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Clinical and electrophysiological study of Guillain-Barre' syndrome with reference to prognosis-A hospital-based study

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Abstract: Introduction: Guillain-Barre Syndrome (GBS) is an acute and often severe polyradiculoneuropathy caused by autoantibody-mediated destruction of the myelin sheath, which presents with ascending paralysis and areflexia. The mortality rate of GBS is less than 5%. We conducted a study in our hospital to identify the epidemiological features, clinical profile, and electrophysiological features of GBS and to determine the various GBS variants present in the studied population. We also aimed to correlate the prognosis of GBS with age, critical time period, and requirements for ventilatory support.
Methods: We conducted a cross-sectional analytical study of 32 adult patients (age > 20 years) meeting the criteria for GBS after a detailed study and 3-month follow-up.
Results: GBS occurred in 71.87% males, mostly in those over 50 years of age. Antecedent events were present in 65.26% of patients, with respiratory tract infections being the most common (43.75%). The most common initial motor symptom was distal weakness (28.12%) with ascending progression. The most commonly involved cranial nerve was the facial nerve (49.99%). Twenty-two patients (68.65%) had a disability grade of 3 at peak. Ten patients developed respiratory weakness, with acute motor axonal neuropathy (AMAN), acute motor and sensory axonal neuropathy (AMSAN), and acute inflammatory demyelinating polyneuropathy (AIDP) cases being 4 (40%), 3 (30%), and 2 (20%), respectively. Postural hypotension was the most common autonomic dysfunction (12.5%). AIDP (71.87%) was the most common variant, and aspiration pneumonia (18.75%) was the most common complication in patients requiring mechanical ventilation (60% of ventilator-assisted patients developed aspiration pneumonia), while urinary tract infection (UTI) (3 cases, 9.37%) was the most common complication in non-ventilator-associated patients. Intravenous immunoglobulin (IVIG) was found to be beneficial, with a 72% recovery rate.
Conclusion: GBS is a disease that primarily affects adult males, with a rapid onset to peak, prolonged duration at peak, need for assisted ventilation, and axonal pattern being poor prognostic factors.

Keywords: G.B.S.; Polyradiculoneuropathy; Autoimmune disorder; Respiratory tract infections; IVIG treatment.

1. Introduction

Guillain-Barre Syndrome (GBS) is an acute, frequently severe, and fulminant polyradiculoneuropathy that is autoimmune in nature [1]. In GBS, autoantibodies are directed against non-self antigens, such as infectious agents or vaccines, which are misdirected to host nerve tissue, affecting peripheral nerves and occasionally cranial nerves through epitope resemblance. The basic pathophysiology is due to an attack on the Schwann cell surface, leading to widespread demyelination or an attack on motor nodes of Ranvier, leading to axonal damage [2]. The autoimmune attack is both cell-mediated and humoral immune mechanisms.

GBS manifests as a rapidly evolving, ascending motor paralysis with areflexia, with or without sensory disturbances [3]. Weakness typically involves hours to a few days and is frequently accompanied by tingling

dysesthesia in the extremities. The legs are usually more affected than the arms, and facial diparesis is present in 50% of affected individuals. The lower cranial nerves are also frequently involved, causing bulbar weakness. Pain in the neck, shoulder, back, or diffusely over the spine is also common in the early stages of GBS, occurring in 50% of patients. Fever and constitutional symptoms are absent at the onset, and if present, cast doubt on the diagnosis. Deep tendon reflexes disappear within the first few days of onset. Cutaneous sensory deficits are usually relatively mild, but functions subserved by large sensory fibers, such as deep tendon reflexes and proprioception, are more severely affected. Bladder dysfunction may occur in severe cases, but if it is a prominent feature and comes early in the course of the disease, diagnostic possibilities other than GBS should be considered. Autonomic involvement is common and may occur even in patients whose GBS is otherwise mild. These features require close monitoring and management as they can sometimes be fatal. Pain is another common feature of GBS, which may be a deep aching pain or dysthetic pain in the extremities. The pain is centimeter and often responds to standard analgesics.

