PROGNOSTIC INDICATORS IN GUILLAIN-BARRÉ SYNDROME WITH SPECIAL REFERENCE TO SERUM ALBUMIN

Submitted in partial fulfilment of the rules and regulations for the requirement of the degree of

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INDEX

INTRODUCTION

Introduction

Guillain Barre syndrome (GBS) is a common cause of neuromuscular paralysis, the annual incidence of which is reported to be 0.81–1.89 per 100,000 person–years.[1] It is characterised by the combination of rapidly progressive symmetrical weakness in the limbs with or without sensory disturbances, hypoflexia or areflexia, with or without involvement of respiratory muscles or cranial nerve-innervated muscles, with or without autonomic dysfunction, in the absence of a CSF cellular reaction. [2] According to the clinical criteria, maximum weakness is reached within 4 weeks, but most patients usually reach their maximum weakness within 2 weeks.[34] Patients then have a plateau phase of varying duration, ranging from 2 days to 6 months (median duration 7 days), followed by a usually much slower recovery phase. [4,5]. In patients with GBS who have inability to walk (severely affected patients), about 25% eventually need artificial ventilation because of weakness of the respiratory muscles. Despite treatment with IVIg or Plasma exchange, about 20% of severely affected patients remain unable to walk after 6 months. [6] Hence, the prognosis of GBS is tough to predict because of the considerable variation in outcome. In the past few decades, the GBS Disability Scale by Hughes et al has been used as an outcome scale in the majority of clinical trials in GBS. [7] Nevertheless, it is essential to foresee the outcome of GBS, as those likely to have a severe disease may require more aggressive therapy. Certain indicators postulated to be of prognostic significance are - higher age (>40 or

>50 years), preceding diarrhoea, severe weakness with consequent low MRC score on admission and high early GBS disability grade. Electrophysiologically, the most consistently described finding predictive of poor outcome has been low mean or summated CMAPs. [7,8] The Erasmus GBS outcome score has been used to predict inability to walk independently after 6 months, and consists of—the GBS disability score at 2 weeks after admission, age and presence of preceding diarrhea. [9]

Hence, the current prognostic models are based predominantly on clinical features, but there is a lack of a serologic biomarker to enhance these models. At present no biomarkers are available to assess the extent of peripheral nerve damage or to predict outcomes in immune-mediated neuropathies. Serum albumin has already been established as a prognostic marker in various pathological conditions like amyotrophic lateral sclerosis, cancer,in geriatric long-term care facility residents,individuals undergoing surgical interventions,patients with kidney disorders, and predicts failure of IVIG therapy in Kawasaki disease. It is unclear whether in these conditions albumin levels are a marker of patients' nutritional status or chronic inflammatory state, which decreases the hepatic synthesis of albumin through the production of proinflammatory cytokines [10].

In this study, we aim to ascertain if serum albumin levels can serve as a prognostic biomarker in patients with GBS. This would help in anticipating treatment outcomes, and in deciding which patients need early and more aggressive therapy in clinical practice

REVIEW OF LITERATURE

Review of Literature

Guillain Barre Syndrome was first described by Jean-Baptiste Octave Landry in 1859 who documented 10 cases of acute ascending paralysis that conformed to the current concept of GBS but lacked information regarding areflexia and CSF albuminocytological dissocation.[11] These discovery of deep tendon reflexes and lumbar puncture set the stage for the seminal paper of Guillain, Barre´ and Strohl in 1916, which described 2 soldiers with similar clinical features, loss of tendon reflexes and albumonocytologic dissociation. [12]. It is the most common and most severe acute paralytic neuropathy characterised by rapid progression of limb weakness, often with sensory and cranial nerve involvement 1–2 weeks after immune stimulation, reaching the maximum severity 2–4 weeks after onset, followed by a plateau.[5,13]. In addition, there is hypoflexia or areflexia, in the absence of a CSF cellular reaction. The diagnosis is largely dependent on clinical assessment, because diagnostic biomarkers are unavailable for most variants of the syndrome.

Epidemiology and preceding infections

Most studies measuring the incidence of GBS were done in Europe and North America,and showed a range of 0·8–1·9 (median 1·1) cases per 100 000 people per

year. [1]. Seasonal variations in the incidence of GBS (seen more commonly in the winter and rainy seasons) has been reported in various parts of India. [14] . This can be explained by the fact that the major preceding infections like gastroenteritis and Influenza tend to occur during these seasons.

Infection or any other immune stimulation produces an abnormal autoimmune reaction against peripheral nerves and their spinal roots in GBS.[15] Molecular mimicry between microbial and nerve antigens is implicated to be the main driving force behind the development of the disorder. Campylobacter jejuni induced gastroenteritis is the most common infection, found in 25–50% of patients, more prevalent in Asian countries.[1617] Other infections known to precede GBS are cytomegalovirus (CMV), Epstein-Barr virus, influenza A virus, Mycoplasma pneumoniae, and Haemophilus influenzae. [1819]. C jejuni is usually associated with acute motor axonal neuropathy (AMAN) variant of GBS, which usually has a more severe weakness and poorer outcome. It is also related to an antibody response to GM1 and GD1a gangliosides [20,21]. GBS has also occured soon after vaccination with Semple rabies vaccine and various types of influenza A virus vaccines. [22]The interval between the prodromal infection and the onset of GBS symptoms varies between 1 week and 3 weeks, with an average of 11 days in some studies.[23].

Clinical spectrum and variants

The diagnostic criteria used for GBS is the Asbury criteria [3], in which the features needed for the diagnosis are progressive weakness in the legs and arms, and areflexia. The additional features mentioned in this criteria are presence of a progressive phase

lasting for days to 4 weeks (often 2 weeks), relative symmetry, mild sensory symptoms or signs (not present in acute motor axonal neuropathy), cranial nerve involvement (especially bilateral weakness of facial muscles), autonomic dysfunction and pain. However, GBS is a heterogeneous disorder and has many variants have been described based on the types of nerve fibers involved (motor, sensory, sensory and motor, cranial or autonomic) and predominant mode of fiber injury (demyelinating versus axonal). Apart from the classic GBS, the first GBS variant was Miller Fisher Syndrome (MFS) which includes a triad of ophthalmoplegia, ataxia, and areflexia without any weakness [24]. Some MFS cases may progress to classic GBS and, 5% of typical GBS cases may have ophthalmoplegia. The pharyngeal-cervical-brachial motor variant was described in up to 3% characterised by ptosis, facial, pharyngeal and neck flexor muscle weakness which eventually involves the arms and spares the legs, sensory system and reflexes. Hence it closely resembles botulism. A paraparetic motor variant is also seen, though much less commonly. It affects the only the legs with areflexia, may be associated with backache and mimicks an acute spinal cord lesion [25]. Other rare entities are the pure sensory ataxic and pandysautonomic variants without predominant weakness. The first description of an axonal variant of GBS was in 1986 [26] , following which an axonal motor variant of GBS termed acute motor axonal neuropathy(AMAN) was reported in 1993 from Northern China [27]. Subsequently, cases acute motor and sensory axonal neuropathy (AMSAN) were also reported [28] . AMAN and AMSAN are associated with C. Jejuni infection which is alone a poor prognostic factor, as mentioned earlier [29]. Patients with AMAN have a more rapid progression of weakness to an earlier nadir than in AIDP resulting in prolonged paralysis and respiratory failure over a few days [30]. In AMAN, patients present with symmetric proximal and distal

weakness without sensory involvement, preceded by C. Jejuni enteritis and may have normal or brisk tendon reflexes.

