Guillain-Barre syndrome – a Sri Lankan profile

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Introduction

Guillain-Barre syndrome (GBS) is a devastating neurological illness, which leads to significant mortality and disability. Its impact is even more serious when considering the fact that most affected individuals are young adults in the prime of their lives. Prompt diagnosis is important as early treatment improves outcome. There has been a resurgence of interest in GBS with the identification of its neurophysiological and pathological subtypes, demonstration of its association with *Campylobacter jejuni* enteritis, and discovery of associated anti-ganglioside antibodies which have some correlation with the disease.

GBS is an acute inflammatory poly-radiculo-neuropathy. It is characterised by acute, hyporeflexic or areflexic, flaccid paralysis. Weakness commonly starts in the lower limbs, but rapidly spreads to involve the upper limbs, and sometimes, the cranial nerves. Sensory symptoms are common, but objective signs unusual. Up to two-thirds of patients have a history of preceding illness, usually a respiratory infection or diarrhoeal illness.

The illness progresses rapidly for a period of up to 4 weeks, followed by a plateau phase of 2-4 weeks, before recovery starts. Death during the acute phase can occur due to involvement of respiratory muscles leading to neuromuscular respiratory failure, aspiration pneumonia, and cardiac autonomic disturbances. Recovery is seldom complete. At one year after the illness, 5-10% of patients would be dead, and 30-40% have residual disability. Only about 50-70% are asymptomatic or are left with only minor symptoms not interfering with their daily lives.

The clinical picture of 'classical' Guillain-Barre syndrome, as described above, is similar throughout the world.[1-10] GBS, however, is pathologically heterogeneous, with the underlying pathological process being demyelination or axonal degeneration.

GBS is an immune mediated disease. The antecedent infection triggers off an immune response which causes damage to neural tissue due to 'molecular mimicry', the presence of identical antigenic epitopes on the pathogen and the peripheral nerves. When these 'shared epitopes' are present on the myelin sheath or the Schwann cells of the peripheral nerves, the immune response damages the myelin, leading to demyelination. When the antigenic epitopes are located on the axonal membrane of the nerves, axonal degeneration results. The pathological type can be neurophysiologically distinguished, enabling classification of GBS into acute inflammatory demyelinating polyradiculoneuropathy (AIDP) or axonal GBS. Axonal GBS is further subdivided into acute motor axonal neuropathy (AMAN) or acute motor-sensory axonal neuropathy (AMSAN), depending on the presence of sensory fibre involvement.

The pathological and neurophysiological type seems to vary according to the geographical location. In North America and Europe, AIDP constitutes 56-87% of GBS cases, and axonal GBS accounts for 3-10%.[2,11-14] In contrast, axonal GBS is commoner in the Far Eastern countries such as China and Japan, ranging from 33% to 98%.[10,15-22] Such distinctions are not merely academic, as the underlying aetiology and the outcome appear to be different. Axonal GBS, especially AMAN in Far Eastern countries, is associated with *Campylobacter jejuni* infection.[12,15,23,24] AMSAN in Western countries is associated with a poor outcome, whereas AMAN in Chinese children is associated with a good prognosis.[15,16,23-25]

Similar data from South Asian countries, especially the Indian subcontinent, are limited. There are no published prospective data on the clinical and electrophysiological patterns, and functional outcome, in patients with GBS in Sri Lanka. Previous studies in Sri Lanka have described management aspects in an ICU setting.[26] and treatment of GBS patients with modified plasma exchange.[27] The third study looked at clinical features and outcome, but was only based on data from retrospective case record evaluation with its inherent drawbacks, and did not have neurophysiological confirmation.[28]

This oration is based on unpublished data from two prospective studies designed to describe the demographic, clinical and neurophysiological characteristics, and the functional outcome at discharge, in patients with Guillain-Barre syndrome in Sri Lanka.

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Study 1 - Guillain-Barre syndrome – a hospital based study*

Study 2 - Guillain-Barre syndrome – a clinical and neurophysiological study*

Both were hospital based studies conducted at the Institute of Neurology, National Hospital of Sri Lanka, Colombo (NHSL). Both prospectively evaluated patients with GBS using similar methodology.

