

# Short Term Rehabilitative Outcome and its Predictors in Guillain Barré Syndrome

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## Abstract

Clinical and electrophysiological data of 34 patients suffering from Guillain Barré Syndrome (GBS) were analyzed. Functional disability and predictors of outcome was determined using Hugh's scale and Medical Research Council (MRC) scale at 0, 2 and at 4 weeks. Good outcome was defined as the ability to ambulate without assistance. 56% patients were males with mean age of 18.41 years (SD  $\pm$ 13.88). Preceding illness was seen in 76.5%. Mean days to disease nadir was 4.6 days. Weakness (50%) was the predominant chief complaint. Mechanical ventilation was required in 41.2 % patients with a mortality of 7.1%. Independent ambulation was achieved by 61.8% and 17.6% with support at the end of study period. Increasing age ( $p < 0.01$ ), days to nadir

( $p = 0.00$ ), duration of ventilation ( $p < 0.001$ ), severity of motor deficit at disease nadir ( $p < 0.001$ ) and high Hugh's score ( $p = 0.00$ ) affected outcome. Mechanically ventilated patients had poorer outcome. Although the recovery from severe GBS was prolonged, most survivors regained independent ambulation.

**Key words:** Guillain Barré Syndrome, prognostic factors, rehabilitative outcome.

## Introduction

The Guillain Barré Syndrome (GBS) is a post infectious severe evolution of demyelinating polyradiculoneuropathy with a postulated autoimmune pathogenesis.<sup>1, 2</sup> With poliomyelitis under control, GBS is now the most important cause of acute flaccid paralysis.<sup>3</sup> GBS has become the most common cause of neuromuscular paralysis in Western countries, with an annual incidence of 0.75 to 2.0 per 100,000 population.<sup>3, 4</sup> In China, the reported an annual incidence of 0.66 per 100,000 for all ages.<sup>5</sup>

GBS diagnosis is made primarily by history and clinical findings.<sup>1</sup> The condition is characterized by progressive and often profound weakness with nadir within one month followed by a variable course of recovery over weeks to several months. Even when intensive care facilities are available, up to 10% patients may die in the acute phase of the illness and 20% are left with some disability one year after onset.<sup>6</sup> Approximately 40% of the patients who are hospitalized with GBS will require inpatient rehabilitation.<sup>7, 8</sup> 5% may die of complications<sup>9</sup>. Relapses are rare, occur at rates of 3-5%.<sup>10</sup>

GBS is classically a demyelinating neuropathy with ascending weakness. Many clinical variants have been documented. Acute inflammatory demyelinating polyradiculoneuropathy (AIDP) is the most widely recognized form in Western countries,<sup>1, 11</sup> but recently acute motor axonal neuropathy (AMAN) and acute motor-sensory axonal neuropathy (AMSAN) also are well recognized.<sup>12, 13, 14</sup>

GBS is a striking problem in India, a good number of young and old persons being affected either with paralysis or respiratory distress or any residual disability. GBS is a disease that often leads to a functional deficit.

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Approximately 85% of patients with GBS achieve full and functional recovery within 6-12 months.<sup>15</sup> The 7-15% who do not recover completely benefit from long term use of assistive devices and rehabilitation strategies.<sup>10</sup>

Various studies have been done to define the diagnostic criteria, antecedent events treatment and prognostic factors affecting outcome.<sup>3, 8, 16, 17</sup> Both plasma pheresis and IVIG are accepted treatment modalities.<sup>18, 19</sup> IVIG is the chosen method of treatment in our centre. Studies from the rehabilitative spectrum are few. There are multiple medical and psychological factors in GBS that can interfere with rehabilitation.<sup>20</sup>

In this study we aimed to document the demographics, clinical characteristics, and complications and to analyze the rehabilitative outcome and the predictors of outcome in patients of GBS.

## **Material and Method**

The study was conducted in the Department of Physical Medicine and Rehabilitation in collaboration with Respiratory Care Unit (RCU), IPGMER, Kolkata during March 2007 to August 2008. The institutional ethical clearance was obtained.