20–30% of patients with GBS can progress to have respiratory failure requiring ventilatory support at an intensive care unit (ICU).[13] Around 25% of patients experience deterioration during or soon after treatment with IVIg or plasma exchange. However, it does not indicate treatment resistence, and implicates that they would have been worse without treatment. [31] The severity and duration of disease is extremely hetereogeneous and can range from mild weakness, from which patients recover spontaneously, to patients becoming quadriplegic and ventilator-dependent without signs of recovery for several months or longer. Eventually, all patients start improving, although recovery could follow a prolonged course and result in severe, permanent disability. During the acute phase, the stable phase, or even during recovery, patients might have signs or symptoms of autonomic dysfunction. [32]

Electrophysiology

Nerve conduction study (NCS) can contribute the reaching the diagnosis and to differentiate between axonal and demyelinating subtypes. Nerve conduction findings can be normal initially and abnormalities are usually maximum 2 weeks after start of weakness.[33]. NCS helps clinicians to classify GBS into AIDP, AMAN or AMSAN.[29] NCS in patients with AIDP is characterised by prolonged distal motor latency, reduced nerve conduction velocity, prolonged F-wave latency, increased temporal dispersion, and conduction blocks. The sural sensory potential is often spared.[34] Features of axonal GBS (AMAN or AMSAN) are decreased motor, sensory amplitudes, or both. Some patients have transient conduction blocks or slowing that quickly recovers during the course of the disease, called reversible conduction failure.[3536] and serial NCS over weeks are required to

reliably distinguish between these two types of GBS. The transient blocks are hypothesised to be caused by impaired conduction at the node of Ranvier, because of the effects of anti-ganglioside antibodies which target the same.

Treatment

Treatment comprises of supportive care to prevent or manage complications and immunological treatment. [32]. Supportive measures include monitoring of respiratory, cardiac and hemodynamic parameters, prompt transfer to ICU when required, prophylaxis for deep vein thrombosis, early initiation of physiotherapy and rehabilitation, and psychosocial support.

A systematic review in 2007 concluded that both IVIg and plasma exchange were equally effective in GBS. [6] Subsequently, several randomised controlled trials (RCTs) studying the effect of immunotherapy in GBS have also demonstrated this.[31,37] However, most of these studies were done in Europe and North America where most patients have the AIDP type of GBS. Immunotherapy should be started as soon as possible in patients requiring the same, prior to irreversible nerve damage taking place. Five plasma exchange sessions (each exchange comprising 2–3 L of plasma according to bodyweight) over 2 weeks is the regimen advised, and it has to be started within the first 4 (preferably 2) weeks from onset in patients with GBS who are unable to walk unaided (Hughes disability score >2).[37,6] .

IVIg is also proven to be effective, in patients unable to walk unaided, when started within the first 2 weeks after onset of weakness. It is recommended to give a total IVIg dose of 2 g/kg bodyweight over 5 days. Both oral steroids and intravenous methylprednisolone do not have any proven benefit in GBS. [38].

Eculizumab (a humanised monoclonal antibody that binds with high affinity to the complement factor C5 and prevents its cleavage to C5a and the proinflammatory, cytolytic C5b-9 complex) has also been investigated as a potential therapy for GBS.[39,40]However a

randomised phase II trial comparing eculizumab and placebo failed to demonstrate a significant difference in the primary outcome (the proportion of patients with restored ability to walk independently [functional grade ≤2] at week 4).[41]

Outcome and prediction of outcome

The outcome of GBS is heterogeneous and varies from person to person. Some patients develop orofacial, bulbar ,respiratory involvement and severe limb weakness within days and remain bedridden or wheelchair bound. Others have weakness from which they recover spontaneously within weeks.Advances in supportive measures and immunotherapy has greatly improved the outcome in GBS. Nevertheless, around 20% of patients with GBS cannot walk unaided 6 months after onset. [22]. Mortality rates in Europe and North America vary between 3% and 7%, and more widely in other countries where data are available.[16,42,43]. The mortality in an Indian cohort of 273 patients was 12.1%.[44]. The cause of death is usually respiratory involvement, or from autonomic dysfunction including arrhythmia. Maximum recovery occurs in the first year, but patients might show further improvement even after 3 or more years.[22]

Prognostic models could help to identify patients who require careful monitoring and aggressive treatment. In order the facilitate this, a scoring system was formulated in 2007, called the Erasmus GBS outcome score (EGOS), which included three variables that were predictive of poor outcome at 6 months in the model, i.e, age, preceding diarrhoea, and GBS disability score at 2 weeks after entry.[9] It could be used 2 weeks after admission to predict the patient's ability to walk at 6 months. The scoring system is as follows:

Table 1. Erasmus GBS outcome score

	Categories	**Score**
Age at onset (years)	>60	1

	41–60 ≤40	0·5 0
Diarrhoea (≤4 weeks)	Absence Presence	0 1
GBS disability score (at 2 weeks after entry)	0 or 1 2 3 4 5	1 2 3 4 5
Erasmus GBS outcome score		1–7

Predictions corresponding to these prognostic scores ranged from 1% to 83% for the inability to walk independently at 6 months.

The modified Erasmus GBS outcome score introduced in 2011, used the Medical Research Council (MRC) Scale for Muscle Strength score instead of GBS disability score and can predict outcome as soon as 1 week after admission, when therapeutic interventions are likely to be more effective. [45].

Table 2. Modified GBS Outcome score

Prognostic factors		**Score**
Age at onset (years)	≤40 41–60 >60	0 1 2

Preceding diarrhoea	Present Absent	1 0
MRC sumscore (at day 7 of admission)	51-60 41-50 31-40 0-30	0 3 6 9
Modified Erasmus GBS outcome score		0-12

Another scoring system used to predict the risk of respiratory insufficiency in GBS is the Erasmus GBS Respiratory Insufficiency Score (EGRIS), which is based on the severity of weakness (expressed as MRC sum score); onset of weakness; and facial palsy, bulbar weakness, or both. [46]

Table 3, Erasmus GBS Respiratory Insufficiency Score

Measure	**Categories**	**Score**
Days between onset of weakness and hospital admission	7 days 4–7 days 3 days	0 1 2
Facial and/or bulbar weakness at hospital admission	Absence Presence	0 1
MRC sum score at hospital admission	60–51 50–41 40–31 30–21 ≤ 20	0 1 2 3 4
EGRIS		0-7

The scoring system ranged from 0 to 7, with corresponding chances of respiratory insufficiency from 1 to 91%.

A study by Durand et al showed that demyelinating GBS and presence of conduction block in the peroneal nerve was associated with a high chance of needing artificial ventilation[47]

Role of biomarkers in prediction of outcome

The drawback of the existing prognostic models is that they are based on clinical features and demographic factors, and there is a requirement to find a serological biomarker that can enable to anticipate the treatment outcome earlier in the course of the disease. In this early phase of disease, it is more likely that intensified treatment is still effective because irreversible nerve damage has not yet occurred.

Petzold et al. studied if neural protein levels in CSF have prognostic value in patients with GBS and found that concentrations of the glial protein markers S100-B and glial fibrillary acidic protein (GFAP) were significantly higher in the CSF of patients with GBS than in controls,but were not associated to outcome. However, elevated levels of the axonal proteins neurofilament heavy chain and tau were associated with poor outcomes, as measured by the GBS disability score. [48].

A simple biomarker that was found to have utility in predicting outcome is GBS by Fokkink et al was serum albumin. [49]. They found that low pretreatment serum albumin level was associated with respiratory failure and lower MRC sum score at nadir . The study also revealed that patients with low serum albumin levels after treatment with IvIg also required mechanical ventilation more frequently and had a poorer GBS disability score and MRC sum score throughout and at the end of follow-up (all $P < .001$). Hence serum albumin was considered a potential biomarker for predicting outcome in GBS, as it is a routinely measured protein already established to have prognostic value in various

conditions like amyotrophic lateral sclerosis and failure of IvIg therapy in Kawasaki disease.[10,50,51].In addition, a low serum albumin level is also an important marker of poor outcome in the setting of acute illness. [5253] Studies focusing on ICU and critically ill patients identified serum albumin as a biomarker for survival and the need for mechanical ventilation.[54,55,56]

The main reason for a decrease in serum albumin levels are increased catabolism, decreased production, and extravasation attributable to increased capillary permeability in the setting of inflammation or severe disease.[50,57,58]. All 3 causes have beenhypothesised to contribute to the observed reduced serum albumin levels in GBS. In addition, high dose IVIG treatment in disorders other than GBS is associated with a reduction of the serum albumin level likely to be due to exhaustion of albumin and IgG recycling pathway via FcRn that binds both proteins. [59,60,61]

The ongoing International GBS Outcome Study (IGOS) is a prospective, observational, multicenter cohort study that aiming to identify the clinical and biological determinants and predictors of disease onset, subtype, course and outcome of GBS which has been started in May 2012, conducted by the Inflammatory Neuropathy Consortium (INC). It includes information about demography, preceding infections, clinical features, diagnostic findings, treatment, course, and outcome and in addition, cerebrospinal fluid and serial blood samples for serum and DNA arecollected at standard time points. The results of this study are still awaited. [62]

AIMS AND OBJECTIVES

Aims of the study

1. To study the correlation between the pretreatment serum albumin levels with the three month clinical outcome in GBS

2. To identify any other clinical and electrophysiological determinants of outcome in GBS

MATERIALS AND METHODS

Materials and Methods

This was an observational (retrospective - prospective) study in patients with GBS. Patients with the diagnosis of GBS admitted to the Neurology ward and Neuromedical ICU in Sree Chitra Tirunal Institute for Medical Sciences and Technology were considered for the study. The retrospective arm of the study included patients fulfilling

the eligibility criteria from January 2012 to the date of IEC approval and the prospective arm included patients consenting for the study from the date of IEC approval to April 2019. A total of 47 patients were included in this study over the study period of 87 months from January 2012 to April 2019.

