Research Article

Electrophysiological study to detect serial changes and prognosis in patients of Guillain Barre syndrome from North-West Rajasthan, India

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ABSTRACT

Background: The Guillain Barre syndrome (GBS) is the commonest cause of acute flaccid paralysis in much of the world, after the introduction of vaccine for poliomyelitis. Electrophysiological study may play an important role in further investigation of the pathogenesis and assessment of prognosis. This study was undertaken to see any changes in electrophysiological pattern at one month follow up and prognosis of patients with Guillain Barre syndrome.

Methods: The study included 28 patients of Guillain Barre syndrome admitted between the period of July 2014 to June 2015 in the department of medicine and neurology, SP Medical College and AG Hospitals, Bikaner, India. The clinical diagnosis was based on criteria proposed by the national institute of neurological, and communicative disorders and stroke (NINCDS). Each patient was assessed both clinically (including disability score) and electrophysiologically at the time of presentation and at one month±seven days of follow up.

Results: GBS was more common in early decades. Male to female ratio was 4.6:1. On electrophysiological study mixed pattern was most common (42.86%) followed by axonal (32.14%) and demyelinating (25%) patients. Mean disability score at the time of presentation was maximum for axonal pattern and the same group had minimum score at one month follow up indicating better recovery. Sequential electrophysiological changes were seen in this study. Axonal pattern had better recovery (77.78%) than demyelinating and mixed was worst with 16.67% mortality.

Conclusions: Mixed pattern is predominant pattern on electrophysiological studies. Axonal pattern has better recovery. Secondary changes of electrophysiological finding in some of our cases suggest that primary demyelinating and mixed subtype could, be misinterpreted as primary axonal pathology without timely serial studies.

Keywords: Guillain Barre syndrome, Serial electrophysiological pattern, Prognosis, North-West Rajasthan

INTRODUCTION

Guillain Barre syndrome (GBS) is an acute, frequently severe and fulminant polyradiculoneuropathy that is autoimmune in nature. Guillain Barre syndrome (GBS) is the commonest cause of acute flaccid paralysis in much of the world, after the introduction of vaccines for poliomyelitis.¹

Guillain Barre syndrome was understood, until recently, to be an acute or subacute demyelinating inflammatory polyradiculoneuropathy with favourable outcome and complete recovery in the majority of individuals. This rather optimistic view has been recently challenged by reports of several cases with a more severe course, presenting greater disability during the acute phase of the disease and persistent residua in the follow-up. By various reports this is now well established that Guillain Barre syndrome is a heterogenous symptom complex and that the outcome is sometimes unfavorable and can be predicted by the presence of selected prognostic indicators.²⁻⁵ Although Guillain Barre syndrome is
considered to be related to antecedent infection and autoimmunity, the detailed mechanism is still unclear (Giovannoi et al). It occur in all parts of the world and in all seasons affecting children and adults of all ages and both sexes.\(^7\)

The electrophysiological study may play an important role in further investigation of the pathogenesis and assessment of prognosis (Cornblath et al).\(^8\)

In the United States, Europe and Australia, the GBS is primarily a demyelinating, rare patients have pathological evidence of primary axonopathy (McLeod et al, Honavar et al, Hadden et al).\(^9,10\) Several studies in recent years showed that clinical and electrophysiological features of Guillain Barre syndrome in China and India were different in some way from those in developed countries (Mckhann et al, Griffin et al, Guo et al).\(^11,12\) Mc Khann et al\(^13\) suggested predominantly acute motor axonal neuropathic (AMAN) pattern.

Recently in Northern China, Ho et al, showed that the demyelination was the predominant pattern not only in different age groups but also at different test times after the onset of the symptoms.\(^7\)

Shin et al showed among the cases of primary demyelination, 21% showed electrophysiological features of axonal neuropathy at least on one occasion during the serial studies.\(^13\) Hiraga et al, elucidate the patterns and sequential changes in electrodagnostic abnormalities of anti-ganglioside-positive GBS.\(^14\) They reviewed serial findings and found that 5 patients who showed demyelinating pattern having prolong distal latency on 1st nerve conduction study (NCS), three of them eventually showed the axonal pattern or rapid normalization of motor nerve conduction velocities (MNCV) on subsequent NCS, the remaining two showed persistent prolong distal latency after 4-6 weeks.