**Inclusion criteria :** Cases were selected from those admitted in RCU and general medical wards. 34 patients diagnosed as Guillain-Barré syndrome (AIDP) as based on National Institutes of Neurological Disorders and Stroke (NINDS) Committee (with modifications proposed by Asbury et al 1990)<sup>21</sup> were selected.

The criteria for case selection was 1) onset of diffuse lower motor neuron paresis-usually rapid in onset, often ascending, usually symmetrical, proximal or distal or both.2) Areflexia or hyporeflexia.3) Sensory involvement if present, less severe than motor impairment.4) Electrophysiological criteria 5) CSF study.

**Exclusion criteria:** 1) Marked persistent asymmetry of weakness.2) Poliomyelitis 3) Diabetic neuropathy 4) Alcoholic neuropathy 5) Porphyria 6) A sharp sensory level. 6) Drugs and metals exposure.

Detailed history and clinical examination were done. Patients were assessed on admission (0), 2 weeks and 4 weeks by standard neuromuscular evaluations. Clinical recovery was defined as the absence of symptoms and signs that interfered with activities of daily living. Factors that were etiologically significant, medical interventions, relevant investigations, need for ventilation, hospital stay, Hugh's disability scale,<sup>17, 18</sup> and Medical Research Council (MRC)<sup>22</sup> scores were noted. Vital signs were regularly monitored and any signs of respiratory distress were checked apart from regular blood gas analysis. The

following features were determined: age, gender, antecedent episodes in the four weeks before onset of weakness, a gastrointestinal or upper respiratory tract infection, time from onset of weakness, distribution of muscle weakness, disability score, MRC sum score, presence of sensory loss, and cranial nerve deficits and requirement of ventilation and factors correlated with it. At study entry and during fourteen weeks of follow up neurological examinations were performed. To assess the distribution of muscle weakness on entry to the study, the strength of some proximal and distal muscles was assessed according to the MRC sum score. Sensory evaluation was performed at each visit in both upper and lower limbs. A good functional outcome was expected on achieving Hugh's disability grade 2 and adequate muscle power of at least grade 3 and above for unassisted gait.

Rehabilitative measures to reduce impairments and disability were started early. Patients went through daily range of motion (ROM) exercises and proper positioning to prevent muscle atrophy and joint contractures. Addressing upright tolerance and endurance was also a significant issue during the early part of rehabilitation. Active muscle strengthening was then introduced slowly. Mobility skills, such as bed mobility, transfers, and ambulation, were targeted. Patients were monitored for hemodynamic instability and cardiac arrhythmias.

Orthoses, assistive devices, modalities like electrical stimulation was given as and when required. In addition pulmonary care, maintaining nutrition, bladder bowel care, skin, eye, mouth care, pain management, deep vein thrombosis prophylaxis and psychological counseling were a part of the rehabilitation program.

Data was analyzed by Statistica version 6 (statsoft incorporation, Tulsa, Oklahoma, 2001), statistical software. Data was summarized by descriptive measures namely mean, standard deviation, median and inter quartile range. Subgroups was made on the basis of age (with 12 years as cut off), gender, and occurrence of enteritis as preceding event and use of ventilation. Numerical variables were compared between relevant subgroups by Mann Whitney U test while categorical variables were compared by Chi Square tests or Fisher's exact test, as appropriate. Friedman's analysis of variance was used to assess change in scores over time followed by Wilcoxon's matched pairs signed rank test for assessing difference between any two time points. All analysis was two tailed with  $p < 0.05$  taken as statistically significant.

## **Results**

Out of 34 patients there were 56% males with a mean age of 18.4 (SD  $\pm 13.88$ ), most being below 30 years.