One limitation of the first study (Study 1) was the lack of sensory conduction data on neurophysiological evaluation, due to technical problems encountered during the study period (lack of proper electrodes, etc.). Sensory conduction findings are important to distinguish AMAN from AMSAN, which may have a bearing on prognosis. The second study (Study 2) was designed to overcome this difficulty, with detailed neurophysiological evaluation by a consultant neurophysiologist at the neurophysiology unit of the NHSL.

This oration will summarise the results of these two studies, which taken together, will provide data regarding 117 patients with Guillain-Barre syndrome, the largest body of data on GBS from Sri Lanka to date.

Purpose

The objectives of these two studies were;

1. to describe the demographic and clinical characteristics
2. to determine the neurophysiological subtypes, and
3. to assess the functional outcome at discharge from hospital

in a population of Sri Lankan patients with Guillain-Barre syndrome.

Methodology

Study 1 was conducted over a two year period, from January 1998 to December 1999, and studied 62 patients with GBS. Prior ethical approval for the study was obtained from the Ethical Review Committee of the Faculty of Medicine, Colombo.

Study 2 was also conducted over a two year period, from January 2002 to December 2003, and studied 55 patients with GBS. Prior ethical approval for the study was obtained from the Ethics Review Committee of the Sri Lanka Medical Association.

Both studies employed similar methodology. All consecutive patients with acute flaccid weakness admitted to a Neurology unit of the National Hospital of Sri Lanka, Colombo during the study period and

providing informed consent were considered for enrolment. The entry criteria (see table 1) were based on accepted diagnostic criteria for Guillain-Barre syndrome.[19,29] Data were collected by medical officers, recorded on pre-validated, standardised data record forms, and entered into a database. Antecedent events during the 4 weeks prior to symptom onset were noted. Muscle power was graded from 0 to 5 according to the Medical Research Council (MRC) scale. Disability was graded from 0 to 6 (0- no symptoms, 6-dead) according to a widely used functional scale (see table 2), modified from Hughes et al.[1,30] Presence of unexplained fluctuations in heart rate or blood pressure requiring treatment was considered as significant autonomic involvement.

Table 1. Entry criteria

Inclusion criteria

Progressive motor weakness of more than one limb
Hyporeflexia or areflexia
Relative symmetry
Progression up to a maximum of 4 weeks
Mild sensory symptoms or signs
Absence of fever at onset

Exclusion criteria

Pronounced or persistent asymmetry of weakness
Sensory level
Other identifiable cause such as poliomyelitis, botulism, hysterical neuropathy, porphyria, diphtheria

Table 2. Disability scale

0 - no symptoms
1 - minor symptoms or signs
2 - able to walk 5 m without assistance
3 - able to walk 5 m with assistance or stick
4 - chair or bed bound
5 - requiring assisted ventilation
6 - dead

All patients had neurophysiological evaluation of the neuropathy during the hospital stay using accepted criteria.[9,15] Cases were classified as acute inflammatory demyelinating polyradiculoneuropathy (AIDP) when evidence of demyelination was present in at least two limbs. Electrophysiological findings considered as indicative of demyelination were prolongation of distal latency, reduction of motor conduction velocity, and/or prolongation of F wave latency. Cases were classified

as axonal GBS when compound motor action potential (CMAP) amplitudes were diminished, in the absence of evidence of demyelination. In Study 2, patients with axonal GBS were further subdivided into acute motor-sensory axonal neuropathy (AMSAN) or acute motor axonal neuropathy (AMAN), depending on the presence of sensory involvement. Patients in whom the electrophysiological features were insufficient to confirm demyelination or axonal degeneration were considered as 'unclassifiable'. Routine needle electromyographic (EMG) studies were not done. Cerebrospinal fluid (CSF) analysis was done as part of routine diagnostic work up. Neurophysiological assessment and CSF analysis are standard investigations in GBS. No additional invasive procedures were carried out for the purpose of the studies.

Treatment with specific immuno-modulatory therapy (plasma exchange or intravenous immunoglobulin), and other ancillary treatments were carried out according to clinical need. The studies did not influence the management of patients.

Outcome measures studied were peak motor deficit, peak functional disability, time taken to reach peak disability (time to nadir), need for intensive care, need for mechanical ventilation, duration of stay in the intensive care unit (ICU), duration of mechanical ventilation, death, and disability at discharge.

The demographic, clinical and neurophysiological findings and functional outcome between the two studies were compared using Student's t test, chi square test or Fisher's exact tests. Functional outcome between the AIDP and axonal GBS groups was also compared.