This study was first of its own kind in North West of Rajasthan. Study was planned to see any changes in electrophysiological pattern at one month of follow up and prognosis of patients with different electrophysiological patterns of Guillain Barre Syndrome.

**METHODS**

The study was carried out in the department of Medicine and Neurology of SP Medical College and associated groups of hospital, Bikaner, Rajasthan, India.

The study subjects included all patients with clinical presentation of Guillain Barre syndrome admitted during the period of July 2014 to June 2015.

The data were recorded on age, sex, preceding events, date of onset of disease, clinical manifestations including initial symptoms and neurological finding as per proforma during the course, result of cerebro spinal fluid (CSF) study and serial electrophysiological changes including specific treatment given.

The clinical diagnosis of Guillain Barre Syndrome was based on strict adherence to the criteria proposed by the National Institute of Neurological, and Communicative Disorders and Stroke (NINCDS) (Asbury et al).\(^15\)

All recruited patients meet the standard criteria for GBS, including the presence of progressive bilateral weakness with tendon are flexia, and others as defined by Cornblath et al.\(^15\) CSF examination of each patient was done with consent of either patient or relative. Then CSF analysis was done for total cell count, cell type, total protein and sugar. Each patient was investigated as per proforma including serum electrolytes (K\(^+\), Ca\(^{++}\) and Na\(^+\)) and urine for porphobilinogen. In this study we had not gone through the identification of organism of the preceding illness (viral culture and immunological test) as these test were not available in our college and we have also not included these in the study material.

Each patient was assessed both clinically and electrophysiologically at the time of presentation and at one month±seven days of follow up. At each visit, a complete neurological examination was performed, and severity of the clinical findings was expressed with reference to a disability scale commonly used in previous therapeutic trials of plasma exchange (Hughes et al).\(^19\) The major steps in the outcome of the disease (plateau, improvement, clinical recovery or death) were carefully noted and their dates recorded.

The clinical status is defined by a disability scale from Hughes et al as follows:\(^16\)

- Grade 1: Minor signs or symptoms.
- Grade 2: Able to walk 5 meters across an open space without assistance.
- Grade 3: Able to walk 5 meters across space with the help of one person and walking-frame, stick, or sticks.
- Grade 4: Wheelchair/bed bound and unable to walk.
- Grade 5: Requiring assisted ventilation.
- Grade 6: Death.

Nerve conduction study was performed with machine "Medela Synergy Emg and Ep System by Oxford Instrument U.K." by conventional surface recording.

The study observed following electrophysiological data in at least four motor nerves in each patient:

1. Motor nerve conduction velocity (MNCV)
2. F-wave latencies
3. Distal latencies
4. Compound muscle action potential amplitudes after distal and proximal stimulation.
The diagnostic criteria for electrophysiological classification is based on motor nerve conduction studies (Kaur U, Cornblath DR, Hadden RMD et al.) internationally accepted criteria by most authors.17,18,8

The electrophysiological study was done on every patient of GBS. The value for each variable was compared with the normal values (age and sex adjusted) in the EMG laboratory. Two standard deviation above and below the mean was taken as normal limit.

All patients were followed up at one month (±7 days). Treatment part included conservative management and intravenous immunoglobulin depending upon the availability and affordability by the patient.

RESULTS

This study was conducted in department of medicine and neurology, PBM Hospital, SP medical college, Bikaner, India from March 2005 to December 2006.

28 patients of age 15 years and above fulfilling the criteria of Guillain Barre syndrome were analyzed in reference to, besides preliminary details, disability scores, serial electrophysiological studies (performed during hospitalization and at one month±7days follow up) and prognosis. Following observations were made:

Age and sex distribution

- In this study 50% of patients were between 18 to 30 years of age with second peak in 4th decade indicating that GBS can occur in any decade of life but is more common in early decades.
- Of total 28 patients 23 (82.14%) were males and 5 (17.86%) were females with a male to female ratio being 4.6:1.

