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OUTCOME OF PLEX IN GUILLAIN–BARRÉ SYNDROME PATIENTS TREATED BEFORE AND AFTER 7 DAYS OF SYMPTOMS ONSET

Original Research

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Conflict of Interest: None
Grant Support & Financial Support: None

ABSTRACT

Background: Guillain-Barré Syndrome (GBS) is an acute, immune-mediated polyneuropathy that often follows infections, characterized by varying degrees of motor weakness, sensory impairment, and autonomic dysfunction. The disease has multiple subtypes, including Acute Inflammatory Demyelinating Polyradiculoneuropathy (AIDP) and Acute Motor Axonal Neuropathy (AMAN), with diverse functional outcomes. Plasma exchange (PLEX) has emerged as a cost-effective and efficient therapeutic option in resource-limited settings, but its impact on various subtypes and functional outcomes requires further exploration.

Objective: To evaluate the effectiveness of plasma exchange (PLEX) as a treatment for GBS and to prospectively analyze the clinical and functional outcomes of patients aged 16 and above across different subtypes of GBS.

Methods: This prospective observational study was conducted over six months at a tertiary care hospital in Rawalpindi. Participants aged 16 and older, meeting inclusion criteria, underwent detailed history taking, clinical examination, and electrophysiological studies, including Forced Vital Capacity (FVC) and EMG, to categorize GBS subtypes. Functional disability was assessed using the Hughes GBS Disability Scale. All patients received five sessions of PLEX initiated on the day of admission. Outcomes were evaluated on the seventh day. Data analysis was performed using SPSS, with quantitative variables presented as means and qualitative variables as percentages.

Results: A total of 40 participants were included, with a mean age of 38.97 ± 5.4 years. Males constituted 63% (n = 25) and females 37% (n = 15). Participants were categorized by Hughes GBS Disability Score into Group 1 (n = 5, Score 2), Group 2 (n = 12, Score 3), Group 3 (n = 20, Score 4), and Group 4 (n = 3, Score 5). Based on EMG findings, 57.5% (n = 23) had AIDP, 30% (n = 12) had AMAN, and 12.5% (n = 5) had AMSAN. After seven days of treatment, 80% of patients in Groups 1 and 2 showed significant improvement, while 75% in Group 3 and 33% in Group 4 demonstrated partial recovery. AIDP had the best response to PLEX, with 24 patients showing improvement, compared to 1 patient with AMAN and 2 with AMSAN.

Conclusion: Patients with GBS exhibit varying functional disabilities and outcomes across different subtypes. PLEX demonstrated significant improvement, particularly in patients with lower initial disability scores and the AIDP subtype. Early intervention and subtype-specific management are critical for optimizing outcomes.

Keywords: AIDP, Electromyography, Guillain-Barre Syndrome, Hughes Disability Scale, Plasmapheresis, Plasma Exchange Therapy, Polyneuropathy

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INTRODUCTION

Guillain-Barre Syndrome (GBS) is an acquired inflammatory disorder affecting the peripheral nervous system. Also referred to as post-infectious polyneuropathy or severe unexplained polyneuritis, it manifests as a critical neurological condition that can impair vital functions such as breathing and sensory perception. Clinical features of GBS encompass a spectrum of symptoms, including gait disturbance, muscular weakness, pain, areflexia with distal predominance, rapidly ascending symmetric flaccid muscle paralysis, variable autonomic involvement, sensory disturbances, and elevated cerebrospinal fluid protein levels without pleocytosis (1). The lifetime risk of developing GBS is estimated at approximately 1 in 1,000 individuals (2). The condition is classified into distinct subtypes based on clinical presentations and electrodiagnostic parameters (3). In Pakistan, GBS is recognized as the leading cause of acute flaccid paralysis, a neurological emergency that can affect individuals across all age groups, including infants, though it is observed more frequently in men. Typically, GBS follows preceding central nervous system symptoms occurring a few days to weeks earlier, often triggered by generic illnesses or precipitating factors such as surgical interventions, trauma, or immunizations. Younger individuals generally have better prognostic outcomes (4). Key factors influencing prognosis include patient age, the progression of the disease, and the requirement for mechanical ventilation. While most studies examining these variables are retrospective in nature (5, 6), only a limited number have employed prospective methodologies.