Retrospective arm:

Inclusion criteria:

1. Age more than 12 years
2. Patients fulfilling the Asbury Cornblath criteria for Guillain Barre syndrome

Exclusion criteria

1. Patient admitted after 1 month of symptom onset
2. Pre-treatment serum albumin level not available in the charts
3. Nerve conduction study not available within 1 month of disease onset
4. Atypical forms of GBS like Miller Fisher syndrome and acute sensory neuropathy
5. Patients with chronic illnesses prior to onset of GBS, like chronic liver disease, chronic kidney disease, malignancies and sepsis which can potentially affect the serum albumin levels

Prospective arm

Inclusion criteria:

1. Age more than 12 years

2. Patients fulfilling the Asbury Cornblath criteria for Guillain Barre syndrome

Exclusion criteria

1. Patient admitted after 1 month of symptom onset
2. Atypical forms of GBS like Miller Fisher syndrome and acute sensory neuropathy
3. Patients with chronic illnesses prior to onset of GBS, like chronic liver disease, chronic kidney disease, malignancies and sepsis which can potentially affect the serum albumin levels
4. Patient not consenting for the study

In the retrospective arm of the study, demographic data, clinical features at admission, electrophysiological data, blood investigations including serum albumin level and CSF investigations, treatment given and disease course was extracted from the patient records using a structured proforma. The details of follow up and the functional status of the patient at 12 weeks of the disease onset was also recorded. A record of follow up at 12 weeks was obtained for all patients which was a scale based assessment of disability (using Guillain-Barré syndrome disability scale, adapted from Hughes et al.,1978) based on the case records.

In the prospective arm of the study, complete neurological examination (cranial nerve examination, muscle power charting, reflexes, and sensory examination at admission, GBS disability scale at admission) was done for all patients at admission. Patients routinely underwent nerve conduction study (CMAP,SNAP and F response) of at least

one upper limb and lower limb at admission. Follow up conduction was routinely done at 3 months after disease onset. All follow up NCS values done till 6 months after onset of symptoms was collected. Complete blood count, renal function tests (blood urea and serum creatinine),serum electrolytes (sodium and potassium) and liver function tests and serum albumin were also routinely done at admission which was collected. CSF study was not mandatory for inclusion in the study. Patient did not undergo CSF study as part of the study. If patient had undergone CSF study as part of his/her clinical care, the data was collected for the study. These details were recorded in a structured proforma. The treatment given to the patients including details of mechanical ventilation, immunomodulatory therapy were also recorded.

All patients were called for follow up at 12 weeks routinely. GBS disability score was used as primary outcome measure and was extracted from the case records. This score was derived from the routine data regarding the functional status and the power recorded during follow up visits for retrospective cases and applied to all prospective cases directly. If the patient did not show up for the review, he/ she was contacted over telephone to know the functional status. An accurate assessment of the GBS disability scale was possible with telephonic follow up even if patient did not report for review.

This was strictly an observational study and the investigator did not influence investigation or treatment decisions.

Statistical analysis

Numerical data were expressed as mean ± standard deviation and categorical data as frequencies.Comparison of categorical variables were analysed by using the chi-square

and Fisher's exact test. Continuous variables were compared using Student's t- test. Data analysis was performed using SPSS version 16.0

RESULTS

Results

A Total of 78 patients with a diagnosis of GBS were evaluated for eligibility. However, 31 were excluded as they did not fit the eligibility criteria. A total of 47 subjects were found eligible for inclusion over a period of 40 months 87 months from January 2012 to April 2019. Out of the 47 cases 25 were prospectively followed up.

Demographic details:

Age and Gender

Among the 47 patients 28 were males and 19 females. There was a slight male preponderance with M:F ratio of 1.5:1. Mean age of patients in the study was 49.25 ± 16.85 years. Out of 47 patients, 23 (48.9%) were aged below 50 years and 24 (51.1%) were aged 50 years and above.

Figure 1

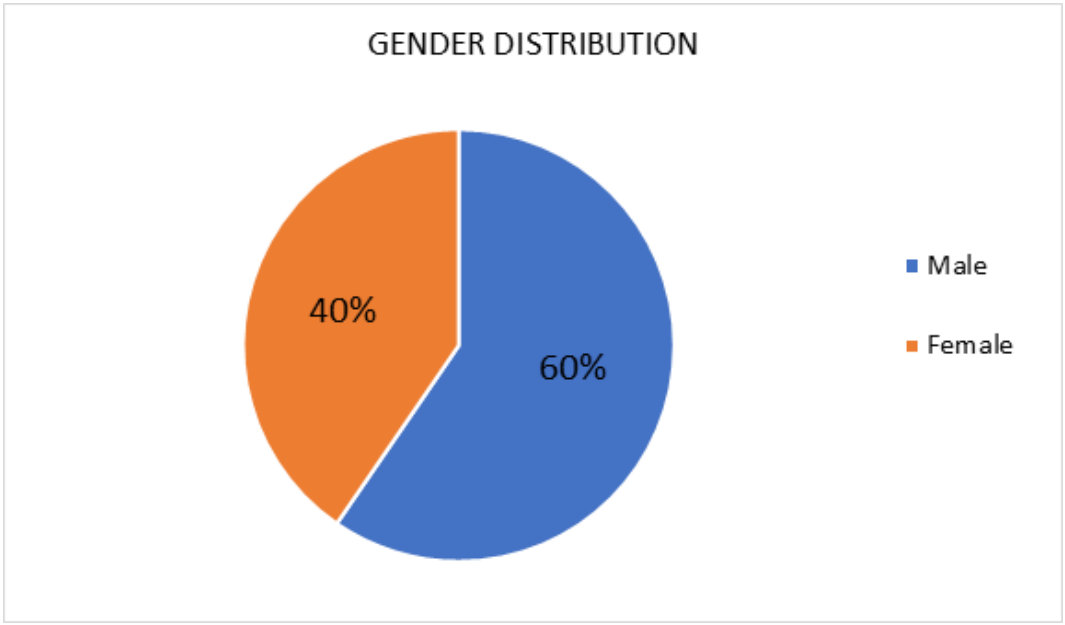
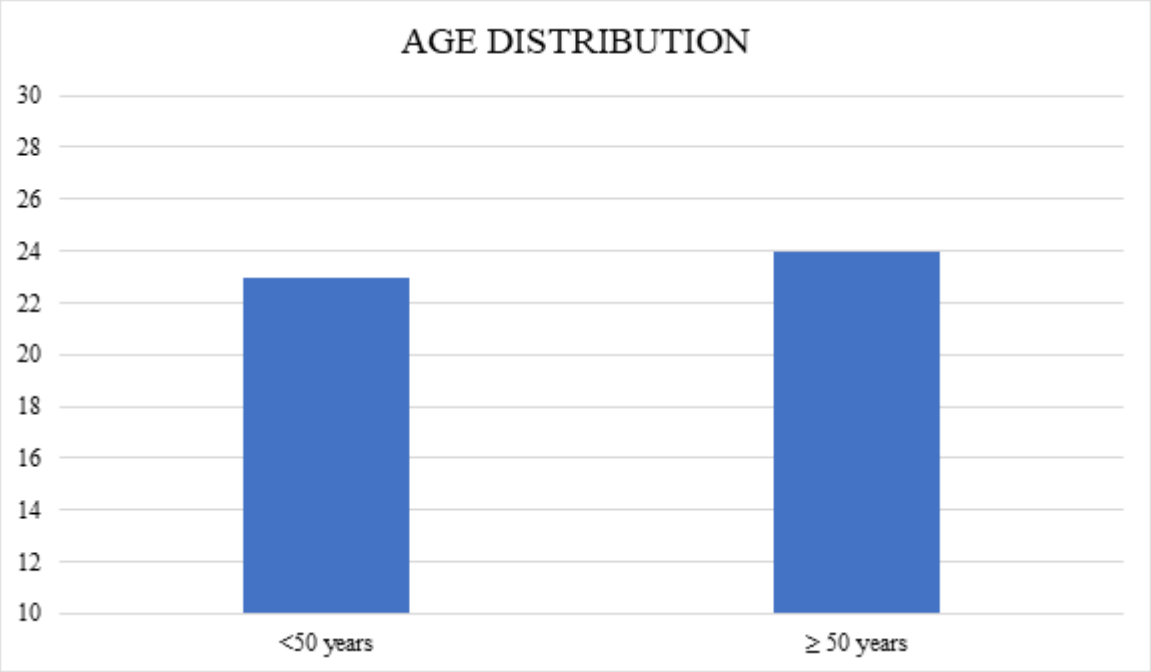