Results

Demographic characteristics

These two studies provide data regarding 117 patients with GBS (Study 1- 62 patients, Study 2 - 55 patients). The demographic features were broadly similar in the two study groups. Two-thirds were males (66.1% in Study 1, 67.3% in Study 2). Age distribution was similar, with young adults being predominantly affected. The mean age in Study 1 was 41.6 (±18.9) years, and in Study 2 was 38.0 (±17.17) years.

A history of antecedent infection in the preceding 4 weeks was common (59.7% in Study 1, 58.2% in Study 2), and this was usually a respiratory infection (54.1% and 53.1% respectively, out of those with antecedent illness).

A preceding diarrhoeal illness was noted in only a few patients (12.9% and 9.4%). There were no cases

related to surgery, vaccination or pregnancy. No definite seasonal variation was observed in the admissions.

Clinical characteristics (Table 3)

The majority (66.1% in Study 1, 60.9% in Study 2) was admitted within seven days of symptom onset, and a further 25.8% and 30.9% respectively presented during the second week of illness.

All patients had limb weakness and hypo/areflexia as they were criteria for inclusion. The illness started with motor symptoms alone in most patients (46.8% and 36.4% respectively), and lower limb involvement was common at onset (87.1% and 61.8%). The maximal recorded weakness was severe (power MRC grade 0-2) in most patients (56.5% and 47.3%). It was mainly noted in the proximal musculature (40.3% and 52.7%). Sensory symptoms were commonly noted (51.6% and 65.5%), with objective sensory signs being unusual (14.5% and 21.8%). Cranial nerve involvement was seen in the majority of patients (50% and 72.7%), with bilateral facial weakness being the commonest (43.6% and 54.5%), and external ophthalmoplegia being rare (2 and 6 patients respectively). Significant autonomic involvement (considered as unexplained tachycardia or fluctuating blood pressure) was observed in many patients (29% and 51%).

Investigations (Table 4)

All patients had neurophysiological evaluation, except one patient in Study 2 who died before assessment. The findings were remarkably similar in the two studies. Acute inflammatory demyelinating polyradiculoneuropathy (AIDP) was the commonest neurophysiological subtype, seen in 42 patients (67.8%) in Study 1, and in 37 patients (67.3%) in Study 2. However, we also observed an unusually high prevalence of axonal degeneration (axonal GBS), seen in 15 patients (24.2%) in Study 1, and in 16 patients (29.1%) in Study 2. Patients with axonal GBS in Study 2 were further subdivided according to sensory findings. Almost all of them were of the acute motor axonal neuropathy (AMAN) type (14 out of 16 patients). Acute motorsensory axonal neuropathy (AMSAN) was rare. Neurophysiological findings were considered as unclassifiable in 5 patients in Study 1, and in one patient in Study 2.

Cerebrospinal fluid (CSF) analysis was done in the acute phase of the illness. CSF protein was elevated (>0.4 g/l) in most patients (67.8% in Study 1, and 69.1% in Study 2), as expected, with levels being more than 1.0 g/l in a large number (30.7% and 43.6%).

Treatment given

The majority of patients (87.5% in Study 1, and

Table 3. Clinical characteristics

	Study 1 (n=62)		Study 2 (n=55)		Total (n=117)	
	no.	*%*	*no.*	*%*	*no*	*%*
Limb weakness	62	100	55	100	117	100
Hypo/areflexia	62	100	55	100	117	100
Onset with motor symptoms	29	46.8	20	36.4	49	41.9
Onset with sensory symptoms	19	30.7	19	34.5	38	32.5
Onset – both sensory & motor symptoms	14	22.6	16	29.1	30	25.6
Onset in lower limbs	54	87.1	34	61.8	88	75.2
Onset in upper limbs	8	12.9	13	23.6	21	18.0
Maximal weakness proximal	25	40.3	29	52.7	54	46.2
Maximal weakness distal	2	3.2	19	34.5	21	18.0
Maximal weakness global	35	56.5	7	12.7	42	35.9
Sensory symptoms	32	51.6	36	65.5	68	58.1
Sensory signs	9	14.5	12	21.8	21	17.9
Cranial nerve involvement	31	50.0	40	72.7	71	60.7
Facial weakness	27	43.6	30	54.6	57	48.7
External ophthalmoplegia	2	3.2	6	10.9	8	6.8
Bladder involvement	14	22.8	7	12.7	21	18.0
Autonomic disturbances	18	29.0	33	60.0	51	43.6