Subtypes such as Acute Inflammatory Demyelinating Polyneuropathy (AIDP) and Acute Motor Axonal Neuropathy (AMAN) present with nearly equal frequency in Pakistan, with AMAN being more prevalent among younger individuals (7). Globally, however, AIDP remains the most common subtype, characterized by immune-mediated myelin destruction in peripheral nerves. In contrast, AMAN involves reduced compound muscle action potential (CMAP) without evidence of demyelination on electrophysiological testing (8). Assessment of therapeutic interventions in GBS has traditionally relied on evaluating the functional abilities of patients during and after treatment. However, functional capacity is not routinely utilized as a predictive marker for determining the necessity of intensive care unit (ICU) admission or hospital stay duration (2, 9). The long-term functional consequences of GBS remain inadequately understood. Addressing this gap, the current study prospectively evaluates the clinical and functional outcomes of individuals aged 16 and above with various GBS subtypes, with a particular focus on plasma exchange as a therapeutic modality.

METHODS

After obtaining ethical approval from the institutional review board, this prospective study was conducted at a tertiary care hospital in Rawalpindi from January 2023 to June 2023. The inclusion criteria encompassed patients aged above 16 years, of either gender, diagnosed with Guillain-Barre Syndrome (GBS) variants, including Miller Fisher Syndrome (MFS). Exclusion criteria included individuals below 16 years of age, patients with hypokalemic periodic paralysis, those with known allergies, individuals undergoing steroid therapy, those with selective IgA deficiency, and patients with severe concurrent conditions such as heart failure with reduced ejection fraction (HFrEF).

Detailed patient histories were taken, including the onset, duration, and progression of symptoms. Additional data were gathered on predisposing factors, such as fever, diarrhea, upper respiratory infections, recent immunizations, diabetes, or other comorbidities. Comprehensive clinical evaluations of pulmonary, circulatory, and neurological systems were conducted alongside the measurement of vital signs, oxygen saturation levels, and single-breath count. Signs indicative of respiratory failure, such as paradoxical abdominal movements, auxiliary muscle use, severe tachypnea, and the inability to speak in full sentences, were meticulously documented. Regular assessments of negative inspiratory force, forced vital capacity, and maximal expiratory pressure were also performed to supplement clinical observations. All participants underwent electrophysiological studies and complete blood counts. In some cases, spinal magnetic resonance imaging (MRI) and additional tests, including antinuclear antibodies and antiganglioside antibody panels, were performed. Based on the Modified Rajabally electrophysiological classification (10, 11), patients were categorized into three subtypes: Acute Inflammatory Demyelinating Polyneuropathy (AIDP), Acute Motor Axonal Neuropathy (AMAN), and Acute Motor and Sensory Axonal Neuropathy (AMSAN). Functional impairment was assessed using the Hughes GBS Disability Scale (12).

The study recruited 40 patients, with a male predominance of 63% (25 patients) and 37% females (15 patients). Patients were grouped based on the Hughes GBS Disability Score: Group 1 consisted of 5 patients (Score 2), Group 2 included 12 patients (Score 3), Group 3 comprised 20 patients (Score 4), and Group 4 included 3 patients (Score 5). Additionally, three groups were formed according to electromyographic (EMG) findings, with 57.5% (23 patients) classified as AIDP, 30% (12 patients) as AMAN, and 12.5% (5 patients) as AMSAN. All patients underwent five sessions of plasmapheresis (PLEX), initiated on the day of admission. Clinical evaluations were conducted on the seventh day to monitor improvement. Quantitative variables were reported as means, while qualitative variables were presented as percentages. Statistical significance between groups was determined using chi-square and t-tests. All analyses were performed using SPSS version 26.

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RESULTS

A total of 40 participants meeting the inclusion criteria were enrolled in this study. The mean age of the participants was 38.97 ± 5.4 years, with a male predominance observed, as 63% (25 participants) were male and 37% (15 participants) were female. Antecedent events were reported in 67% (27 participants), with diarrhea being the most frequently observed symptom. Preceding infections were noted in 65% of the cases. Patients were classified into groups based on the Hughes GBS Disability Score and electrophysiological subtypes to analyze clinical and functional outcomes.