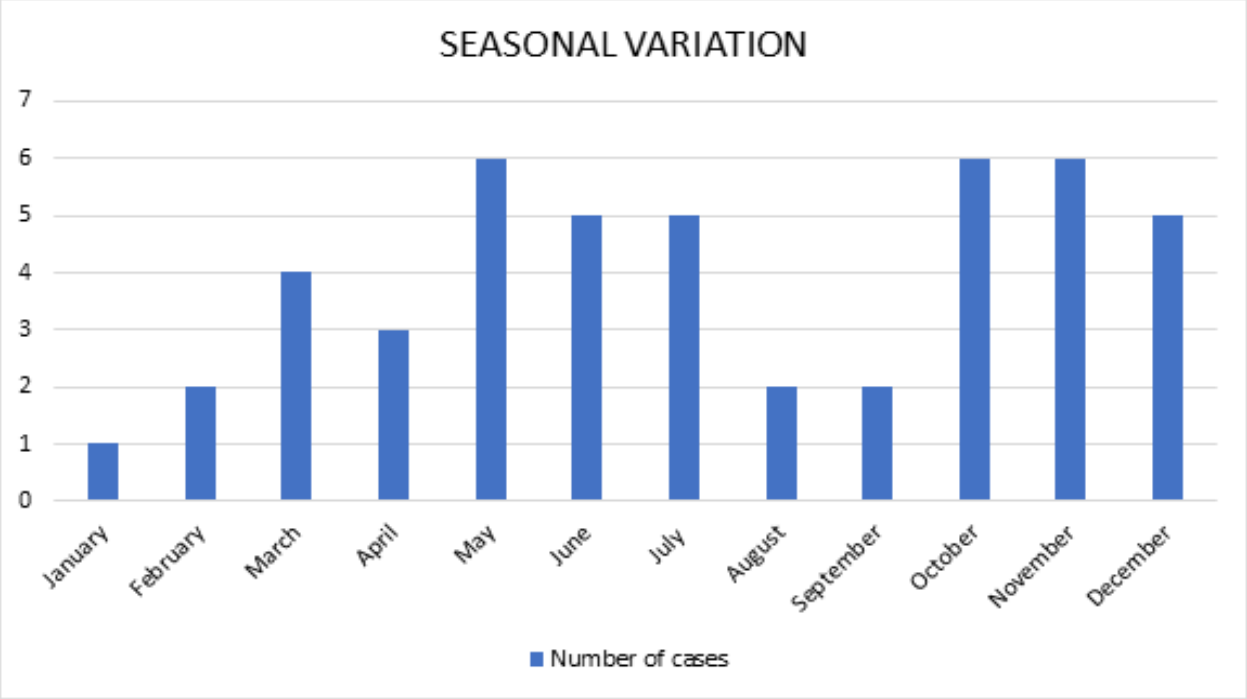
Figure 2



Seasonal variation

The cases of GBS were maximum between May to July and October to December, suggestive of a higher prevalence during the rainy and winter seasons.

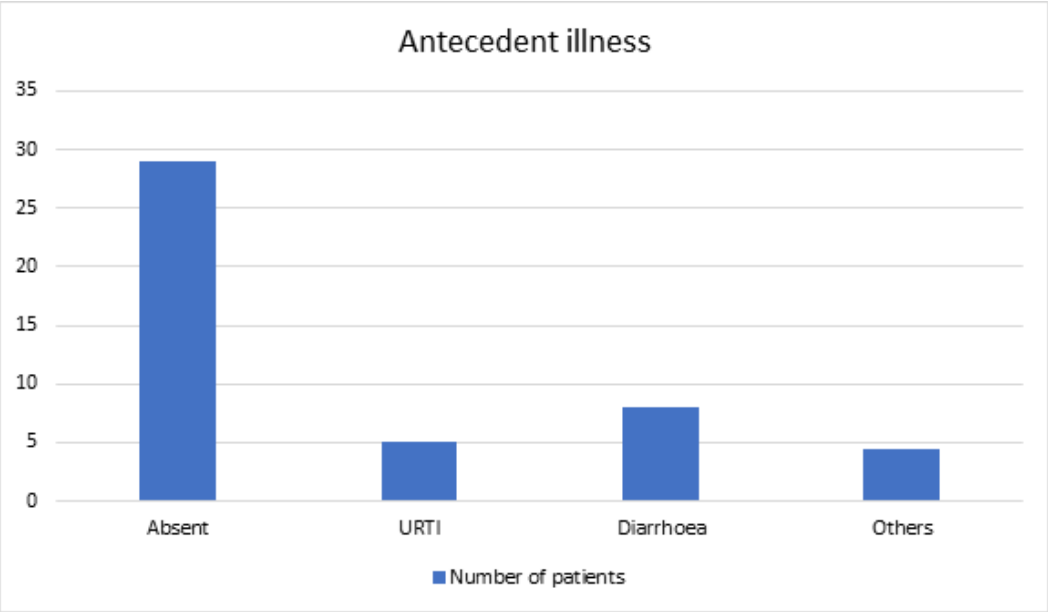
Figure 3



Antecedent illness

Of the 47 patients, 18 (38.3%) were preceded by an infection within 4 weeks prior to onset. 5 patients had upper respiratory tract infections, 8 patients had diarrhoea, and 5 patients had other infections- likely to be of viral etiology.

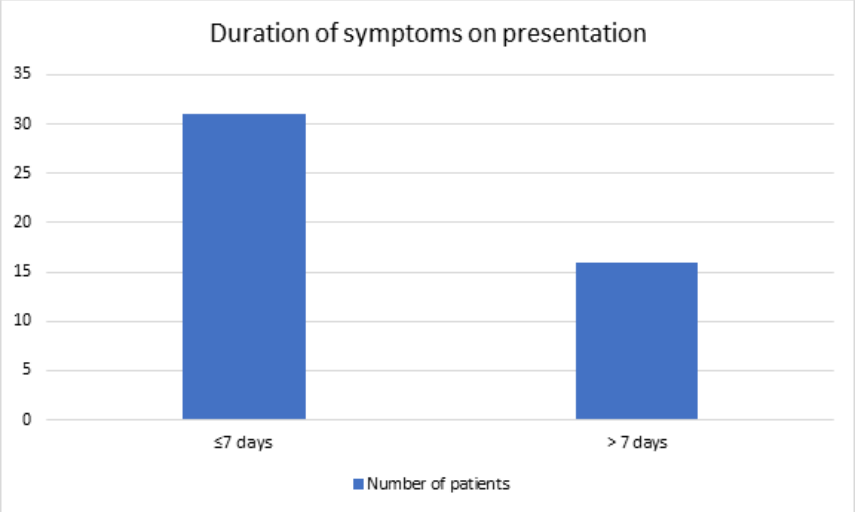
Figure 4



Duration of symptoms at presentation

The mean days between onset of disease and admission was 8.13±6.35. Out of 47 patients 31 (66%) were admitted within 1 week of onset and the rest 16 (34%) within 4 weeks

