Original Article

Characteristics and Acute Rehabilitation of Guillain-Barré Syndrome in Singapore

YS Ng,[1] *MRCP*, YL Lo,[2] *M Med*, PAC Lim,[3,4] *MD*

Abstract

Introduction: The objectives of this study are to describe the demographics, clinical characteristics, complications and functional outcomes in patients with Guillain-Barré syndrome (GBS) or the Miller-Fisher syndrome (MFS) variant admitted to our institution. We also aim to identify prognostic outcome indicators. Materials and Methods: A retrospective review of the case records of all patients discharged from our hospital with a diagnosis of GBS or MFS over a 2-year period was performed. The clinical characteristics charted included the time of symptom onset to nadir. The Modified Barthel Index (MBI) and Expanded Grading Scale (EGS) for GBS were the functional outcome measures used. Results: Thirty-one cases were reviewed and 8 (25.8%) had the MFS variant. Twenty-two (71%) patients were male, with a mean age of 42.3 years. Weakness and numbness (74%) were the most common initial symptoms; 9 (29%) patients were paraparetic and 7 (22.6%) were tetraparetic. Ten (32.3%) patients had respiratory involvement and 8 (25.8%) had urinary retention. Intravenous immunoglobulin (IVIG) was prescribed in 13 (41.9%) patients. The mean duration to disease nadir was 8.1 days. The mean MBI scores at nadir and discharge were 54.7 and 77.3, respectively, and this gain was highly significant (P <0.01). The majority (84%) of patients were employed at admission and although most returned to work, 63% (17/27) of the patients had residual symptoms or signs 3 months after discharge. Conclusion: The clinical characteristics and complication frequency closely follows that previously described in Western populations, although our cohort was younger and had a higher proportion of the MFS variant. Predictors of a poorer functional outcome include a high EGS score at nadir, tetraparesis, respiratory involvement, urinary retention and the need for nasogastric enteral feeding. Patients who had MFS or received IVIG had greater functional gains. Good functional outcomes occurred in a large majority of patients.

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Introduction

The Guillain-Barré syndrome (GBS) is an acute, frequently severe evolution of a demyelinating inflammatory polyradiculopathy with an autoimmune pathogenesis.[1] In developed countries, GBS is the most common cause of acute neuromuscular paralysis.[2,3] Epidemiological studies give incidence rates of 1 to 2 per 100,000 in the United States and United Kingdom.[4] Approximately 3% to 11% of patients die and 20% suffer from functional deficits years later.[4-6] The Miller-Fisher syndrome (MFS) is the most common GBS variant involving ophthalmoplegia, ataxia and areflexia with minimal weakness.[2,3] Most studies on GBS have focused on diagnostic criteria (both clinical and electrodiagnostic), antecedent events, immunopathogenesis, clinical subtypes and treatment.[3,7] In addition, studies have attempted to identify prognostic factors with regard to a poor outcome. These factors include older age, need for respiratory support, rate of progression, abnormal physiologic characteristics of peripheral nerve function, type of infecting organism, severe paresis and time of

[1] Registrar
[3] Head and Senior Consultant
Department of Rehabilitation Medicine
[2] Consultant
Department of Neurology
Singapore General Hospital, Singapore
[4] Clinical Associate Professor
Department of Physical Medicine and Rehabilitation
Baylor College of Medicine, Houston, Texas, USA
Address for Reprints: Dr Yee-Sien Ng c/o Dr Peter AC Lim, Department of Rehabilitation Medicine, Singapore General Hospital, Outram Road, Block 6 Level 9, Singapore 169608.
Email: ng.yee.sien@singhealth.com.sg or grulac@sgh.com.sg

symptom onset to nadir.[2,6,8-10] The nadir is thought to be the point of maximal neurological dysfunction where outcome and therapeutic intervention are considered critical.[4] Plasmapheresis or intravenous immunoglobulin (IVIG; Intragam P, CSL Ltd, Parkville, VIC, Australia) are currently accepted therapies for GBS, and both have been shown to improve functional outcomes and shorten hospital stays.[2,3,8] Comparisons between these 2 modalities have not been conclusive, and some centres use both.[5]

From the rehabilitation perspective, studies are few and limited mainly to reviews collated from scattered case reports and case series. There are multiple medical and psychological complications that may develop from GBS and these may persist, interfering with rehabilitation or leading to permanent disability.[10,11] In addition, the prevalence of chronic disability secondary to GBS is unknown. However, given the young age at which GBS can occur, the number of individuals with residual functional deficits of GBS is probably significant.[2] There is little epidemiological data for GBS in Asian populations, and even less on functional outcomes and complications during rehabilitation.