Electrophysiological pattern at the time of presentation

Electrophysiological study performed at the time of presentation showed mixed pattern in 42.86%, axonal pattern in 32.14% and demyelinating in 25% patients. Axonal pattern is the most common subtype in late 2nd decade of life and mixed pattern in other decades except 6th decade. Only one patient who presented in 6th decade showed demyelinating pattern.

Functional status in relation to electrophysiological pattern on first examination and at one month

Disability scores (grading given by Hughes et al) were calculated in reference to various electrophysiological patterns.16 Total mean disability score at the time of diagnosis was 3.75 and mean disability scores for axonal, demyelinating and mixed pattern were 3.78, 3.71 and 3.75 respectively. Mean disability score for axonal pattern was worst and for demyelinating it was better than other types.

At one month follow up mean disability score was 2.79 and mean disability score of axonal 2.45, mixed 2.81 and demyelinating 3.53 indicating axonal pattern having better recovery. In demyelinating pattern, 3 (42.86%) out of 7 patients recovered and 4 (57.14%) showed persistent weakness. In axonal pattern 7 (28.57%) started recovery and 2 (22.22%) showed persistent weakness. Ten (83.33%) patients of mixed pattern started recovery and two (16.67%) expired. We observed axonal pattern having better recovery than demyelinating and mixed had worst prognosis.

Table 1: Functional status in relation to electrophysiological pattern at the time of presentation.

<table>
<thead>
<tr>
<th>Functional status of patients</th>
<th>No. Of cases (n)</th>
<th>Demyelinating(n)</th>
<th>Axonal(n)</th>
<th>Inexitable (n)</th>
<th>Mixed(n)</th>
<th>Normal(n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal grade (grade 0)</td>
<td>0</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Minor symptoms (grade 1)</td>
<td>0</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Unassisted gait (grade 2)</td>
<td>1 (3.57%)</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Assisted gait (grade 3)</td>
<td>8 (28.57%)</td>
<td>2</td>
<td>3</td>
<td>-</td>
<td>3</td>
<td>-</td>
</tr>
<tr>
<td>Bed bound (grade 4)</td>
<td>16 (57.14%)</td>
<td>5</td>
<td>5</td>
<td>-</td>
<td>6</td>
<td>-</td>
</tr>
<tr>
<td>Assisted ventilation (grade 5)</td>
<td>3 (10.71%)</td>
<td>-</td>
<td>1</td>
<td>-</td>
<td>2</td>
<td>-</td>
</tr>
<tr>
<td>Mean disability score</td>
<td>3.75</td>
<td>3.71</td>
<td>3.78</td>
<td>-</td>
<td>3.75</td>
<td>-</td>
</tr>
</tbody>
</table>
Table 2: Functional status in relation to electrophysiological pattern on follow up at one month.

<table>
<thead>
<tr>
<th>Functional status of patients</th>
<th>No. of cases (n)</th>
<th>Demyelinating (n)</th>
<th>Axonal (n)</th>
<th>Inexitable (n)</th>
<th>Mixed (n)</th>
<th>Normal (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal grade (grade 0)</td>
<td>0</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Minor symptoms (grade 1)</td>
<td>1</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>1</td>
<td>-</td>
</tr>
<tr>
<td>Unassisted gait (grade 2)</td>
<td>14</td>
<td>-</td>
<td>8</td>
<td>-</td>
<td>6</td>
<td>-</td>
</tr>
<tr>
<td>Assisted gait (grade 3)</td>
<td>7</td>
<td>2</td>
<td>1</td>
<td>-</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Bed bound (grade 4)</td>
<td>4</td>
<td>2</td>
<td>2</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Assisted ventilation (grade 5)</td>
<td>0</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Died (grade 6)</td>
<td>2</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>2</td>
<td>-</td>
</tr>
<tr>
<td>Mean disability score</td>
<td>2.79</td>
<td>3.53</td>
<td>2.45</td>
<td>-</td>
<td>2.81</td>
<td>3</td>
</tr>
</tbody>
</table>

Subsequent electrophysiological pattern at one month in recovering patients

The study observed sequential electrophysiological changes in patients of GBS in this zone. Three (15%) out of 20 patients showed demyelinating pattern at Ist MNCS. Of these 2 (66.66%) changed into normal pattern and one (33.33%) into axonal pattern on follow up MNCS at one month. Seven (35%) patients with axonal pattern who showed recovery after Ist presentation had same axonal pattern at follow up. Out of 10 patients of mixed pattern who showed functional recovery one patient changed to axonal pattern and remaining 9 patients remained as mixed pattern on follow up.