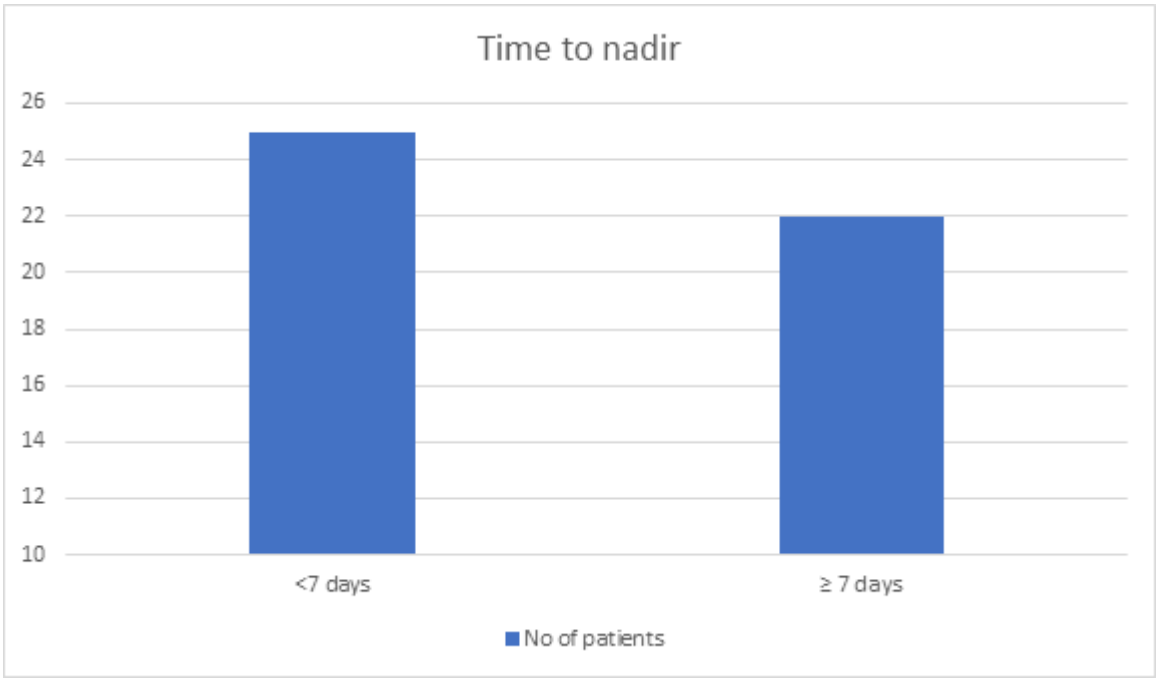
Figure 5



Onset to nadir

Based on the duration from onset to nadir, the patients were divided into two groups of less than 7 days and greater than 7 days. Among the patients in this study, majority 25 (53.2%) patients had an onset to nadir less than 7 days, however an almost equal number (22 [46.8%]) patients had an onset to nadir greater than or equal to 7 days.

Figure 6



GBS disability score at admission

A GBS disability score of 4 was the most common score at admission and was seen in 17 (36.1%) patients. 35 (74.5%) patients had a GBS disability score greater than 3 indicating the inability to walk without support before initiating treatment.

Table 4. GBS disability score at admission

GBS Disability score	No of patients (%)
1	2 (4.3%)
2	10 (21.3%)
3	12 (25.5%)
4	17 (36.1%)
5	6 (12.8%)
Total	47 (100%)

MRC Sum score at admission

Majority of the patients (46.8%) had an MRC sum score between 51 and 60 at admission. 5 (10.6%) patients had a score <= 30 and 10 (21.3%) patients each had a score of 31-40 and 41-50

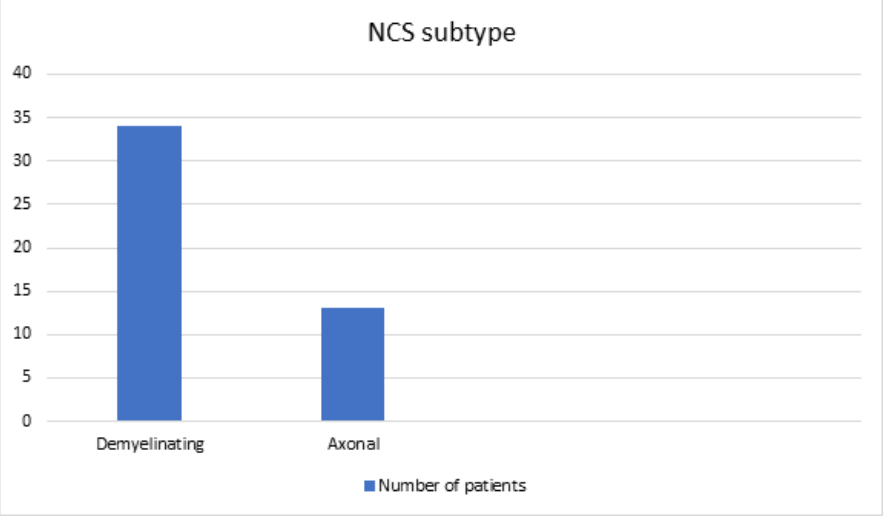
Table 5. MRC sum score at admission

MRC sum score	No of patients (%)
51-60	**22 (46.8%)**
41-50	**10 (21.3%)**
31-40	**10 (21.3%)**
<= 30	**5 (10.6 %)**
Total	**47 (100%)**

Nerve conduction study at admission

Out of the 47 patients, 34 (72.3%) had NCS suggestive of a demyelinating subtype, and 13 (27.7%) had NCS suggestive of an axonal subtype

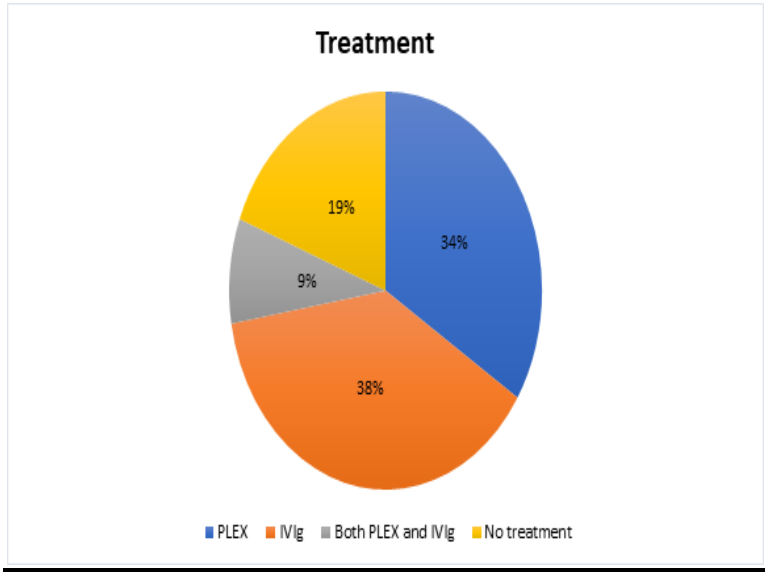
Figure 7



Treatment

Almost equal number patients received plasmapheresis (16 [34%]) and IvIg (18 [38%]). 4 patients received both plasmapheresis and IvIg and 9 patients received no treatment