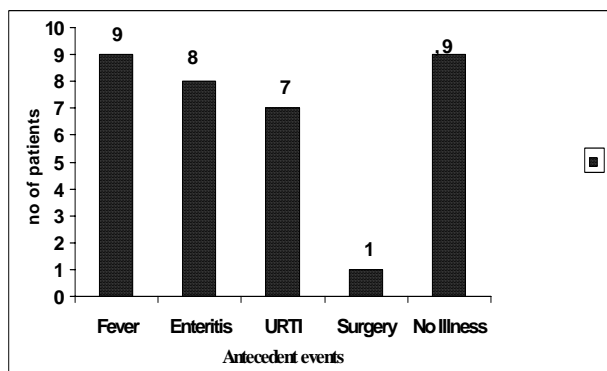


Figure1: Antecedent events prior to onset.

There were 20 patients from urban locality (58.8%) and 14 patients from rural areas (41.1%).

76.4% patients conformed to the classic description of a preceding illness (Figure 1). Maximum latent period was 26 days and the minimum was 1 day the average being 5-8 days.

The onset of paralysis was in most cases insidious and progressive in 30 patients and only 4 had an acute onset within hours to 2 days .The maximum days to disease nadir being 12 days and minimum is 1 day. The mean days to disease nadir are 4.6 days. (SD± 2.32), median 4.00 days (Q R± 3.00).

Modes of progression of the disease on admission is represented in the table 1.

Modes of progression of Paresis	No (%)
BLL to BUL and Cr Nn with resp Support	14 (41)
LL no progression	3 (8.8)
BLL and BUL, no progression	16 (47)
Cr Nn along with UL with gradual involvement of BLL	1 (2.9)

Table 1. Modes of Progression. (BLL: both lower limbs, LL: lower limbs, BUL: both upper limbs, Cr Nn: Cranial Nerves.)

The presenting complaint was mostly weakness (50%) and weakness with tingling and numbness (29%). Some patients presented with tingling only (11.8%) and myalgia (8.8%). The pattern of muscle involvement varied in axial distribution but was fairly symmetrical. In the sensory examination, it was seen that subjective feelings of tingling and numbness were most common, followed by pain in lower back and lower extremities seen in 3 patients.

The lower extremities reflexes were involved in all 34 cases and upper extremities reflexes in 31 cases. During recovery, the upper limb reflexes were quick to recover than the lower limbs which remained absent in 13 cases at the end of study, especially the ankle jerk.

Bilateral Facial nerve was involved (26.5%), lower motor neuron type. 15 patients (44.1%) had bulbar weakness (9<sup>th</sup> and 10<sup>th</sup> nerves) complaining of difficulty in swallowing, pooling of saliva and dysphagia. No other cranial nerve involvement was observed. The facial nerve and the palatal and pharyngeal palsies were transient in all cases.

On admission retention of urine was seen in 8 patients (23.5%). In most cases patients were catheterized and they regained control over the bladder in few days. 5.9% had constipation. Autonomic signs and symptoms were observed in the 35.3%. One patient each had developed hypertension and hypotension. Arrhythmias were uncommon.

Nerve conduction study (NCS) showed low motor unit action potential in all the 31 patients examined for this.

25 patients (73.52%) were treated with standard regime of intravenous immunoglobulin.

The Hugh’s disability scoring system showed a progressive improvement over time from a mean value of 4.35 initially to a mean of 1.42 at the end of study (Friedman’s ANOVA test had a p<0.001).

The Medical Research Council (MRC) score showed a steady improvement over time from a mean value of 15.26(SD±11.66) initially to a mean score of 52.53(SD±9.17). However age and the status of ventilation affected the MRC scores as shown in Figures 2 and 3.

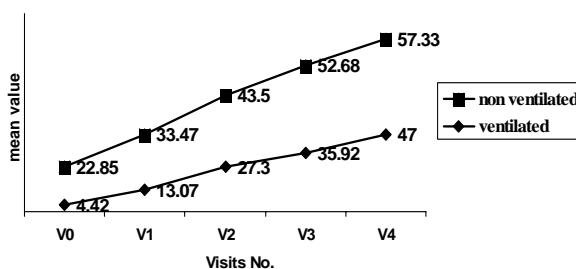


Figure 2: MRC scores across time in ventilated and non ventilated patients.

