (40%). It is comparable with other Asian studies as well.[9,10,13,21]

Functional outcome and mortality is affected by the variant of GBS. The mortality rate in this study was 5%, which is comparable to other studies by Bhagat *et al*.[16] A study by Akbayram, showed increased morbidity and mortality in

axonal variant.[21] Similarly, this study showed increased mortality and morbidity in axonal variant.

According to Hughes grading disability score, 47 (76%) patients presented in this study had grade 4 or 5 *i.e.* severe disability needing assistance or mechanical ventilation at admission. At 6 months' follow-up 57 (96%) patients showed remarkable improvement and walked independently similar to study by Manorenj *et al.*[13]

The mean length of stay was 11.2 days and median was 8.5 days, 56 days being the longest stay observed in AMAN. Prolonged length of stay *i.e.*, more than 10 days were observed in 22 (35%) patients, comparable to previous studies.[13] Out of the total number of patients, 10 (30%) of AIDP, 3 (43%) of AMSAN and 7 (39%) of AMAN had prolonged stay. The most common reason for prolonged stay was bulbar involvement or respiratory distress present in 50% of these patients.[22]

Most of the patients 32 (52%) in this study were treated with plasmapheresis, which is comparable to other local studies done by Yakoob *et al.*[11] Although one of the RCTs done by Asghar *et al*. on plasmapheresis *versus* IVIg showed significant improvement in mean disability score at four weeks in patients treated with IVIg ($p<0.05$) as compared to the plasmapheresis group.[6] However, in the present study, the mean improvement was comparable between the two groups and results were insignificant ($p >0.05$). Studies showed that intravenous immunoglobulin (IVIg) and plasma exchange are both effective treatments in GBS, IVIg is the preferred treatment only for practical reasons.[8,20] However, supportive care is still the most important component of management.[20]

There is a strong need of multicenter prospective study with extensive inclusion of patients to further evaluate functional outcomes of GBS and its associated complications, co-morbidities and treatment patterns.

As the study was collected from retrospective chart review patients and attendants' memory, recall bias and data gaps are likely. It is a single, private center study that limits the selection of patients and generalization of results.

CONCLUSION

Guillain-Barré syndrome is a rare autoimmune disease of the peripheral nervous system with considerable mortality and morbidity. AIDP is the most common variant of GBS found in this study. However, there is high prevalence of axonal variant (40%) as compared to Western (6%-7%) population. AMAN had a significantly worse prognosis as compared to AIDP. Most patients (85%) had good outcome. Most of the patients were treated with plasmapheresis, although there was no significant difference in the mean improvement of both AMAN and AIDP.

ETHICAL APPROVAL:

The study was approved from the Institutional Review Board (IRB) of Shifa International Hospital, Islamabad, Pakistan prior to the initiation of research work, collection of data, Ref No. 068-558-2019, which is in accordance of ICH and GCP guidelines.

PATIENTS' CONSENT:

As this is a retrospective observational study, no patients' consent is required

CONFLICT OF INTEREST:

The authors declared no conflict of interest.

AUTHORS' CONTRIBUTION:

MS: Concept and design, data analysis, manuscript writing, manuscript review and editing.
SM: Concept and technical design, respondent coordination and data collection, data editing and analysis, manuscript writing, manuscript review and editing.
HY: Data collection, data analysis, manuscript editing, and manuscript review.
FM: Data collection, data analysis, and manuscript review.

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