Figure 8



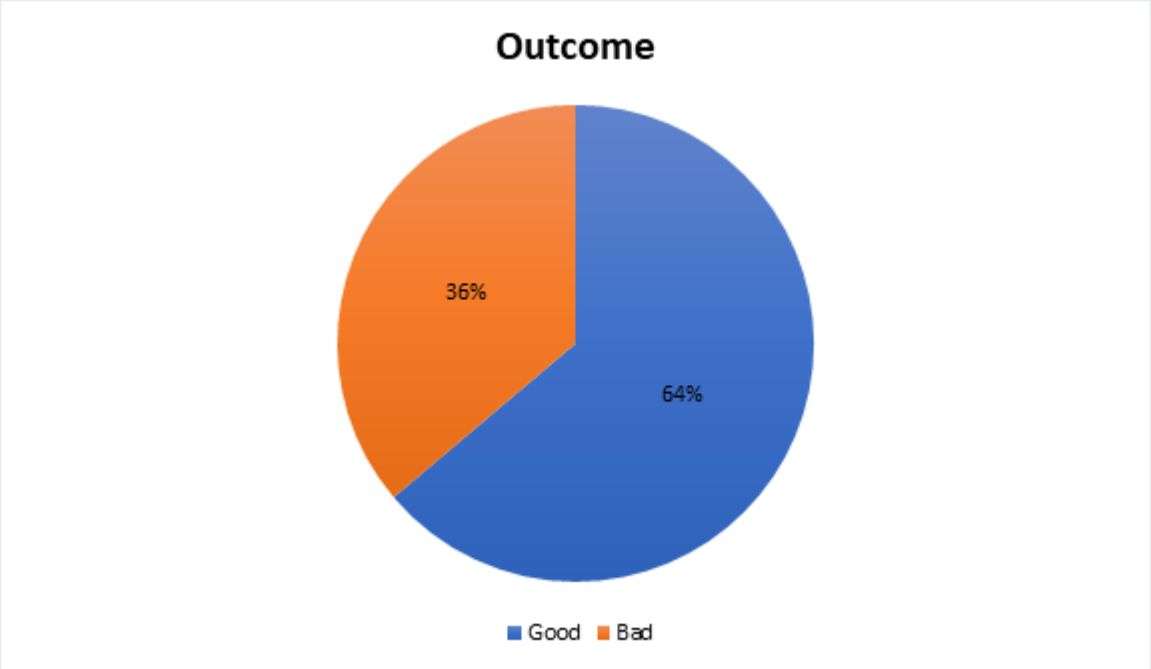
ICU admission, mechanical ventilation and complications

28 (59.6%) patients required ICU stay, 6 (12.8%) patients required ventilator, 8 (17%) patients had infections. 2 (4.3%) patients developed deep vein thrombosis

OUTCOME

A GBS disability score of 0-1 was taken as good outcome and a score of 2 or above was taken as bad outcome. 30 (63.8%) patients had good outcome and 17 (36.2%) patients had a bad outcome.

Figure 9



Predictors of outcome

Age

Patients were divided into <50 and > 50 years of age. There was no significant correlation between age and outcome.

Table 6. Age as a predictor of 3 month outcome

	Outcome				p
	Good		Bad		
Age	N	%	N	%	

<50	16	69.6	7	30.4	
>50	14	58.3	10	41.7	0.423
Total	30	63.8	17	36.2	

MRC sum score

There was no significant correlation found between MRC sum score and outcome

Table 7. MRC sum score as a predictor of 3 month outcome

	Outcome				p
	Good		Bad		
MRC sum score	N	%	N	%	
51-60	15	68.2	7	31.8	
41 - 50	8	80.0	2	20.0	0.338
31 - 40	5	50.0	5	50.0	
<= 30	2	40.0	3	60.0	
Total	30	63.8	17	36.2	

Preceding infection

No significant correlation was found between presence or absence of infection and type of infection with outcome.

Table 8. Preceding infections as a predictor of 3 month outcome

	Outcome				p
	Good		Bad		
Preceding infection	N	%	N	%	

Present	13	72.2	5	27.8	
Absent	17	58.6	12	41.4	0.345
Total	30	63.8	17	36.2	

Table 9. Preceding infections as a predictor of 3 month outcome

	Outcome				p
	Good		Bad		
Preceding infection	N	%	N	%	
Absent	17	58.6	12	41.4	
URTI	4	80.0	1	20.0	
GI infection	6	75.0	2	25.0	
Other infection	3	60.0	2	40.0	0.712
Total	30	63.8	17	36.2	

Serum albumin

The median albumin level was 3.8 gm/dl and patients were divided into those with serum albumin ≤3.8 gm/dl (n= 24) and serum albumin >3.8 gm/dl (n=23). A lower albumin was associated with higher age, longer duration of symptoms on presentation and longer time time initiation of therapy (p= 0.034, p= 0.006, and p= 0.003 respectively). There was no correlation between serum albumin and the sex of the patient, time to nadir, duration of hospital stay, necessity and duration of ICU stay and necessity and duration of ventilator

Table 10. Association of serum albumin with demographic and clinical factors

	Serum albumin ≤3.8 gm/dl (n= 24)	Serum albumin >3.8 gm/dl (n=23)	P value
Age (years)	54.38 ± 14.485	43.91 ± 18.146	0.034

Sex **Male** **Female**	 13 (54.2%) 11 (45.8%)	 15 (65.2%) 8 (34.8%)	0.440
Duration of symptoms on presentation (days)	10.58 ± 7.627	5.57± 3.449	0.006
Time to initiation of treatment (days)	12.35 ± 8.002	6.11± 2.349	0.003
Time to nadir (days)	8.63 ± 5.991	6.22 ±3.477	0.101
Duration of hospital stay (days)	16.21 ± 11.221	16.09 ± 19.566	0.979
ICU stay **Yes** **No**	 16 (66.7%) 8 (33.3%)	 12 (52.2%) 11 (47.8%)	0.312
Duration of ICU stay (days)	19.8 ± 9.792	21.25 ± 19.74	0.805
Ventilator **Yes** **No**	 3 (12.5%) 21 (87.5%)	 3 (13%) 20 (87%)	0.955
Duration of ventilator (days)	16 ± 7.937	26.33 ± 8.505	0.199

No correlation was found between serum albumin and respiratory weakness, bulbar involvement, MRC sum score at nadir, discharge and 3 month follow up, GBS disability score at nadir, discharge and 3 month follow up, and outcome at 3 months

Table 11. Association of serum albumin with outcome

	Serum albumin ≤3.8 gm/dl (n= 24)	Serum albumin >3.8 gm/dl (n=23)	P value
Respiratory weakness			

Yes **No**	3 (12.5%) 21 (87.5%)	3 (13%) 20 (87%)	0.955
Bulbar involvement **Yes** **No**	 7 (29.2%) 17 (70.8%)	 3 (13%) 20 (87%)	0.177
MRC sum score at nadir	41.25 ±15.693	48.74 ± 9.951	0.058
MRC sum score at discharge	52.21 ±7.437	53.78 ±8.118	0.491
MRC sum score at 3 month follow up	55.82 ±6.558	56.1 ±7.44	0.897
Hughes score at nadir **1** **2** **3** **4** **5**	 1 (4.2%) 4 (16.7%) 5 (20.8%) 11 (45.8%) 3 (12.5%)	 1 (4.3%) 6 (26.1%) 7 (30.4%) 6 (26.1%) 3 (13%)	0.702
Hughes score at discharge **0** **1** **2** **3** **4**	 0 4 (16.7%) 8 (33.3%) 11 (45.8%) 1 (4.2%)	 2 (8.7%) 4 (17.4%) 10 (43.5%) 6 (26.1%) 2 (8.7%)	0.310
Hughes score at 3 month follow up **0** **1** **2** **3** **4**	 6 (27.3%) 7 (31.8%) 6 (27.3%) 2 (9.1%) 1 (4.5%)	 8 (40%) 5 (25%) 5 (25%) 1 (5%) 1 (5%)	0.917
Outcome at 3 months **Good** **Bad**	 14 (58.3%) 10 (41.7%)	 16 (69.6%) 7 (30.4%)	0.677

NCS subtype

Based on NCS subtype, patients were divided into those with demyelination (n=34) and axonal (n=13) subtypes. No correlation was found between NCS subtype and age,

sex, time to nadir, duration of hospital stay, necessity and duration of ICU, necessity and duration of ventilator.