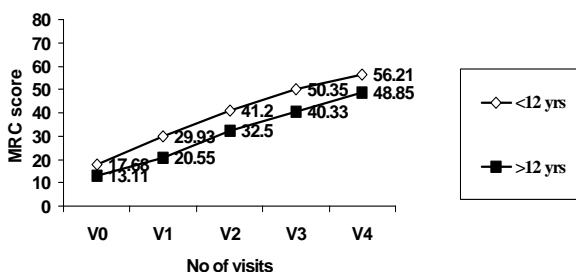


Figure 3: MRC scores across time in two age groups.

14 (41.2%) developed respiratory impairment and had to be placed on mechanical ventilation. One patient on ventilation expired. Mean duration of ventilation was 18.7 days and median value was 12 days. There is significant correlation between the ventilation duration and poorer outcome ( $p < 0.001$ ) in both the Hugh's scale and MRC scale at the end of study period. Correlation between Spearman rank test was 0.382 (fair correlation) with Hugh's score at baseline and 0.14 (poor correlation) with MRC score at baseline (V0). However at the end of study period (V4), ventilation duration showed a good correlation with Hugh's score (0.476) and a good inverse correlation with MRC score (-0.602). So longer the duration of ventilation, poorer was the outcome of the patients. Several factors which showed association with respiratory involvement were: Bulbar involvement ( $p$  value  $< 0.001$ ), Cranial nerve involvement ( $p$  value 0.017), Sensory involvement ( $p$  value 0.035).

Autonomic involvement ( $p$  value 0.036). Age had a significant correlation with ventilation ( $p = 0.010$ ) and days to disease nadir ( $p = 0.001$ ). However in this present study factors which failed to show any significant association was gender, upper limb involvement, antecedent event, Nerve Conduction Study result and treatment.

The complications during hospital stay were seen in majority (73.52%), table 2. There were no cases of deep vein thrombosis, heterotrophic ossification and severe cardiac arrhythmias.

<b>Complications</b>	<b>% of patients</b>
Transient urinary retention	23.5
Constipation	0.9
Pneumonia	8.8
Pain	26.5
Contactures	14.7
Hypotention and hypertention	5.9
Dysphagia	44.1
Pressure sore	2.9
Death	2.9
Urinary tract Infection	2.9
Tracheostomy	2.9

Table 2: Complications during hospital stay.

Out of 34 patients, there were 4 drop outs during follow up and one death during in-patient stay. 61.8% of the study population achieved the ability for independent mobility. Children in this study, showed a better recovery pattern than those above 12 years ( $p < 0.05$ ). Around 33.3% of this population was unable to do manual work. A percentage of 17.6% achieved the ability to ambulate with support such as canes, walkers and orthoses. Upper extremity recovery was good in all these cases. Activities of daily living were mostly achieved by the patients apart

from those having difficulty during gait. 2.9% (one patient) remained confined in bed. Fatigue was an often complaint. Postural hypotension was another complaint in few patients especially after inpatient discharge. 64.3% had no sensory symptoms while the remaining had pain and paraesthesia.

## Discussion

Despite numerous studies, there is still some uncertainty concerning GBS outcome. This could be due to the fact that most studies are based on small populations that analyzed retrospectively or focus on patients admitted to clinical trials, which usually include more severely affected individuals. Moreover, one reason explaining the discrepancies in the epidemiologic results is the difference in diagnostic criteria used for defining GBS, a problem that can be overcome by considering only the studies based on NINDS<sup>21</sup> criteria.