Several types of GBS are recognized, primarily by electrodiagnostic and pathologic distinctions. The most common variant is Acute Inflammatory Demyelinating Polyneuropathy (AIDP). Additionally, there are two axonal variants, which are often clinically severe: Acute Motor Axonal Neuropathy (AMAN) and Acute Motor Sensory Axonal Neuropathy (AMSAN). One of the current variants is Miller Fisher syndrome (MFS), which presents as rapidly evolving ataxia and areflexia of limbs without weakness. It also presents as Ophthalmoplegia and pupillary paralysis. The mortality rate is < 5%, and the cause of death is pulmonary complications. Approximately 85% of patients with GBS achieve full functional recovery within several months to years. Between 5-10% of patients with GBS have one or more late relapses, which are classified as chronic inflammatory demyelinating polyneuropathy (CIDP) [4].

The requirement for mechanical ventilation is associated with more severe weakness on admission, rapid progression tempo, and symptoms. Hence, to find out the correlation between disease severity and the treatment given, this study was carried out with a 3-month follow-up to prognosticate and hence bring out the factors determining the patient's recovery.

The aim of this study is to investigate the epidemiological features of GBS, analyze the clinical profile of GBS, and understand various GBS variants.

2. Materials and Methods

This study included 32 adult patients (age > 20 years) who were diagnosed with Guillain-Barre Syndrome and fulfilled the Brighton criteria for G.B.S. They were admitted to the Department of General Medicine at M.K.C.G. Medical College and Hospital in Berhampur from March 2021 to November 2022.

2.1. Study Design

This study was a descriptive cross-sectional analytical study.

2.2. Inclusion Criteria

Patients who fulfilled the Brighton's criteria for G.B. Syndrome and those with clinical variants of G.B. Syndrome were included in this study.

2.3. Exclusion Criteria

Patients with an equivocal diagnosis, inadequate clinical details, or laboratory investigations were excluded from the study. The following clinical entities were also excluded:

1. Acute Myelopathies
2. Vasculitic Neuropathies
3. Lyme Polyradiculitis
4. CMV Polyradiculitis
5. Poliomyelitis
6. Hypokalemic/Hyperkalemic Periodic Palsies
7. Porphyria
8. Botulism
9. Patients with inadequate clinical details or laboratory investigations.

The patient's data, type of antecedent event, interval between the antecedent event and onset of neurological symptoms, and seasonal trends were recorded in a pre-designed protocol. Detailed clinical examination findings, pattern of weakness and sensory and anatomical disturbances, presence of respiratory muscle weakness, requirement for ventilator assistance, and mortality were documented. Repeated examination of muscle power was performed on alternate days until discharge, followed by a follow-up examination at the end of 3 months. Autonomic function tests were performed at admission and repeated at the peak of disability. Nerve conduction studies were performed using standard techniques. Statistical analysis was carried out using Chi-square test, pie charts, bar diagrams, and related statistical techniques using S.P.S.S. version 20.

3. Results

This study included a total of 32 hospitalized patients with Guillain-Barre Syndrome (GBS) who fulfilled the Brighton criteria from March 2021 to November 2022. The average duration of hospital stay was 20.87 days. Of the patients, 23 (71.87%) were male and 9 (28.12%) were female. The patients' ages ranged from 23 to 63 years with a mean age of 46 years. Fourteen patients (43.75%) were over 50 years old and 8 patients (25%) were between 41 and 50 years old.

The majority of cases (11 cases, 34.5%) occurred between April and June, but no significant increase in incidence during any particular season could be inferred.

Motor weakness was the first symptom of illness in 21 (65.62%) of the cases, with distal weakness involving lower limbs present in 9 (28.12%) of cases and proximal and distal weakness of upper and lower limbs present in 7 (21.87%) cases. Bulbar weakness was present in 2 (6.25%) cases. Sensory symptoms were present in 11 (34.37%) of cases, with paraesthesia (12.5%), numbness (9.375%), and back pain (9.375%) being the most common. Ataxia was present in 1 (3.125%) of patients. Ascending form of paralysis was observed in 21 patients (65.62%), descending type of paralysis in only 3 patients (9.37%), and simultaneous involvement of both proximal and distal muscles in 8 patients (25%).

Cranial nerve dysfunction was observed in 17 patients (53.125%), with facial nerve palsy present in all 16 patients. Unilateral involvement was observed in only 3 (9.37%) patients, while bilateral involvement was present in the rest (13 patients, 40.62%). Eight patients (25%) had 9th and 10th cranial nerves involvement. One patient had total external ophthalmoplegia involving the 3rd, 4th, and 6th cranial nerves, as well as severe ataxia and weakness of lower limbs, leading to a diagnosis of the Miller-Fisher variant. Patients with respiratory paralysis were treated with ventilator support. The development of respiratory distress was monitored by periodic assessment of maximal inspiratory force and expiratory vital capacity, and neck muscle weakness was observed by counting single breaths.