Table 12. Association of NCS subtype with demographic and clinical factors

	Demyelinating (n= 34)	Axonal (n=13)	P value
Age (years)	50.26 ± 17.514	46.62 ± 16.091	0.517
Sex **Male** **Female**	 19 (56%) 15 (44%)	 9 (69%) 4 (31%)	0.404
Time to nadir (days)	7.32 ± 5.25	7.77 ±4.549	0.789
Duration of hospital stay (days)	13.53 ± 9.407	23 ± 25.09	0.063
ICU stay **Yes** **No**	 20 (59%) 14 (41%)	 8 (62%) 5 (39%)	0.865
Duration of ICU stay (days)	18.37 ± 14.595	25.38 ± 14.793	0.267
Ventilator **Yes** **No**	 3 (8.8%) 31 (91%)	 3 (23%) 10 (77%)	0.19
Duration of ventilator (days)	24.67 ± 11.504	17.67 ± 6.807	0.416

An axonal NCS was associated with a lower MRC sum score at nadir and at discharge compared to a demyelinating one (p= 0.017, p=0.013 respectively). The difference was not found to be statistically significant in the MRC sum score at 3 month follow up. No correlation was found between NCS subtype and respiratory weakness, bulbar involvment Hughes score at nadir, discharge and 3 month follow up , and 3 month outcome.

Table 13. Association of NCS subtype with outcome

	Demyelinating (n= 34)	Axonal (n=13)	P value
Respiratory weakness **Yes** **No**	 3 (8.8%) 31 (91%)	 3 (23%) 10 (77%)	0.19
Bulbar involvement **Yes** **No**	 6 (18%) 28 (82%)	 4 (31%) 9 (69%)	0.325
MRC sum score at nadir	47.79 ±10.725	37.38 ± 17.529	0.017
MRC sum score at discharge	54.68 ±6.004	48.54 ±10.03	0.013
MRC sum score at 3 month follow up	57.06 ±5.18	52.4 ±10.319	0.062
Hughes score at nadir **1** **2** **3** **4** **5**	 2 (5.9%) 7 (21%) 10 (29%) 12 (35%) 3 (8.8%)	 0 3 (23%) 2 (15%) 5 (39%) 3 (23%)	0.551
Hughes score at discharge **0** **1** **2** **3** **4**	 2 (5.9%) 5 (15%) 14 (41%) 12 (35%) 1 (2.9%)	 0 3 (23%) 4 (31%) 4 (31%) 2 (15%)	0.44
Hughes score at 3 month follow up **0** **1** **2** **3** **4**	 11 (34%) 10 (31%) 8 (25%) 3 (9.4%) 0	 3 (30%) 2 (20%) 3 (30%) 0 2 (20%)	0.1
Outcome at 3 months **Good** **Bad**	 22 (65%) 12 (35%)	 8 (62%) 5 (39%)	0.84

Treatment

On comparing the patients who received plasma exchange (n=16), with those who received IvIg (n=18), those who received plasma exchange tended to have a longer duration of ICU stay than those who received IvIg (p= 0.041). No correlation was found between type of treatment and age, sex, duration of symptoms on presentation, time to initiation of treatment, time to nadir, duration of hospital stay, necessity and duration of ICU stay, necessity and duration of ventilator.

Table 14. Association of treatment with demographic and clinical factors

	Plex (n= 16)	Ivlg (n=18)	P value
Age (years)	45.81± 19.904	50.67 ±17.644	0.456
Sex **Male** **Female**	 11 (69%) 5 (31%)	 8 (44%) 10 (56%)	0.154
Duration of symptoms on presentation (days)	7.63 ± 5.29	9.11± 7.955	0.531
Time to initiation of treatment (days)	9.56 ± 5.727	9.89± 7.918	0.893
Time to nadir (days)	8.06 ± 5.26	6.83 ± 5.597	0.516
Duration of hospital stay (days)	18.25 ± 9.263	12.72 ± 7.226	0.06
ICU stay **Yes** **No**	 14 (88%) 2 (13%)	 10 (56%) 8 (44%)	0.041
Duration of ICU stay (days)	17.58 ± 8.795	14.64 ± 7.284	0.394
Ventilator **Yes** **No**	 2 (13%) 14 (88%)	 1 (5.6%) 17 (94%)	0.476
Duration of ventilator (days)	15 ± 7.071	13	0.856

Those who underwent plasma exhange had a better GBS disability score and better outcome at 3 months follow up compared to those who received IvIg (p= 0.03, p=0.02). No correlation was found between treatment and respiratory weakness, bulbar involvment, MRC sum score at nadir, discharge and 3 month follow up, Hughes score at nadir and discharge.

Table 15. Association of treatment with outcome

	Plex (n= 16)	Ivlg (n=18)	P value
Respiratory weakness **Yes** **No**	 2 (13%) 14 (88%)	 1 (5.6%) 17 (94%)	0.476
Bulbar involvement **Yes** **No**	 4 (25%) 12 (75%)	 4 (22%) 14 (78%)	0.849
MRC sum score at nadir	42.75 ±16.831	45.22 ± 9.039	0.592
MRC sum score at discharge	54.75 ±6.768	51.72 ±7.061	0.212
MRC sum score at 3 month follow up	58.4 ±5.138	54.27 ±6.628	0.067
Hughes score at nadir **1** **2** **3** **4** **5**	 1 (6.3%) 1 (6.3%) 5 (31%) 7 (44%) 2 (13%)	 0 3 (17%) 5 (28%) 9 (50%) 1 (5.6%)	0.649
Hughes score at discharge **0** **1** **2** **3** **4**	 2 (13%) 3 (19%) 6 (38%) 4 (25%) 1 (6.3%)	 0 3 (17 %) 5 (28%) 9 (50%) 1 (5.6%)	0.418
Hughes score at 3 month follow up **0** **1** **2** **3** **4**	 9 (60%) 4 (27%) 1 (6.7%) 0 1 (6.7%)	 3 (20%) 3 (20%) 6 (40%) 3 (20%) 0	0.030
Outcome at 3 months	14 (88%)	9 (50%)	

Good **Bad**	2 (13%)	9 (50%)	0.020

A multivariate analysis was not done as potential confounders like age, preceding illness, MRC sum score at nadir and NCS subtype which may potentially influence the 3 month outcome did not show any statistically significant correlation with the same on univariate analysis.

DISCUSSION

Discussion

Our study showed a significantly higher preponderance of GBS in males compared to females in a ratio of 1.5:1. This is similar to previous studies in the US and India which showed a ratio of 1.2:1 and 1.5- 1.7 :1 respectively [14,63,64]. The number of cases of GBS were more between May to July and October to December, which is predominantly in the monsoon and post monsoon season. A study by Mathew et al showed a higher prevalence of GBS cases in the monsoon and winter seasons due to a higher incidence of influenza and gastroenteritis during these seasons. [14]. We did not find a high prevalence in the winter months, probably because the climate changes seen in this region comprises mainly of summer and monsoon seasons.

38.3 % of the patients had an antecedent infection. This a slightly lower compared to previous studies which showed that approximately 40-70% of GBS cases are associated with an antecedent infection. [65]

GBS disability score of 4 was seen in a majority of patients (36.1%) on admission, which is similar to the study done by von Koningsveld et al. This is probably because ours is a tertiary referral centre and most of the cases referred are those with a significant disability requiring active intervention. [9]

Majority of the patients had an NCS suggestive of a demyelinating GBS (72.3%), while the remainder (27.7%) had an axonal GBS. This is consistent with the preexisting literature that approximately 80% of GBS are demyelinating.[66]

59.6% patients required ICU stay and 12.8% patients required mechanical ventilator. The number of patients kept in ICU is higher than that observed in previous data.[67] This may be because our institute is a tertiary care centre and as mentioned earlier, the referral bias leading to admission of patients with severe illness. There is also a protocol of admitting patients even with relatively milder illness in ICU, if they appear to be in a stage of progression. The number of patients requiring ventilatory support (12.8%) was also less compared to the pre exisitingdata of 20-30%, probably due to the same reason.[13] There was no mortality in due to GBS in the study duration.

A GBS disability score at 3 months of 0-1 was taken as good outcome and a score of 2 or above was taken as bad outcome. 30 (63.8%) patients had good outcome and 17 (36.2%) patients had a bad outcome. Significant predictors of outcome included in the EGOS and mEGOS were age, MRC sum score at admission and at 1 week, GBS disability score at 2 weeks and preceding infections[9,45] , however our study did not show a similar correlation. A large study from India evaluating the outcome predictors in GBS also did not show a significant association with preceding diarrhoeal illness and outcome [68], however, it did show a significant association between age, peak disability grade and upper and lower limb power <3 with outcome. IvIg was the only treatment given in this study for disabled patients. These differences may be attributed due to differences in the demographics and treatment, as early and aggressive treatment with IvIgor plasma exchange have been given to the patients in our study.