A higher incidence in males 55% in comparison to 44% in females were seen in this study. A higher incidence of GBS in males has been reported in most studies<sup>3,5</sup>, with a male to female ratio ranging from 1.1:1 to 2:1. This finding is similar to what has been observed in two other autoimmune disorders of the peripheral nervous system: multifocal motor neuropathy with conduction blocks and chronic inflammatory demyelinating. The study population was mostly below the age of 30 years (79%). The youngest being 2 years of age and the oldest 49 years. It supports the view that GBS occurs in younger age group in Asian population.<sup>23</sup>

26 patients (76.47%) had some form of illness preceding the weakness. The examined period is too short to determine the presence of a seasonal trend. The largest proportion had non specific febrile illness followed by enteritis and upper respiratory tract infection which is consistent with other studies.<sup>24, 25</sup> In adults a higher frequency of enteritis was seen.<sup>26, 27</sup> Antecedent event like enteritis did not seem to affect the outcome of the disease ( $p > 0.05$ ). This was not consistent with other reports,<sup>6</sup> which may be because of small study population and a greater number of patients in the younger age group having a better outcome at the end of study period. It is of note that in one case (2.9%) GBS followed surgery. The incidence of post-surgery GBS is low and its etiology remains uncertain.<sup>2</sup>

The presenting symptom was pure motor weakness in 50% of the population and associated with paraesthesia 29%. Back and thigh pain was seen in 8.82% this was also reported by Italian and Taiwan study group<sup>17, 22</sup>.

The length of time from when the first symptoms appear to the point of maximal neurological dysfunction is

reported as the “disease nadir.” The point of disease nadir has frequently been referred to as the point at which outcome and therapeutic intervention has been considered critical but this has never been established. The mean days to disease nadir is 4.6 days ( $SD \pm 2.32$ ). The shorter time to disease nadir was predicted to have a poorer prognosis and severity in this study which corroborates with the Italian study group.<sup>17</sup>

The present study showed patients having motor weakness more on lower limbs. Sensory symptoms too were mostly in the lower limbs. Upper limb paralysis was identified in a higher proportion of patients who subsequently received mechanical ventilation, but this did not reach statistical significance.

Electro diagnostic studies revealed that demyelinating pattern was the commonest pattern overall especially in children less than 12 years. The least common was the axonal variety. There is no significant co-relation between age groups and NCS pattern. (Chi square p value test 0.118).

Regarding treatment, IV immunoglobulin was the mainstay of treatment in 25 patients. However there was no significant difference observed in worsening of symptoms and outcome between and those receiving immunoglobulin and those without. Though studies<sup>28</sup> have found no convincing evidence of the benefits of IVIG the authors enumerated several confounding factors that may have affected data..

Respiratory involvement had has been unequivocally associated with worse functional outcome in the literature on GBS.<sup>17, 29, 30</sup> The presence of increasing age, bilateral facial palsy, bulbar involvement, autonomic dysfunction, and rapid disease progression were also associated with an increased likelihood of mechanical ventilation.<sup>31</sup> Patient-dependent factors such as gender, upper limb involvement, antecedent event and the nerve conduction study result did not predict the progression to mechanical ventilation. Patients with GBS in the ICU are prone to develop pneumonia and upper respiratory tract complications.<sup>32</sup> 3 patients in this study developed pneumonia, which is less than previously reported.<sup>29</sup> Measures that may have assisted in the management of patients with GBS include chest physical therapy and intermittent mandatory positive pressure ventilation, elevating the head of the bed and minimizing aspiration, performing serial respiratory function measurements to monitor improving diaphragmatic function, and maintaining a surveillance system of the infectious organisms present in a particular ICU. Ventilation requirement is a significant prognostic factor in functional outcome, as evident in Hugh’s score and MRC score of the patients.

Paraesthesia did not affect functional outcome in our study and this is consistent with previous reports.<sup>29</sup>

Micturition disturbances as retention were a common problem. This was consistent with previous reports and detrusor areflexia, non relaxing urethral sphincter, disturbed bladder sensation and detrusor over activity have all been known to occur<sup>33</sup>. None of the patients required prolonged indwelling catheterization which is consistent with the reports that urological dysfunction usually resolves and improves<sup>33</sup>. All patients with retention had paraparesis or tetraparesis.

Tetraparetic patients who required nasogastric feeding had poorer outcomes. The severity of paresis have been correlated with poorer outcomes<sup>34</sup>. The requirement of nasogastric feeding indicates the involvement of bulbar cranial nerves and a more severe illness.