Table 4. Investigations

	Study 1 (n=62)		Study 2 (n=55)		Total (n=117)	
	no.	*%*	*no.*	*%*	*no*	*%*
Neurophysiology						
Demyelination (AIDP)	42	67.8	37	67.3	79	67.5
Axonal degeneration (axonal GBS)	15	24.2	16	29.1	31	26.5
AMAN	-	-	14	25.5	-	-
AMSAN	-	-	2	3.6	-	-
Unclassifiable	5	8.1	1	1.8	6	5.1
Not done	-	-	1	1.8	1	0.9
Cerebrospinal fluid analysis						
Elevated protein	42	67.8	38	69.1	80	68.4
Cells > 5/mcl	8	12.9	10	18.2	18	15.4

83.7% in Study 2) were given immuno-modulatory treatment, in addition to general medical care. This was mainly in the form of plasma exchange (77.4% in Study 1, and 63.7% in Study 2). Out of them, most patients had only one exchange (37.1% in Study 1, and 48.6% in Study 2). Only a few patients received intravenous immunoglobulin (IVIg) therapy (6 in Study 1, and 19 in Study 2).

Clinical course and functional outcome
(Tables 5,6,7)

The peak motor deficit was reached within 7 days in most patients (51.6% in Study 1, and 43.6% in Study 2). The mean time to nadir was 8.45 days ($\pm$5.56) and 10.6 days ($\pm$10.6) respectively. Peak disability at nadir was severe (grade $\geq$ 4) in the majority of patients (67.7% in Study 1, and 80% in Study 2), and was considered mild (grade $\leq$ 2) in only 3 and 9 patients respectively.

A large number of patients required admission to an intensive care unit (ICU); 28 patients (45.2%) in Study 1, and 24 (43.6%) in Study 2. Respiratory involvement was the commonest cause for admission to the ICU. Mean duration of stay in the ICU was 20.6 ($\pm$14.6) days and 17.46 ($\pm$11.81) days, respectively. Respiratory involvement (vital capacity <20 ml/kg) was a common complication, seen in 29 patients (46.8%) in Study 1, and in 23 (41.8%) in Study 2. A large

proportion of them required mechanical ventilation (27.4% in Study 1, 32.7% in Study 2). Mean duration of ventilation was 15.1 ($\pm$13.9) days and 13.61 ($\pm$9.03) days, respectively.

Majority needed to be in hospital for more than two weeks (56.5% in Study 1 and 43.6% in Study 2), with the mean duration of hospital stay at the NHSL being 21.6 ($\pm$13.4) days and 18.93 ($\pm$12.06) days. At the time of discharge, many patients had significant residual disability. A large number (40.7% and 44%) were chair-bound or bed-bound on discharge. Only a minority (17% and 36%) had mild disability, being able to walk home without assistance. Death (functional grade 6) occurred in 3 patients in Study 1, and 5 patients in Study 2, during the hospital stay.

Comparison between Study 1 and Study 2

The two studies were broadly similar in all the aspects studied; demographic features, main clinical features, neurophysiological types, CSF findings, and functional outcome (Tables 3,4,5,6, and 7). Statistically significant differences were noted only with regard to site of symptom onset (lower limbs commoner in Study 1, p=0.016), cranial nerve involvement (more in Study 2, p=0.012), autonomic involvement (more in Study 2, p=0.007), number of patients with mild disability at peak of illness (peak disability $\leq$ grade 2 more in Study

Table 5. Clinical course and functional outcome

	Study 1 (n=62)		Study 2 (n=55)		Total (n=117)	
	no.	*%*	*no.*	*%*	*no*	*%*
Peak disability $\geq$ grade 4	34	54.8	44	80	78	66.7
Time to peak motor deficit –						
1-7 days	32	51.6	24	43.6	56	47.9
8-14 days	22	35.5	17	30.9	39	33.3
15-21 days	5	8.1	8	14.5	13	11.1
more than 21 days	3	4.8	6	10.9	9	7.7
Needed ICU care	28	45.2	24	43.6	52	44.4
Respiratory involvement	29	46.8	23	41.8	52	44.4
Needed assisted ventilation	17	27.4	18	32.7	35	29.9
Duration of ventilation –		(n=17)		(n=18)		(n=35)
1-7 days	4	23.5	5	27.8	9	25.7
8-14 days	9	52.9	6	23.3	15	42.9
15-21 days	0	0	4	22.2	4	11.4
more than 21 days	4	23.5	3	16.7	7	20.0
Death	3	4.8	5	9.1	8	6.8