In this study, we aim to document demographics and acute injury variables in a group of GBS patients admitted to our institution, including medical complications and functional outcomes during acute rehabilitation. In addition, a comparison of the demographics, clinical variables, complications and functional outcomes with similar studies done in other Western and Asian populations will be made. Finally, we aim to identify prognostic indicators affecting functional outcomes on discharge, and the magnitude of functional gain during their rehabilitation stay.

Materials and Methods

The case records of all patients discharged with a diagnosis of GBS and/or the Miller-Fisher variant from January 2000 to December 2001 in our institution were reviewed. The Department of Neurology managed all the patients and each patient received an individualised rehabilitation programme according to their disease severity. The attending neurologist made interventional decisions, including the need for mechanical ventilation and IVIG.

As far as possible, patients completed their rehabilitation programme in the Department of Neurology and were discharged home directly from the department. A rehabilitation physician was consulted for patients who could benefit from further acute intensive rehabilitation and appropriate patients were transferred to the Department of Rehabilitation Medicine in our institution. Patients who required less intensive, but more prolonged, rehabilitation were transferred *directly* from the Department of Neurology to a dedicated subacute comprehensive rehabilitation facility located away from our institution *after* a period of acute rehabilitation. Further data on patient stay in the subacute rehabilitation facilities were unobtainable.

Patients received an average of 2 hours a day of physical and/or occupational therapy in the Department of Neurology. Patients transferred to the Department of Rehabilitation Medicine benefited from a multidisciplinary team approach led by a rehabilitation physician. Besides physical and occupational therapy, inputs were obtained from other members of the team, such as speech-language pathologists and the medical social worker. Case conferences were held on a weekly basis to review and co-ordinate care.

The demographics, clinical details and medical complications were culled from admission to discharge from the institution. The duration to nadir refers to the time of symptom onset to point of maximal neurological dysfunction. The main functional outcome measure used was the Modified Barthel Index (MBI),[12] with scores ranging from 0 (maximal disability) to 100 (full functional independence). The Expanded Grading Scale (EGS)[8] grades severity utilising clinical features specific to GBS, including involvement of cranial nerves, pattern of motor involvement and the need for mechanical ventilation. Scores range from 0 (healthy) to 9 (complete tetraparesis and need for ventilation), with an additional score of 10 indicating death. The results of both scales were charted within 24 hours of the nadir, and within 48 hours of discharge from the institution.

The SPSS version 9.0 software (SPSS Inc., Chicago, IL, USA) was used for statistical analysis. Unless otherwise indicated, statistical analyses performed are parametric when 2 groups were compared and a P value <0.05 was considered significant.

Results

Thirty-one patients were diagnosed with GBS and 8 (25.8%) patients had the MFS variant. Twenty-two (71%) patients were male and 58% were Chinese, 26% were Malay and the rest were of other races. The mean age was 42.3 years (range, 21 to 81 years). The difference in the mean ages between the GBS and Miller-Fisher variant groups was not significant ($P = 0.12$).

The most common preceding events involved the respiratory tract (32%) followed by non-specific fever with chills (23%). Weakness and numbness of the limbs (74%) were the most commonly reported initial symptoms on admission, followed by aches and pains of various bodily parts (23%) and ophthalmologic symptoms (19%).

On admission, 9 (29%) patients were predominantly paraparetic, 7 (22.6%) were tetraparetic and the rest, except for 1 (only eye findings) patient, had mild patchy muscle

weakness. Pathological eye signs, cranial nerve, bulbar muscle or facial weakness was documented in 11 (35.5%) patients. More patients with MFS had eye signs (Fisher's exact test, P <0.01), compared to the GBS patients.

Subsequently, 16 (51.6%) patients required monitoring in the intensive care unit. Ten (32.3%) patients had significant respiratory involvement documented by a diminished peak expiratory flow rate or on spirometric examination. Five (16.1%) patients had to be mechanically ventilated. There was no significant difference in the number of MFS and GBS patients with respiratory involvement (Fisher's exact test, P = 0.38). Thirteen (41.9%) patients received intravenous immunoglobulin therapy (IVIG) and none had plasmapheresis.