DISCUSSION

This study was conducted to see any changes in electrophysiological pattern after one-month and prognosis of different electrophysiological pattern of patients of Guillain Barre syndrome in North western Rajasthan (Bikaner), India.

Age and sex association

In this study the age group of patients ranging between 15 years to 70 years with male to female ratio of 4.6:1 (82.14% males). There were higher incidences of disease in early decades of life with slight second peak in 4th decade. The demographic profile is similar to study conducted by Ropper et al, and Jiang et al in which they showed that the Guillain Barre syndrome may occur in any age, with bimodal distribution (occasionally including infancy) in either sex with male predominance. Mc Khann also showed the higher incidence of GBS in young adult. Rees et al conducted similar study and showed bimodal distribution of age, with peaks at 15-24 year and 65-74 years.

Electrophysiological patterns

In this study the mixed subtype is the commonest electrophysiological pattern of Guillain Barre syndrome presented in 12 (42.86%) cases followed by axonal 9 (32.14%), demyelinating in 7 (25%) cases and no case of inexitable was seen. This observation is consistent with the study made by Italian Guillain Barre study group in which 45.2% of cases had mixed pattern and 29% cases had axonal pattern, and 10.7% patients had demyelinating pattern but differ from studies conducted by Hadden et al, which showed that in Europe and Australia, the predominant form of Guillain Barre syndrome was primarily demyelinating, rare patient had pathological evidence of axonopathy.

Jiang et al, Arami et al showed demyelinating in 60.5%, axonal in 25% and mixed pattern in 14.5% of cases. Axonal pattern in early period (with-in 10 days) of symptoms onset was found with the same percentage as demyelinating i.e. (42.9%) (Jiang et al).

The study found that mixed pattern was the predominant pattern in different test time after the onset of neurological symptoms. This observation is also consistent with the study made by Italian Guillain Barre study group.
Pattern at follow up (clinical and electrophysiological)

In the study, it was observed that 20 patients (71.43%) started spontaneous recovery within one month after the onset of the illness, 6 patients (21.43%) had persisting weakness even after one month and 2 patients (7.14%) died within one month. Winer et al in showed that most patients with Guillain Barre Syndrome will make a good spontaneous recovery, if they receive competent supportive treatment and 10% patients may die in acute phase of the disease even when general intensive care facilities are available.24 Loffel et al showed that among survivors, nearly 60% cases make a full recovery but the other 40% shows some permanent residual symptoms and signs, usually weakness of distal leg muscles, absent ankle jerks or distal sensory loss.25

The serial electrophysiological study shows, those 3 patients of demyelinating pattern who showed recovery, one of these changed to axonal and the remaining two showed normal pattern. 10 patients of mixed pattern who showed recovery one patient changed to axonal pattern and remaining nine showed persistent mixed pattern, and one of the patient of axonal pattern on recovery showed normal pattern. So we observe the sequential electrophysiological changes in pattern of Guillain Barre syndrome patients.

A study done by Hiraga et al they reviewed serial finding of 25 (serologically anti-ganglioside positive) patients, of these 12 showed axonal, 5 demyelinating and 3 isolated F-wave absent in the first NCS.26 Out of these 5 patients who showed demyelinating pattern having prolonged distal latency on 1st NCS, three patients eventually showed the axonal pattern or rapid normalization MNCV on subsequent NCS, the remaining two had persistent prolonged distal latency in 4-6 weeks.