Nerve conduction studies were performed on all patients. Fifteen patients had decreased motor conduction velocities consistent with demyelination neuropathy, 8 patients had decreased amplitude of action potentials consistent with axonal pattern of neuropathy, and 9 patients had mixed patterns of neuropathy with both demyelinating features (prolonged distal latency and reduced conduction velocity) and features of axonopathy (reduced C.M.A.P.).

Statistical analysis was performed using Chi-square test, pie charts, and bar diagrams with S.P.S.S. version 20.

Aspiration pneumonia was observed most frequently in patients with bulbar dysfunction requiring assisted ventilation. Septicemia occurred in one patient who was also diabetic. Deep venous thrombosis occurred in one patient due to prolonged immobilization as they were suffering from ataxia and was treated with low molecular weight heparin. The details are provided in Table 3.

Out of the 32 patients with G.B.S., Acute Inflammatory Demyelinating Polyneuropathy (A.I.D.P.) was the most common variant, forming 23 cases (71.87%), followed by Acute Motor Axonal Neuropathy (A.M.A.N.) forming 5 cases (15.62%). Acute Motor Sensory Axonal Neuropathy (A.M.S.A.N.) was found to be an uncommon variant, forming only 3 cases (9.375%). Only 1 patient (3.125%) was diagnosed with the Miller-Fisher Variant.

Possible prognostic factors were analyzed similarly.

The outcome at the end of three months was correlated with the severity of paralysis [M.R.C. grading] at Plateau Period. Nine patients had the power of grade 0-1, among whom three patients had a good outcome

and six patients had a poor outcome. Sixteen patients had the power of grade 2-4, out of which 14 patients had good outcomes and only two patients had poor outcomes. The difference in the outcome in the two groups was found to be statistically significant regarding the severity of paralysis and final outcome [P = 0.005].

The presence or absence of bilateral facial palsy was compared with respect to the outcome. Nine patients had bilateral facial palsy, of which five patients had a good outcome and four patients had a poor outcome. Sixteen patients had no bilateral facial nerve involvement, of which 12 patients had a good outcome and four patients had a poor outcome. The difference is not statistically significant [P = 0.317].

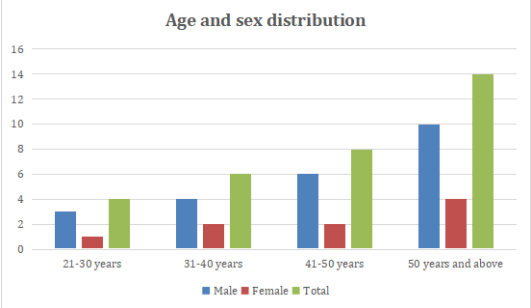

Figure 1. Age and sex distribution

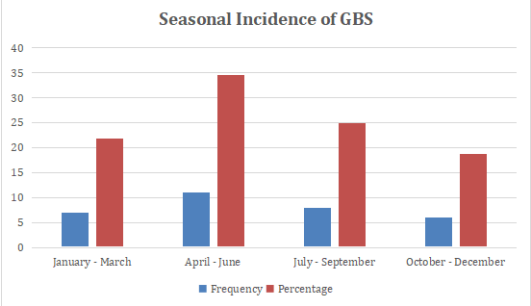

Figure 2. Seasonal Incidence of G.B.S.

Table 1. First symptom of illness

Symptom of illness		No of cases	Percentage
Motor symptoms	Prox. +distal weakness of ul & ll	7	21.87
	Proximal weakness	3	9.3
	Distal weakness	9	28.12
	Bulbar weakness	2	6.25
	Total	21	65.62
Sensory symptoms	Paraesthesia	4	12.5
	Numbness in legs	3	9.375
	Back pain	3	9.37
	Ataxia	1	3.12
	Total	11	34.37%
Mode of onset of G.B.S.	Ascending paralysis	21	65.62
	Descending Paralysis	3	9.37
	Involvement of all 4 Limbs	8	25
	Ascending paralysis	21	65.62

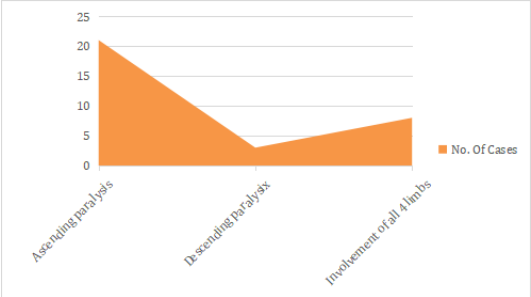

Figure 3. Mode of onset of G.B.S.