The mean duration to nadir was 8.1 days. The mean MBI at disease nadir and discharge was 54.7 (range, 2 to 93) and 77.3 (range, 9 to 98) respectively, and this improvement was highly significant (P <0.01). The mean MBI gain was 22.6 (range, 4 to 60). The mean EGS at disease nadir and discharge was 5.45 (range, 3 to 9) and 3.87 (range, 1 to 8) respectively; this improvement was also highly significant (P <0.01). Patients who received IVIG had lower MBI and EGS scores at nadir (P <0.01 for both scores). These patients also had lower MBI and EGS scores at discharge

Table 1. Analysis of Possible Functional Outcome Predictors in GBS/MFS

Parameter	Mean MBI at Nadir	Mean MBI at discharge	Mean MBI gain	MBI gain *P* value	Sp.ρ
Sex					
Males (n = 22)	57.1	78.5	15.4	0.51	
Females (n = 9)	48.9	74.6	17.6		
Diagnosis					
GBS (n = 23)	56.4	75.8	19.4	0.05	
MFS (n = 8)	49.6	81.6	32.0		
Intravenous immunoglobulin					
Yes (n = 13)	28.9	61.2	32.2	0.02*	
No (n = 18)	73.3	89.0	15.7		
EGS at nadir					
6 to 10 (n = 18)	27.3	59.5	15.7	0.01*	
0 to 5 (n = 13)	74.4	90.1	32.2		
Time to nadir					
1 to 7days (n = 17)	51.6	75.9	17.0	0.53	
>7days (n = 14)	58.4	79.1	14.7		
Motor impairment on admission					
Paraparetic (n = 9)	58.9	78.7	19.6	0.37*	
Tetraparetic (n = 7)	14.6	49.6	35.0		
Respiratory involvement					
Yes (n = 10)	23.2	55.6	32.4	0.06	
No (n = 21)	69.7	87.7	18.0		
Nasogastric feeding required					
Yes (n = 8)	11.75	49.4	37.6	0.03*	
No (n = 23)	69.61	87.0	17.4		
Initial numbness on admission					
Yes (n = 21)	56.3	80.0	23.7	0.61	
No (n = 10)	51.2	71.1	20.5		
Urinary retention					
Yes (n = 8)	15.3	52.1	19.8	0.01	
No (n = 23)	68.4	86.1	11.0		
Time to nadir (Days)				0.32	-0.19
Age (y)				0.05	-0.18

* indicates the non-parametric Mann-Whitney *U* test used for comparison between two groups,
EGS: Expanded Grading Scale; GBS: Guillain-Barré syndrome; MBI: Modified Barthel Index;
MFS: Miller-Fisher syndrome; n: number of patients; Sp.ρ: Spearman's rho (Spearman's rank correlation)

(P <0.01 for both scores), but had bigger functional gains on the MBI compared with the group who did not receive IVIG (P = 0.02).

Table 1 shows the possible predictors of MBI scores. Tetraparetic patients and patients with respiratory involvement had lower MBI nadir scores (P = 0.01 and P = 0.03, respectively). Predictors of a lower discharge MBI score include an EGS score of ≥6 at nadir (P <0.01), tetraparesis on admission (P = 0.02), presence of respiratory involvement (P <0.01), need for nasogastric enteral feeding (P <0.01) and urinary retention requiring catheterisation (P <0.01). There was no significant correlation between the time of symptom onset to nadir, MBI at nadir (ρ = 0.095, P = 0.61) and MBI at discharge (ρ = 0.04, P = 0.84). There were very good correlations between the EGS and MBI scores across the cohort of patients at nadir (ρ = -0.92) and at discharge (ρ = -0.82).

The Miller-Fisher variant had better functional gains (P = 0.05) on the MBI, as was an EGS score of ≤5 at nadir (P = 0.01). There were no gender differences with respect to the quantum of MBI gain and scores at nadir or discharge.

During their hospital stay, 8 (25.8%) patients experienced urinary retention and all required urinary tract catheterisation. All of these patients were either paraparetic or tetraparetic and 1 patient had strong urge symptoms. Eight (25.8%) patients required nasogastric tube feeding during hospitalisation. One patient developed pneumonia and underwent nasogastric tube insertion. Cardiovascular or autonomic dysfunction, such as electrocardiographic changes, labile blood pressure readings or palpitations occurred in 4 (12.9%) patients. Aches and pain of varying degrees were reported in 22 (71%) patients; 12 had limb pain, 5 had back pain and 5 had generalised pain. Paracetamol (15 patients) was the most commonly prescribed analgesic and vitamin B preparations (10 patients) were also commonly prescribed for altered sensation. Mood changes, which included depression and anxiety, were documented in 14 (45.2%) patients. There were no cases of deep venous thrombosis (DVT), decubitus ulcers, contractures or heterotopic ossification.