Table 6. Outcome – Peak disability

	Study 1 (n=62)		Study 2 (n=55)		Total (n=117)	
	no.	*%*	*no.*	*%*	*no*	*%*
0 - no symptoms	0	0	0	0	0	0
1 - minor symptoms or signs	0	0	1	1.8	1	0.9
2 - able to walk 5 m without assistance	3	4.8	8	14.5	11	9.4
3 - able to walk 5 m with assistance	17	27.4	2	3.6	19	16.2
4 - chair or bed bound	22	35.5	26	47.3	48	41.0
5 - requiring assisted ventilation	17	27.4	13	23.6	30	25.6
6 - death	3	4.8	5	9.1	8	6.8

Table 7. Outcome – Disability at discharge

	Study 1 (n=59)		Study 2 (n=50)		Total (n=109)	
	no.	*%*	*no.*	*%*	*no*	*%*
0 - no symptoms	0	0	0	0	0	0
1 - minor symptoms or signs	0	0	9	18	9	8.3
2 - able to walk 5 m without assistance	10	17.0	9	18	19	17.4
3 - able to walk 5 m with assistance	25	42.4	10	20	35	32.1
4 - chair or bed bound	24	40.7	22	44	46	42.2
5 - requiring assisted ventilation	0	0	0	0	0	0

(8 patients died during hospital stay – 3 in Study 1, 5 in Study 2)

2, p=0.0403), and number of patients with mild disability at discharge (disability at discharge ≤ grade 2 more in Study 2, p=0.233). There were no statistically significant differences between the two studies in the other parameters studied.

Functional outcome: AIDP vs. axonal GBS
(Table 8)

We compared the functional outcome in the two main neurophysiological subgroups, AIDP and axonal GBS. Outcome was noted to be poorer in patients with axonal GBS. In this group, hospital stays were longer (p=0.0104), ICU stays were longer (p=0.038), duration of ventilation was longer (p=0.05, of borderline

significance), peak disability was more severe (p=0.0128), and disability at discharge was more severe (p=0.0044). Recovery was better (disability ≤ grade 2 on discharge) in the patients with AIDP (p=0.0058). There were no significant differences between the two groups in age distribution, sex distribution, time to nadir, and the number needing ICU care or ventilation.

Discussion

With the eradication of poliomyelitis being almost a reality, GBS has emerged as the commonest, and the most important, cause of acute flaccid paralysis. These two prospective studies conducted over a period of four years, taken together, provide a large collection

Table 8. Functional outcome – AIDP vs. Axonal GBS

	AIDP no. (n=79)	Axonal GBS no. (n=31)	X^2	p
Male sex	54	18	1.04	0.3072
Time to peak disability < 1 week	27	9	0.27	0.6049
Peak disability ≥ grade 4	53	28	6.19	0.0128
Peak disability ≤ grade 2	11	1	2.62	0.1054
Needed ICU care	34	15	0.26	0.6116
Needed assisted ventilation	21	11	0.86	0.3551
ICU stay >2 weeks	14	11	4.31	0.0380
Duration of ventilation >2 weeks	4	6	-	0.0502*
Hospital stay >2 weeks	40	24	6.57	0.0104
Disability at discharge ≥ grade 4	26	19	8.11	0.0044
Disability at discharge ≤ grade 2	25	2	7.6	0.0058

* denotes p value obtained on Fisher's exact testing, where numbers were small

of data on 117 patients regarding this uncommon, yet serious, neurological illness. The two studies were comparable, as they were conducted in the same setting, over a similar duration, with identical inclusion and exclusion criteria, and using similar methodology. The results from the two studies were broadly similar, allowing these data to be collated and analysed together. This also highlights the similarity between the two patient populations, and therefore the validity and reproducibility of the data from the two studies.