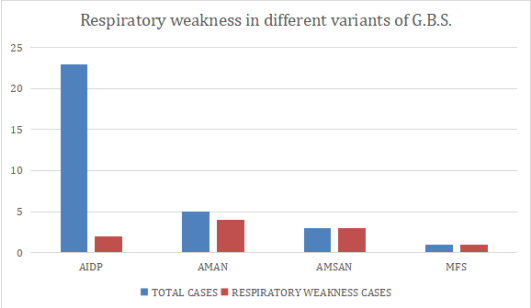

Figure 4. Respiratory weakness association in different variants of G.B.S.

Table 2. Nerve conduction study of cases

Type	No of cases	Percentage
Demyelinating	15	46.87
Axonal	8	25
Mixed	9	28.125

Table 3. Complications

Complications	No of cases	Percentage
Aspiration Pneumonia	6	18.75
Septicemia	1	3.12
DVT	1	3.12
UTI	3	9.37

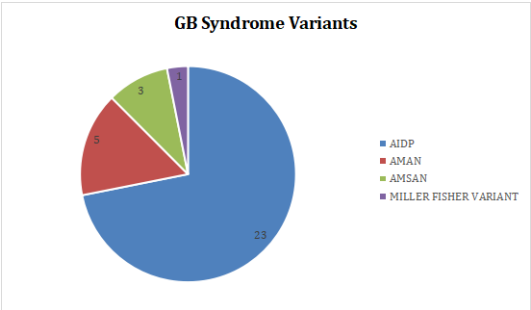

Figure 5. Respiratory weakness association in different variants of G.B.S.

Table 4. Other possible prognostic neurological signs

	Neurological signs	No. of patients	Good outcome	Poor outcome	P value
Severity of Paralysis	Power grade 0-1	9	3 (33.33%)	6 (66.67%)	0.005
	Power grade 2-4	16	14 (87.5%)	2 (12.5%)	
B/L Facial Palsy	Present	9	5 (55.56%)	4 (44.44%)	0.317
	Absent	16	12 (75%)	4 (25 %)	
Obj. Sensory loss	Present	3	1 (33.33%)	2 (66.67%)	0.17
	Absent	22	16 (72.73%)	6 (27.27%)	
Autonomic dysfunction	Present	9	5 (55.56%)	4 (44.44%)	0.317
	Absent	16	12 (75%)	4 (25%)	
Bulbar Paralysis	Present	6	4 (66.67%)	2 (33.33%)	0.935
	Absent	19	13 (68.42%)	6 (31.58%)	

4. Discussion

A total of 32 patients were included in this study. The maximum number of patients were above 50 years of age (43.75%), and 25% of patients were between 41-50 years of age. With 23 cases (71.87%), there was a male preponderance in our study, which is in conformity with the report by Robert M. *et al.* [5]. No specific seasonal incidence of G.B.S. could be inferred with the majority of studies in literature. However, a few studies have noted a seasonal clustering of cases. Kaur *et al.* reported an increased incidence in summer and autumn [6], and Peter C Dowling [7] also noted an increase in summer. In my study, there was a seasonal clustering during summer (April-June) with an incidence of 11 patients (34.5%) during this time period, followed by the spring season (January-March) with an incidence of 7 patients (21.87%) [7].

The first symptoms of illness in the form of motor weakness were present in 21 (65.62%) cases, and 11 patients (34.37%) had sensory symptoms as their presenting symptom. However, Robert *et al.* reported the first symptom as sensory in 83% and motor in 17% of patients [5]. Allan H Ropper in his meta-analysis reported an 85% incidence of paresthesia [8]. In a study by Winter *et al.*, 75% patients had paraesthesia. Robert M. *et al.* described an 83% incidence in paraesthesia [5]. Objective sensory loss occurred in only three patients (9.375%) in the form of diminished touch, vibration, and joint position sense, which occurred in glove and stocking distribution. This is much lower than the 40% reported by Allan H. Ropper in his meta-analysis [8]. Winter *et al.*, noted sensory loss in 52% of his patients. This lower incidence of sensory symptoms may be due to a small sample size.