Fourteen (45.2%) patients were discharged home directly after rehabilitation in the Department of Neurology and 5 (16.1%) were rehabilitated in the Department of Rehabilitation Medicine prior to discharge. Twelve (38.7%) patients were transferred from the Department of Neurology to a subacute rehabilitation facility after a period of acute rehabilitation. There was a strong association between an MBI score at nadir of <50 (indicating total or severe dependency in functional activities of daily living) and transfer to a subacute rehabilitation facility rather than being discharged home (Fisher's exact test P <0.01). There were no relapses of GBS or mortalities in this cohort during their hospital stay.

Twenty-seven patients returned for follow-up and 17 (63%) patients still experienced residual symptoms or exhibited signs related to the primary illness at a mean of 3 months post-discharge.

Twenty-six (84%) patients were working prior to hospitalisation. Of these, 23 returned for follow-up and 18 (78%) resumed work at a mean of 9 weeks after discharge.

Discussion

Two thirds of our patients had preceding symptoms, with the largest proportion of them having flu-like symptoms, and this is consistent with other studies.[5,13-15] Certain infecting organisms, such as *Campylobacter jejuni*, had reportedly worse outcomes.[2,13] Two of our patients had positive dengue viral serologies, an infection endemic to tropical Asian countries. Further studies are indicated to establish the role of tropical organisms, such as dengue, in the pathogenesis and resultant clinical features of GBS with their corresponding functional outcomes.

At symptom onset, three-quarters of the patients had weakness and numbness of the limbs. This finding was also reported by Taiwanese and Italian GBS study groups.[5,14]

Most of our patients had favourable functional outcomes, with highly significant improvements in the MBI and EGS scores. This concurs with previous large published studies, with 75% to 87% having complete recoveries.[4-6] More than two thirds of our patients had MBI discharge scores >75, indicating only mild to minimal disability; only 3 patients had severe disability on discharge with MBI scores <50.

Similar to previous epidemiological data, our study indicates that males are twice more likely to be afflicted, and that there is no correlation between gender and functional outcomes.[4,5,8] It also seems to support previous observations that GBS in Asian populations seems to occur in younger individuals.[5,6] The impact of the age of the patient on functional outcomes is more conflicting; some reports indicate that older adults had poorer outcomes,[2,14,15] but not in others[8] mainly because of difficulties in controlling for comorbidities that are more prevalent in the elderly. There was no correlation between older age and functional outcomes in our study, but this should be interpreted with caution as our sample size was small.

The mean period from symptom onset to nadir is about 7 to 12 days and our study nadir falls within this range.[4,5,13,14] The clinical severity at nadir, as measured by the EGS, correlates well to a Scandinavian GBS report using the same scale.[8] Generally, an increase in the time to nadir is thought to be a poor prognostic indicator for functional outcome,[6] but there have been exceptions.[5,8] We found no correlation between the time to nadir and functional outcome

scores. In practice, it can be difficult to define the point of nadir clinically as GBS itself has a myriad of manifestations, where different bodily systems may be at varying stages of clinical severity. This lack of consistency has been reported in previous studies.

Our patients who received IVIG showed significantly greater gains in the MBI, similar to previous intervention studies.[3,13] However most centres, including ours, may not intervene if the patient has already begun to show neurological recovery or has not deteriorated significantly. The latter was demonstrated by the group who did not receive IVIG and this group had much higher MBI and lower EDS nadir scores.[6]

Respiratory involvement unequivocally had worse functional outcomes in the literature on GBS. This was true of our study, although patients had greater functional gains compared to those who did not have respiratory involvement.[5,6,8,10,13] Given the same level of respiratory involvement, which is about one third of all GBS patients, half of whom required mechanical ventilation, our rate of pneumonia is much lower than previously reported.[8,13] This could reflect different infecting strains that resulted in GBS or prior vaccination.

In our cohort, tetraparetic patients and those who required nasogastric tube feeding had poorer outcomes. The severity of paresis has been correlated to poorer outcomes previously.[8] The requirement for nasogastric enteral feeding probably reflects involvement of the bulbar cranial nerves and more severe clinical disease.

Micturitional disturbances occurred in about a quarter of our patients and urinary retention was the most common symptom. This was consistent with previous reports and detrusor areflexia, non-relaxing urethral sphincter, disturbed bladder sensation and detrusor overactivity have been known to occur.[16] The need for urinary catheterisation was a poor prognostic indicator in our study. However, only 1 patient required an indwelling catheter on discharge, which is consistent with earlier reports that urological dysfunction usually improves and resolves.[2,13,16] All patients who had urinary retention had either paraparesis or tetraparesis, again likely reflecting more severe disease.