A few patients complained of pain with occasional flares. Pain in GBS has a neuropathic, musculoskeletal and visceral autonomic quality, all of which have been described.<sup>35, 36</sup> Various topical agents, Paracetamol, Tricyclic Antidepressants and NSAIDs had been prescribed with good results. Simple physical measures such as gentle massage and cold packs together with reassurance were also helpful.

There were no cases of deep vein thrombosis or heterotrophic ossification identified through routine clinical screening which have been reported previously.<sup>8</sup> Despite preventive rehabilitative measures were advised throughout; there were cases of decubitus ulcers and contractures. Early mobilization from bed with assisted transfer to a chair was encouraged in all patients, whenever possible, as soon as head control was achieved, even whilst ventilation continued. This contributed to the prevention of contractures and limb pain and improvement in patient’s morale.

The number of dysautonomic patients was relatively small in this study. This group has been reported to be notorious for fatal arrhythmias<sup>29</sup> but our small study group precludes further analysis.

A relapse rate of 13% and a death rate of 11 to 18% have been reported<sup>17</sup>. There were no relapses in this study although there was one death (7.1%) in the ventilated population.

It is encouraging to note that majority of the patients 61.7% had a good outcome and were able to ambulate without assistance. 33.3% of this population was unable to do manual work. Upper extremity recovery was good in all these cases. 17.6% of the study population achieved the ability to ambulate with support. In the Italian study group<sup>17</sup> 15% of the 108 survivors had disability grade 3

and more 2 years after onset. Activities of daily living were mostly achieved by the patients apart from those having difficulty during gait. 2.9% (one patient) of the study population remained confined in bed. Fatigue was an often complaint. Sensory deficits were few and similar to previous studies<sup>34</sup>. Children below 12 years of age showed a better recovery pattern than those above 12 years ( $p < 0.05$ ). This was consistent with available literature.<sup>17, 29</sup>

Several studies have shown that the mortality and outcome in terms of residual disability correlate with the severity of motor deficit at the nadir of the disease and that mechanical ventilation is a particularly poor prognostic feature.<sup>6, 17, 29</sup> This study strongly corroborates with these prognostic factors previously identified. Rapidly progressive disease leading to quadriplegia within one week was shown to be a poor prognostic factor in one series,<sup>23</sup> but this could not be confirmed in the present series. Cardiac arrest are also a significant causes of mortality but, as in the present series, sudden death due to cardiac arrhythmias in patients with Dysautonomia is uncommon. The prognostic factors identified in this study were increasing age, days to nadir, requirement of ventilation, duration of ventilation, high Hugh's grade and severity of motor deficit at disease nadir. One of the most important prognostic factors for the outcome of patients with Guillain-Barré syndrome is the severity of muscle weakness<sup>6</sup> Children had a better recovery of power than adults while gender was not found to be significant. Requirement of ventilator and duration of ventilation was strongly associated with poor motor recovery ( $p < 0.000$ ).

The Hugh's disability scale is used frequently and is easy to administer. The Hugh's disability score at nadir was an individual predictor functional outcome. However it does not measure cognitive impairments which have been reported in severely affected individuals Functional outcome as measured by the Hugh's score and MRC score did correlate with the requirement for ventilator support and agrees with other epidemiologic studies that generally evaluated outcome by ambulatory function.<sup>15</sup>

Our study had a few limitations. Our sample size was small and did not represent the entire spectrum of GBS.

## Conclusion

The requirement for ventilator support had the most significant impact on outcome. The presence of bilateral facial palsy, bulbar involvement, autonomic dysfunction, and rapid disease progression were also associated with an increased likelihood of mechanical ventilation. Upper limb involvement, considered to be a factor for ventilator dependence in other studies, was not shown to be a statistically correlated factor in this study. Compared to

other studies, number of fatal autonomic dysfunctions were found to be few after comprehensive rehabilitation approach was utilized in this study. The prognostic factors identified in this study were increasing age, days to nadir, requirement of ventilation, duration of ventilation, severity of motor deficit at disease nadir and high Hugh's score.

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