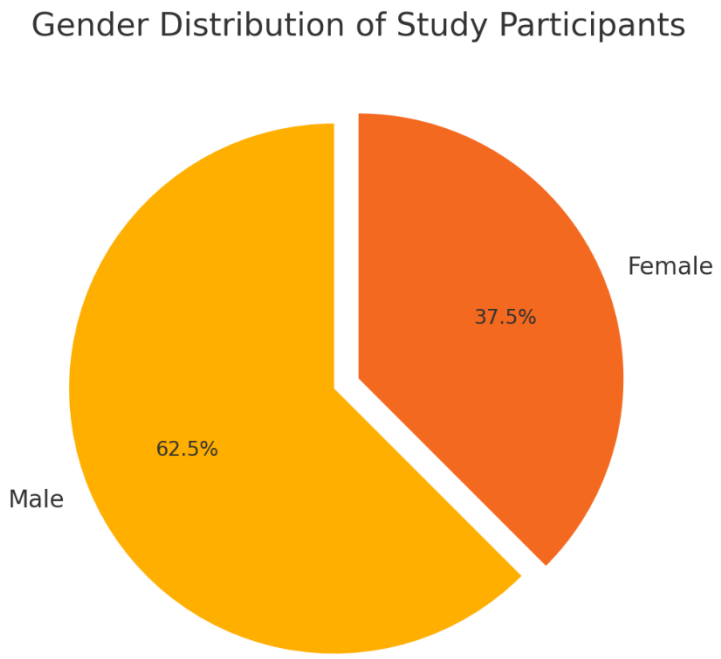

Table 1.1 (Gender)

Male	**25 (63%)**
Female	15 (37%)

Table 1.2a (Patients group according to Hughes Score)

Sr No.	No. of patients	Hughes Score
Group 1	05	02
Group 2	12	03
Group 3	20	04
Group 4	03	05

Table 1.2b (Subtype according to EMG)

Sr No.	No. of patients	Subtype
1	23	AIDP
2	12	AMAN
3	05	AMSAN

Among the Hughes score-based groups, Group 1 included 5 patients with a Hughes score of 2, Group 2 had 12 patients with a score of 3, Group 3 included 20 patients with a score of 4, and Group 4 consisted of 3 patients with a score of 5. Electrophysiological subtyping revealed that 57.5% (23 participants) had acute inflammatory demyelinating polyradiculoneuropathy (AIDP), 30% (12 participants) had acute motor axonal neuropathy (AMAN), and 12.5% (5 participants) had acute motor-sensory axonal neuropathy (AMSAN). On the

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seventh day of assessment following plasmapheresis, 80% of patients in Group 1 showed improvement, with 4 participants achieving a Hughes score of 1. In Group 2, 75% (9 patients) exhibited significant recovery, with 5 patients improving to a Hughes score of 2 and 4 achieving a score of 1. In Group 3, 15 patients showed betterment of symptoms, with 5 improving to a score of 2 and 10 improving to a score of 3. No patients in Group 3 reached a Hughes score of 1. In Group 4, only one patient demonstrated recovery, with a Hughes score improvement to 4, suggesting that additional therapeutic strategies beyond plasmapheresis might be necessary for severe cases.