The number of dysautonomic patients was comparatively low and could have reflected differences in monitoring.[6] All presented with cardiovascular abnormalities and occurred in patients who were more severely involved. This group had been previously reported to be at high risk for cardiac arrhythmic deaths and have longer rehabilitation stays, but our small numbers preclude further analysis.[13]

A large number of patients reported pain, with occasional excruciating flares. Pain in GBS may have neuropathic, musculoskeletal or even visceral autonomic characteristics, all of which have been described.[11,13] Various topical and pharmacological agents, including paracetamol, tricyclic antidepressants, antiepileptics and non-steroidal anti-inflammatory drugs, were prescribed based on the pain character with good results.

Paraesthesia did not affect functional outcomes in our study and this is consistent with previous reports.[13] However, it may be disabling and leads to co-ordination and balance issues, as well as safety concerns, and may require specific rehabilitation strategies, such as sensory reintegration exercises. Vitamin B preparations were commonly prescribed for paraesthesia. Although their efficacy has not been proven clinically, patients have reported symptomatic improvements.

Anxiety, insomnia, depression and fatigue were fairly commonly reported symptoms and understandable in previously healthy, working adults. Psychosocial manifestations have been shown to seriously affect many patients even after they have physically recovered and early intervention by neurologists and psychiatrists may be necessary.[10] Hallucinations are a rare complication of GBS; 2 of our patients developed these in association with frank psychotic symptoms. This has been attributed to the sensory and motor denervation in GBS, resulting in confusion between internally and externally generated thoughts and sensations.[17]

There were no cases of DVT or heterotopic ossification identified through routine clinical screening which may have underestimated its true incidence in our study, although these have been described previously.[13] There were also no complications of immobility, such as decubitus ulcers or contractures. Preventive rehabilitation nursing was also emphasised throughout.

A relapse rate of about 13% and a death rate of between 11% and 18% have been reported.[6,14] There were no relapses or deaths in our study. These adverse outcomes might also have occurred in the subacute rehabilitation facility, where data was unobtainable.

Almost half of the patients were discharged home from our institution. The association between a low MBI score and transfer to a subacute rehabilitation facility is a potentially useful one. This result should be validated by larger studies as it could prove important in discharge planning and allocation of hospital resources.

It is encouraging to note that the majority of patients who were actively employed at the time of admission were able to return to work. However, the long-term functional sequelae and associations between ageing and GBS have not been thoroughly investigated;[13] more than half of our patients had residual, albeit mild symptoms. Whether this can cause long-term disability is unknown, although

outpatient therapies seem to benefit patients.[6,15]

We had more patients with the MFS variant, which is consistent with Asian GBS studies, as compared to Western reports.[5,13] In addition, the age distribution between the 2 groups is similar, although previous epidemiological data indicate that MFS patients were older.[5] Subgroup analysis of MFS patients indicate that although their initial and discharge functional status did not differ significantly from the rest of the patients, their absolute functional gain was higher. More surprising is the higher number of MFS patients with respiratory involvement.

The EGS is a more specific scale measuring clinical severity in GBS. Although it has not been used frequently, we found it easy to administer as each grade is well-demarcated.[7] There were good correlations between the EGS and the more widely used MBI and we found that the EGS score at nadir was an independent predictor in functional outcome. The MBI may not be the best general self-care scale as it does not measure cognitive impairments, which have been reported in more severely affected individuals.[6] Other functional outcome measures that contain cognitive components, such as the Functional Independence Measure, may be more useful.[6,18]

There were several limitations in our study. Our sample size was small and may not be truly representative of the entire spectrum of GBS patients. We did not include paediatric patients, as our institution was primarily an adult facility. Some of our patients were discharged to a subacute rehabilitation facility; hence our medical complication rate may have been underestimated. For this reason, analysis of factors affecting length of stay in acute rehabilitation was also difficult. Long-term disabilities and vocational and psychosocial outcomes could not be studied due to the short follow-up period.

Conclusions

The demographics, clinical characteristics and frequency of complications are very similar to those described in earlier cohorts of GBS patients. However, our patients were younger and there were more patients with the MFS variant. Good functional gains were the norm for the majority of patients, and most had minimal disability on discharge. Predictors of a poorer functional outcome include a high EGS score at nadir, tetraparesis, respiratory involvement, urinary retention and need for nasogastric enteral feeding. Patients with MFS, and those who received IVIG had greater functional gains. Respiratory involvement was not uncommon in MFS. The EGS scale was easy to administer, had good correlations with the MBI, and had prognostic value. The majority of patients returned to work, but long-term disability and psychosocial outcomes after severe GBS need further study.

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