According to the description by Winter *et al.*, muscle weakness usually starts in legs and ascends to arms in most cases. The meta-analysis of series by Allan H. Ropper showed ascending paralysis in 60%, descending paralysis in 20%, and involvement of all four limbs simultaneously in 20% cases [8]. This was similar to our study. Seventeen patients (53.125%) had cranial nerve dysfunctions. This is in conformity with the 50% incidents reported by Winter *et al.* and 60% in Allan H. Ropper's meta-analysis. Kaur *et al.* reported an incidence of 41% in a study from North India [6,8,9].

Respiratory failure was present in 10 patients (30.30%). Allan H. Ropper, in his meta-analysis showed that 10% of patients have respiratory failure. Winter *et al.* noted a 23% incidence of respiratory failure [8,9]. The average duration of mechanical ventilation in our patients was 18 days. Electrophysiological studies were conducted in all patients, and 15 (46.87%) of them showed demyelinating pattern, 8 (25%) of them showed axonal pattern, and 9 patients

Many authors have reported that a proportion of patients have normal nerve conduction and varying severity of nerve involvement, with the population ranging from 9% to 20%. The A.I.D.P. subtype predominates among all G.B. Syndrome variants, as demonstrated in various studies. In this study, 23 patients (71.87%) were diagnosed with A.I.D.P., 5 patients (15.62%) with A.M.A.N., three patients (9.375%) with A.M.S.A.N., and one patient (3.125%) with Miller Fisher syndrome. A.I.D.P. is the predominant subtype in the United States and Europe (up to 90%), while the Axonal type predominates in China (70% A.M.A.N., 25% A.I.D.P., 5% others). Hadden *et al.*, noted 71% A.I.D.P., 4% A.M.A.N., 2% A.M.S.A.N., and 1% Miller Fisher subtype in their study. Zhahirul Islam *et al.*, showed A.I.D.P. in 82% of cases and A.M.A.N. in 15% of cases. Gupta *et al.*, noted A.I.D.P. in 70% of cases, A.M.A.N. in 20% of cases, and Miller Fisher variant in 5% of cases in India [10–12].

The possible prognostic factors analyzed in the study were the severity of muscle weakness at peak, the presence of objective sensory loss, the presence of bilateral facial paralysis and autonomic dysfunction, and the presence of bulbar palsy. However, only the severity of muscle weakness at peak was found to be statistically significant, while the rest of the parameters were not statistically significant. The study by NK Singh *et al.*, showed similar results, with the severity of paralysis at peak adversely affecting the outcome in patients [13].

In summary, the rapid progression to peak paralysis, prolong plateau phase, delayed onset of recovery from paralysis, requirement of mechanical ventilatory support, and severity of muscle weakness at peak are significant prognostic factors of outcome in G.B.S.

The study's limitation was the sample size, as only 32 patients were admitted to the General Medicine ward during the study period, and many observations did not match those made by others. The lack of availability of treatment modalities such as Plasma exchange, modified plasma exchange, and immunoadsorption therapy prevented the beneficial effects of those modalities from being studied and inferred in this study.

5. Conclusion

Guillain-Barré syndrome (G.B.S.) can occur in individuals of all age groups, with a higher incidence in those over 50 years old. However, age does not appear to be correlated with prognosis. G.B.S. affects both males and females, with males being affected more often than females at a ratio of 2.56:1 in this study. In 65.26% of cases, patients reported a definite antecedent event prior to the onset of G.B.S. Onset of G.B.S is characterized by both motor and sensory symptoms, although objective sensory deficits are seen in very few patients. Factors associated with poor recovery from the illness include rapid progression from onset to peak paralysis, prolonged duration of peak paralysis, delayed onset of recovery from paralysis, need for ventilatory support, and severity of paralysis.

Demyelinating pattern was the most common electrophysiological abnormality in this study, followed by the mixed pattern. Conduction abnormalities were not consistent across all nerves studied, and varying degrees of involvement may occur due to multifocal demyelination. Nerve conduction study results with axonal and mixed patterns of neuropathy are associated with a poor prognosis. In our study, the mortality rate in G.B.S. was 9.375%. A.I.D.P. was the most common subtype in the studied population, followed by the A.M.A.N. variant. Intravenous immunoglobulin (I.V.I.G.) showed significant clinical improvements in patients.

The main limitation of this study was the small sample size, as only 32 patients were admitted to the General Medicine ward during the study period. Additionally, treatment modalities such as plasma exchange, modified plasma exchange, and immunoadsorption therapy were not available, and thus, their beneficial effects could not be studied and inferred in this study.

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Conflicts of Interest: "Authors declare that they do not have any conflict of interests."

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