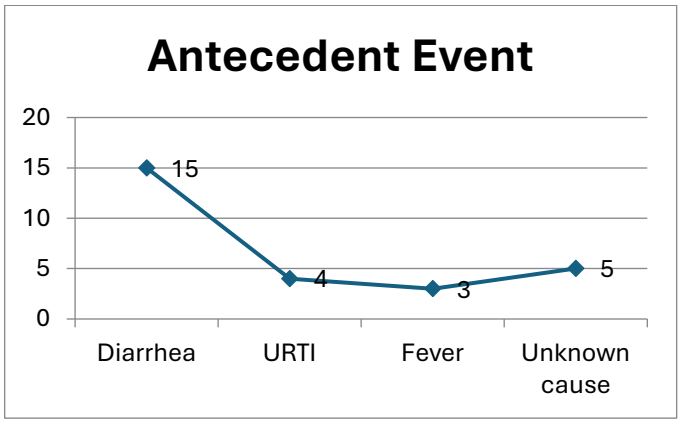


Chart 1: Antecedent events in patients with GBS

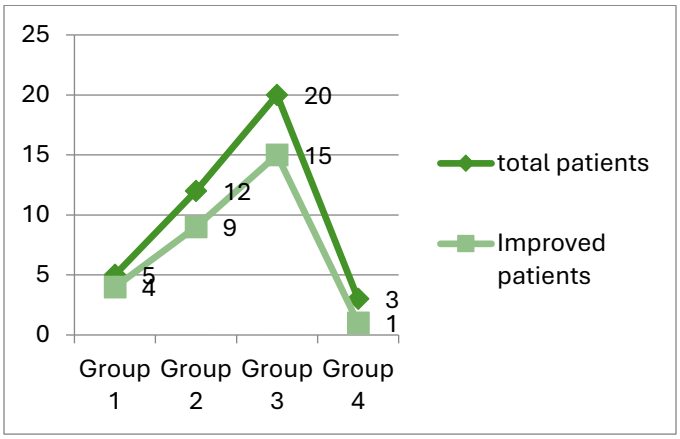


Chart 2: Trends in Clinical Improvement

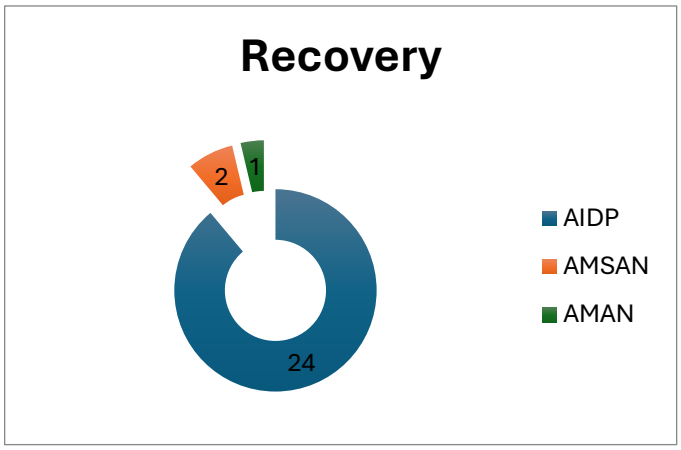
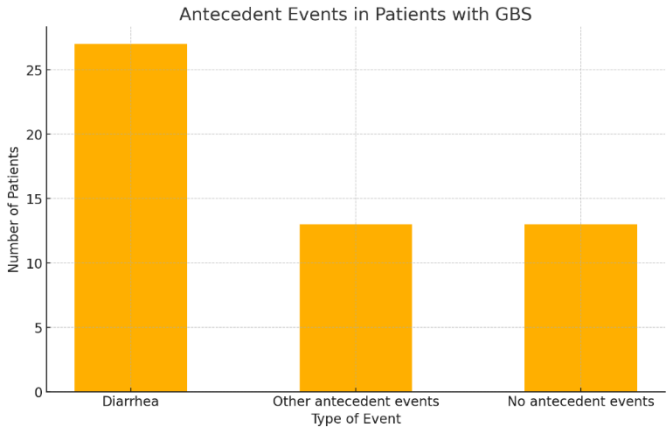


Chart 3: Improvement Trend in Subtypes



Subgroup analysis based on electrophysiological subtypes indicated that patients with AIDP exhibited better outcomes, with 24 participants demonstrating improvement. In contrast, only 1 participant in the AMAN group and 2 in the AMSAN group showed clinical recovery. Functional improvement was notably poorer in patients with axonal variants compared to those with demyelinating types. Cranial nerve involvement was observed in 40% of participants, with the facial nerve being the most frequently affected (60% of cases). Patients with cranial nerve involvement demonstrated a significantly lower mean change in Hughes score (0.11 ± 0.02) compared to those without cranial nerve involvement (0.41 ± 0.06; p = 0.000). Sensory symptoms, including tingling and paralysis, were reported in 50% of patients, while 5% exhibited autonomic dysfunctions, such as bradycardia and positional hypotension. Cerebrospinal fluid (CSF) analysis revealed elevated protein levels in 75% (30 participants), normal CSF in 15% (6 participants), and pleocytosis in 10% (4 participants). These findings underscore the variability in clinical and diagnostic presentations across the study population.

DISCUSSION

Guillain-Barre Syndrome (GBS) is a rare but serious post-infectious immune-mediated neuropathy characterized by inflammatory damage to the peripheral nervous system. It presents with a range of symptoms, including numbness, weakness, paralysis, and sensory disturbances (13). The mean age of onset has been reported as 42.8 years (14), although cases have been documented across all age groups. Consistent with earlier research, the present study identified a male predominance with a ratio of 1.6:1, and 63% of participants were male (15, 16). Antecedent infections were observed in 67% of patients, with diarrhea being the most frequently reported symptom. These findings align with prior studies associating GBS with infections such as Campylobacter jejuni, cytomegalovirus, Epstein-Barr virus, and influenza, typically occurring within two weeks of symptom onset. The study population predominantly presented with the

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classic form of GBS (88%), while atypical variants accounted for 12%, including cases of paraparetic variation and distal paresthesia with bifacial paralysis. This distribution mirrors findings by Bogliun et al. (17). Cranial nerve involvement was noted in 40% of participants, with the facial nerve being the most commonly affected, consistent with reports by Bhargava et al. (15) and Dhadke et al. (18). Patients with cranial nerve involvement exhibited poorer functional improvement, as evidenced by a lower mean change in Hughes scores compared to those without cranial nerve involvement ($p = 0.000$).