Most series of GBS report a male preponderance. Only a slight excess of males (M:F ratio 0.8 to 1.3:1) has been reported from the Caucasian populations,[1,2,5,6,31-33] while a relatively higher proportion (1.9 to 2.3:1) has been reported from the Asian countries.[7-9,16,34] Our finding of a male: female ratio of 2:1 was similar to the Asian figures. Interestingly, comparatively higher male prevalence rates have been noted with cases of AMAN,[9,15] and the high prevalence in males reported from Asian series may be due to the higher frequency of axonal GBS.

Some studies have previously shown a bimodal age distribution with peaks occurring in young adults and elderly,[6,31-33,35] or an increase with age with a peak in the elderly.[3,4,5,36,37] The main exceptions to this have been the reports of GBS occurring predominantly in children from Northern China.[10,15,16] In our series, the majority were young adults, as noted by Kaur et al and Dowling et al.[7,33]

An antecedent infection was noted in 59% in our patients. This figure is similar to many series where such an event was recorded in 55-71.5% patients. This was usually a respiratory infection, similar to descriptions from the Western countries.[31,37,38] Unlike reports from the Far Eastern countries, a preceding diarrhoeal illness was not a prominent feature in our study.

We did not find a seasonal preponderance, a finding seen in studies from European countries.[3-5,31,36,39] Lack of a seasonal variation in GBS, in spite of its obvious association with infection, is attributed to the opposite seasonality of the antecedent respiratory and gastrointestinal infections.[31] This is in contrast to the marked seasonal preponderance of GBS seen in summer epidemics of AMAN in Northern China, where it is associated with campylobacter enteritis.[10,15-17] Clinical and laboratory features in our patients were characterised by prominent motor weakness with hyporeflexia or areflexia, common sensory symptoms but few objective sensory signs, cranial nerve involvement usually with bilateral facial weakness, and elevated CSF protein with few cells. These are similar to the previous descriptions of 'classical' GBS.[1-9, 33]

Immuno-modulation by plasma exchange or intravenous immunoglobulin (IVIg) is the mainstay of therapy in GBS. The studies did not influence the decisions regarding institution of treatment or the type of treatment. Five plasma exchanges are usually recommended, but most of our patients received only one due to the logistic difficulties and the cost per procedure. IVIg, the most widely used treatment in the Western countries, was hardly used due to its prohibitive cost in Sri Lanka.

The clinical course of GBS in our patients is similar to what has been described previously. Assisted ventilation was required in 25.6%, similar to the figures of 23-33% previously reported.[1,5,10,33,34] The mean duration of ventilation was 15.1 days and 13.6 days in the two studies, similar to previous findings from elsewhere.[2,9,34] The mean duration of hospital stay was 21.6 days and 18.9 days respectively, compared to a range of 21-66 days in other studies.[3,5,7,9,29] Mean time to nadir was 8.45 days and 10.6 days in the two studies, compared to 5-9 days reported in the literature.[2,5,7,9,10] Hospital mortality was 6.8%, comparable to the mortality rates seen in most series (3.9-11.1%).

The description of 'an axonal form of Guillain-Barre syndrome' in 1986,[25] transformed the outlook on GBS and rekindled interest in its aetiology and pathological mechanisms, stimulating a large amount of new research. Hitherto considered a homogeneous clinical and pathological entity of an acute demyelinating neuropathy, it paved the way to the recognition of many cases of acute flaccid paralysis due to axonal neuropathy as of GBS, such as the summer outbreaks of AMAN from Northern China.[10,15-23] AIDP was the neurophysiological type in 67.5% in our study, and 26.5% had axonal GBS. These figures lie in between the predominantly demyelinating picture seen in the Western countries, and the acute axonal forms seen in the Far East. Our rate of axonal GBS was much higher than the rates (3-10%) described from the Western countries.[2,11,12,6] However, we did not observe the predominance of axonal GBS over AIDP. Out of the patients with axonal GBS, the majority (14 out of 16) were of the AMAN type, similar to other Far Eastern data. Outcome in patients with axonal GBS is reported to be less favourable, when compared to AIDP.[12,23,24,25] Our findings were similar, on comparing the pooled data on AIDP and axonal GBS from the two studies.

Limitations

Although originally planned, we were unable to perform sensory conduction studies in Study 1 due to technical problems encountered with the sensory recordings. Sensory studies are essential to enable proper classification of GBS, especially the axonal syndromes into acute motor or acute motor-sensory axonal neuropathies (AMAN, AMSAN). This limitation

was overcome in the second study. The patients with axonal GBS in Study 2 were mostly of the AMAN type, and the AMSAN group was too small (2 out of 16) to enable any meaningful comparisons between these two groups.