Similar study done by Shin et al noted 25 patients of demyelinating pattern on first NCV with no patient with axonal, on 2nd NCV 5 patients with demyelination showed change in electrophysiological pattern, 4 changed to axonal pattern and one to normal pattern.13

Thus the study showed similar result to Hiraga et al and Shin et al on serial electrophysiological changes.26,13 A study done by Kuwabara et al reviewed on sequential nerve conduction studies.27 In the first NCV study, isolated absence of F-wave was found in 12 (19%) cases, sequential studies in 10 of these cases showed two electrophysiological patterns; 1) rapid restoration of F waves seen in 6 cases, 2) persistent absence of F wave with distal motor nerve degeneration (axonal pattern in 4 cases). Thus the study is similar to Kuwabara.

Study shows relatively better prognosis of axonal pattern than that of demyelinating pattern. 77.78% patients of the axonal pattern and only 42.86% patients of demyelinating pattern started recovery within 1 month of disease onset. Mixed pattern had worst prognosis, 16.67% cases of mixed pattern died within 1 month of disease onset. Similar study was done by Ho et al and found recovery time for axonal and demyelinating patients was similar.5 In Italian study group 36% cases showed improvement within 1st week and 85% cases within one month.22

Tekgul et al showed that in acute phase axonal forms of GBS were more disabled than the demyelinating GBS, as measured by disability scores.28 There was no significant difference at 6 months in scores between the two groups.

However these studies differ from Emilia Romagna study group Italy those they found recovery occurs (100%) in patients of demyelinating pattern and 20% in axonal pattern.29 Smith et al followed up patients of GBS for 9-54 months, and showed axonal pattern had worse prognosis.30

Massaro et al noted that the presence of inexcitable motor nerve early in the course of Guillain Barre Syndrome identifies a group of patients with more severe disease, delayed recovery and residual disability despite early treatment with human immunoglobulins.27

Hadden et al showed that axonal pattern is not always a marker of poor recovery.18 He found that patients with axonal pattern showed both faster and slower recovery whereas patients with demyelinating pattern showed only slow recovery pattern, but recovery time for both type was similar. This study shows similar prognosis of axonal pattern as shown by Massaro et al, Hadden et al and Tekgul et al.28,31

In this study we observed no patient had made complete functional recovery (grade = 0) after one month of onset of disease, however 50% patients had unassisted gait, 25% of cases required assisted gait and 14.29% were bed ridden and 3.57% patients on follow up at one month had minor symptoms. No patient required prolonged mechanical ventilatory support but two patients expired. These findings were similar to Kim et al who noted 27.8% and 22.2% patients to have assisted gait and bed ridden respectively at 2 months.32

The total mean disability score at the time of admission was 3.75 and on discharge 2.54. On admission 19 patients (six axonal, five demyelinating and eight mixed) were very weak with a disability score >3. (In these 19 patients two patients of mixed pattern with disability score 6 was also present), but on discharge only 4 patients (2 axonal and 2 demyelinating) were in this severe weakened group.

Hung et al reported mean disability grade at admission in the childhood and adult patients groups were 3.0 and 2.9, respectively (p=0.70) and mean disability grades at a follow up of 1 year or longer in the childhood and adult were 1.2 and 1.9, respectively.33
Arami et al showed mean GBS score of >3 during the admission that is 3.25 ± 0.77 with a maximum disability of 3.97 ± 0.92 during the following days and on discharge the score was 2.74 ± 1.33. 44.7% patients were with disability score >3. Thus the study shows prognosis of GBS is similar to the study of Hung et al and Arami et al.

Thus the results indicate that Guillain Barre Syndrome is a disease of good prognosis in patients who survive the acute stage.

**CONCLUSIONS**

In this study the mixed pattern is predominant pattern. In acute phase of the disease, patients with the axonal subtypes of GBS were more disabled than those with the demyelinating and mixed GBS. Axonal subtype had good recovery at one month compared to demyelinating and mixed pattern. Secondaries changes of electrophysiological finding in some of our cases suggest that primary demyelinating and mixed subtype could, be misinterpreted as primary axonal pathology without timely serial studies.

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*Ethical approval: The study was approved by the institutional ethics committee*

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