Electrophysiological classification revealed that the demyelinating variant (AIDP) was the most common subtype (57.5%), followed by axonal neuropathy (30%) and AMSAN (12.5%). These findings align with previous studies indicating a higher prevalence of AIDP in Western populations (15, 16). However, patients with axonal variants showed significantly poorer functional outcomes compared to those with AIDP. Sensory symptoms, including tingling and paralysis, were reported in 50% of participants, while 5% exhibited autonomic dysfunctions such as bradycardia and positional hypotension. Cerebrospinal fluid (CSF) analysis demonstrated elevated protein levels in 75% of patients, consistent with prior studies reporting albuminocytological dissociation in GBS (15, 17). While pleocytosis was observed in 10% of patients, it remains an atypical finding in GBS and warrants consideration of alternative diagnoses such as viral, lymphomatous, or carcinomatous polyradiculoneuropathies (20). The early detection of elevated CSF protein, often within the first two weeks, underscores its utility in supporting a diagnosis of GBS.

In this study, plasmapheresis (PLEX) was administered to all patients, with five sessions initiated on the day of admission. Significant improvement was observed across most Hughes score groups after seven days, particularly in those with milder initial disability scores. Patients with AIDP exhibited the most pronounced functional recovery following PLEX. These findings are supported by a Cochrane review from 2012, which highlighted the efficacy of PLEX when initiated within the first week of symptom onset (21). Comparisons with trials by Farkkila et al. (1987), McKhann et al. (1985), and Raphael et al. (1987) further reinforce the observed benefits of early PLEX intervention. The cost-effectiveness of PLEX also makes it a preferred treatment option in resource-limited settings, as noted by Chaudhari et al. (15). The study's strengths include its prospective design and the comprehensive evaluation of clinical and functional outcomes in a resource-constrained setting. However, several limitations must be acknowledged. The small sample size and single-center design limit the generalizability of the findings. The exclusive use of PLEX without comparison to intravenous immunoglobulin (IVIG) restricts the scope of therapeutic insights. Additionally, the short follow-up duration of seven days precludes an understanding of long-term outcomes. A larger, multicenter study with extended follow-up and direct comparisons between PLEX and IVIG is warranted to validate these results and provide broader clinical recommendations. The findings of this study contribute to the growing body of evidence supporting the early use of PLEX in managing GBS, particularly in patients with AIDP. However, further research is essential to explore therapeutic strategies for severe cases and axonal subtypes, which remain associated with poorer prognoses.

CONCLUSION

Patients presenting with Guillain-Barre Syndrome (GBS) who exhibit early respiratory or facial nerve involvement are at a heightened risk of severe complications, necessitating prompt admission to intensive care. Among the subtypes studied, the axonal variants were associated with the poorest clinical outcomes, while the demyelinating variant demonstrated a more favorable prognosis. Early recognition of critical signs, accurate classification of GBS subtypes, and timely initiation of treatment, particularly plasmapheresis (PLEX), were crucial in improving outcomes, especially in patients with lower initial disability. Antecedent events and elevated cerebrospinal fluid (CSF) protein levels were prominent findings, further emphasizing the diagnostic and therapeutic relevance of these factors. Plasmapheresis emerged as a cost-effective and widely accessible treatment option, demonstrating significant functional improvement and reinforcing its role in resource-limited settings.

Author	Contribution
Jamshaid Iqbal	Conceptualization, Methodology, Formal Analysis, Writing - Original Draft, Validation, Supervision
Abdul Hameed Khan	Methodology, Investigation, Data Curation, Writing - Review & Editing
Sarah Azam	Investigation, Data Curation, Formal Analysis, Software
Sidra Fazal	Software, Validation, Writing - Original Draft
Muhammad Waleed Ahmed	Formal Analysis, Writing - Review & Editing
Muhammad Raza	Writing - Review & Editing, Assistance with Data Curation
Muhammad Farrukh Habib	Writing - Review & Editing, Assistance with Data Curation

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