We did not routinely investigate for an underlying aetiology in all patients, and in the cases investigated for an antecedent infection as part of the diagnostic work-up, the yield was low. Detailed investigations for aetiology should form a part of future studies, especially conditions such as *Campylobacter jejuni* infection, as the clinical features and the outcome may vary according to the underlying cause that triggers off GBS.

This was a hospital based study, and hospital-derived data cannot be readily extrapolated to a population at large. However, most patients with GBS seek admission to hospital due to the serious nature of the illness. The Institute of Neurology, NHSL is the final referral centre for neurological illness in Sri Lanka, and most patients with GBS are transferred there for tertiary care including plasma exchange. Furthermore, community based data are virtually impossible to obtain in GBS, due to its low incidence, and the need for hospital evaluation to establish the diagnosis. Almost all the reports in the literature are based on hospital derived data. Therefore, we believe these findings would be representative of the disease pattern in Sri Lanka.

Conclusions

Our results suggest that the pattern of clinical characteristics in Sri Lankan patients with GBS is similar to the classical picture of GBS described from other countries.

The neurophysiological characteristics lie in between the two ends of the spectrum represented by the West and the Far East, raising the possibility of an intermediate phenotype of GBS, which we can only speculate at. It may be interesting to observe whether a similar pattern exists in our neighbouring countries in South Asia, especially the Indian subcontinent. More research needs to be done to explore this possibility, as well as identify the aetiological factors and factors governing outcome in our population. We also need to look at the disease pattern and outcome in children, a group in which data on GBS are scanty. It is indeed surprising that only a handful of studies have been carried out on GBS in this country to date, considering the serious nature of the illness. A large multicentre study would be the way forward, to generate sufficient numbers needed to arrive at meaningful conclusions, especially regarding aetiology.

If our efforts to eradicate poliomyelitis from Sri Lanka are to succeed, we need to be able to rapidly and properly evaluate all patients with acute flaccid

paralysis. GBS constitutes the majority of these patients. Facilities essential for diagnosis, such as neurophysiological assessments, are not available in most hospitals in the periphery where these patients would first present. Evaluation for underlying aetiological factors is vital, as recent studies have repeatedly shown the diversity in neuropathology and outcome in relation to aetiology. Facilities for aetiological diagnosis, even of the commonest responsible agents such as Campylobacter jejuni and common viruses, are not available even in the best of centres in Sri Lanka.

Treatment for GBS with plasma exchange or intravenous immunoglobulin is effective. However, these are available only in a handful of teaching hospitals in the country. Even where available, cost and logistic constraints preclude the delivery of ideal treatment (such as five plasma exchanges), as noted in our studies. Good supportive care is imperative in the acute phase, where ICU care and assisted ventilation can be life saving. Facilities for ICU care and ventilation are grossly inadequate in Sri Lanka, especially in the outstations.[40] The lack of diagnostic and treatment facilities in the centres where these patients are first seen and acutely managed results in an influx of these patients to the National Hospital of Sri Lanka, Colombo (NHSL). This leads to unnecessary and avoidable delays in providing effective care which may adversely affect outcome, especially when requiring ventilation. This also entails enormous 'hidden' costs of transport, which we can ill afford.

IVIg is at least as equally effective as plasma exchange (PE). It is the preferred treatment in Western countries, especially considering its ease of use. The costs of the two treatments are considered to be similar, when one considers the cost of ancillary materials and skilled manpower needed in PE, which is a labour-intensive and time-intensive procedure. PE may not be a reality in all peripheral hospitals, due to its inherent need for prohibitively expensive equipment and technical expertise. However, provision of IVIg in the peripheral hospitals, at least in the main provincial and base hospitals, could possibly transform the outcome in our patients with GBS. If effective treatment can be administered early at the time and place of presentation, the need for ICU care, ventilation, and prolonged hospital stays, and transfers to the NHSL for PE can all be minimised.

GBS exacts a heavy toll on the patients, their families, and the health care delivery systems. The impact of disability on a young adult in his or her prime, with the resultant loss of earning capacity, sexual difficulties, effects on marital harmony, loss of self esteem, and psycho-social consequences, cannot be measured in mere economic terms. It is imperative that facilities for the effective management of this devastating illness are made readily available in all parts of the country.

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