No significant correlation was found between serum albumin and outcome, development of respiratory weakness or bulbar involvement. This is contrary to the results found in previous studies [4969] A lower albumin was associated with higher age, longer duration of symptoms on presentation and longer time time initiation of therapy (p= 0.034, p= 0.006, and p= 0.003 respectively). The mean serum albumin was 3.8 gm/dl in our population , and 11(23.4%) patients had hypoalbuminemia prior to treatment, which was a higher proportion than that found in the study by Fokkink et al. This could probably be explained by the differences in the overall preexisting nutritional status of the population which is different in an Indian and Western population, which could be a potential confounder.

An axonal NCS was associated with a lower MRC sum score at nadir and at discharge compared to a demyelinating one (p= 0.017, p=0.013 respectively). The difference was not found to be statistically significant in the MRC sum score at 3 month follow up. This is consistent with the existing knowledge. Patients with AMAN have been found to have a more rapid progression and severity of weakness compared to AIDP resulting in prolonged paralysis and respiratory failure over a few days.[30] No correlation has been found between the NCS subtype and outcome or need for mechanical ventilation in our study.

Those who received plasma exchange tended to have a longer duration of ICU stay than those who received IvIg (p= 0.041). This can be explained by the fact that all patients who required plasma exchange were kept in the ICU for monitoring of hemodynamic parameters during the procedure.

Those who underwent plasma exchange had a better GBS disability score and better outcome at 3 months follow up compared to those who received IvIg (p= 0.03, p=0.02). This is contrary to to the previous randomised controlled trials showing that both are equally efficacious [31,37]. However, a smaller study done in China showed that plasma exchange had a higher efficacy than IvIg. [70] It also analyzed the changes in immunoglobulin and complement of the two methods of treatment and found that that immunoglobulin IgG, IgA, IgM, C3 and C4 of the patients with GBS were significantly lower in the plasma exchange group compared to the IVIg group post treatment. Similarly, a study done in Egypt in paediatric population also revealed that there was significant reduction in the duration of hospitalization and an increase in the number of children with complete recovery in cases treated with plasmapheresis compared to IvIg.[71] In AIDP patients with axonal involvement, plasma exchange has been reported to be of greater potential benefit than IVIG[72]. One study done in India comparing plasma exchange and IvIg suggested that plasmapheresis was marginally superior to the IVIg in improving disability [73]. Large scale studies comparing the differences in efficacy between IvIg and plasma exchange have not been done previously in India. It has been found that the cost of plasmapheresis was significantly lower as compared to IVIG [74]. This makes the fact that plasma exchange may be more efficacious than IvIg an important finding in developing countries like India, where plasma-derived products (IVIG) are not easily available, and affordable plasma exchange is preferred.

CONCLUSION

Conclusion

1. In our cohort of patients, there was a male preponderance and a seasonal clustering of cases in the monsoon and post monsoon seasons

2. The number of patients kept in the ICU were higher compared to preexisting data, and the number of patients requiring ventilatory support was less, probable due to better monitoring in the ICU and early aggressive treatment

3. The most common electrophysiological subtype was demyelinating followed by axonal.

4. The was no correlation found between low pretreatment serum albumin levels and long term outcome.

5. Axonal subtype of GBS was associated with a more severe weakness at nadir and discharge compared to the demyelinating subtype, and it recovered to an almost comparable state at 3 month follow up.

6. Patients treated with plasma exchange have been found to have a better outcome and GBS disability score at 3 months compared to those treated with IvIg.

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ANNEXURE

श्री चित्रा तिरुनाल आयुर्विज्ञान और प्रौद्योगिकी संस्थान, त्रिवेन्द्रम
तिरुवनन्तपुरम - ६९५०११, केरल, इंडिया
SREE CHITRA TIRUNAL INSTITUTE FOR MEDICAL SCIENCES AND TECHNOLOGY, TRIVANDRUM
Thiruvananthapuram - 695 011, Kerala, India
(An Institute of National Importance under Govt. of India)
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Institutional Ethics Committee

(IEC Regn No. ECR/189/Inst/KL/2013)

13.04.2018

SCT/IEC/1169/FEBRUARY-2018

Dr. Poornima Narayanan Nambiar
Senior Resident
Department of Neurology
SCTIMST, Thiruvananthapuram

Dear Dr. Poornima Narayanan Nambiar,

The Institutional Ethics Committee reviewed and discussed your application to conduct the study entitled "SERUM ALBUMIN AS A POTENTIAL PROGNOSTIC INDICATOR IN GUILLAIN BARRE SYNDROME (IEC/1169)" on 17th February, 2018.

The following documents were reviewed:

Original submission

1. Covering Letter addressed to the Chairperson, IEC, SCTIMST dated 18.01.2018 with checklist
2. TAC Approval Letter
3. IEC Application Form
4. Project Proposal
5. Proforma
6. Patient Information Sheet and Informed Consent Form in English and Malayalam
7. CV of Principal Investigator and Co-Principal Investigators

Revised submission

1. Covering Letter addressed to the Chairperson, IEC, SCTIMST dated 04.04.2018 with checklist
2. TAC Approval Letter
3. IEC Application Form
4. Project Proposal
5. Proforma
6. Telephonic follow up interview proforma
7. Patient Information Sheet and Informed Consent Form in English and Malayalam
8. CV of Principal Investigator and Co-Principal Investigators

The following members of the Ethics Committee were present at the meeting held on 17th February, 2018 at G. Parthasarathi Board Room, AMCHSS, SCTIMST

SL. No.	Member Name	Highest Degree	Gender	Scientific /Non Scientific	Affiliation with Institution(s)
1.	Dr. R V G Menon	M Tech, PhD	Male	Lay Person (Chairman)	No
2.	Dr. Rema M. N	MD	Female	Basic Medical Scientist	No
3.	Dr. Kala Kesavan. P	MBBS, MD	Female	Basic Medical Scientist	No
4.	Dr. K R S Krishnan	M.E., Ph.D.	Male	Medical Technology	Yes
5.	Dr. S S Giri Sankar	LL.M. Ph.D.	Male	Legal Expert	No
6.	Dr. Aneesh V Pillai	BA. LLB (Hons.), LLM, Ph. D, SET (Law)	Male	Legal Expert	No
7.	Mr. Satheesh Chandran	MSW, PGDPM	Male	Lay person/ NGO/ Social Scientist	No
8.	Dr. Harikrishna Varma PR	Ph.D(Materials Science)	Male	Medical Technology	Yes
9.	Dr. P. Manickam	BSMS, MSc (Epid).,PhD	Male	Health Science Expert/ Social Scientist	No
10.	Dr. Christina George	MD Psychiatry	Female	Clinician	No
11.	Dr. Harikrishnan S	MD, DM (Cardiology) DNB (Cardiology)	Male	Clinician	Yes
12.	Dr.Lekha Pandit	MD.DM Neurology, PhD (Bioscience)	Female	Clinician	No
13.	Dr. V. Raman Kutty	M D, M Phil, M P H	Male	Health Sciences Expert/Clinician	Yes
14.	Dr. Mala Ramanathan	PhD	Female	Social Scientist (Member Secretary)	Yes

IEC Decision

The IEC approved the conduct of the study in the present form.

Remarks:
The Institutional Ethics Committee expects to be informed about the progress of the study, any SAE occurring in the course of the study, any changes in the protocol and patient information/informed consent and asks to be provided a copy of the final report.

There was no member of the study team who participated in voting / decision making process. The ethics committee is organized and operated according to the requirements of Good Clinical Practice and the requirements of the Indian Council of Medical Research (ICMR).

Sincerely,

Mala Ramanathan
Member Secretary, IEC

PROFORMA

1. Identification data

1.1 Unique ID number: ----------

1.2 Serial number: ----------

1.3 Age: ----------

1.4 Sex: ---------- (1= Male, 2= Female)

1.5 Address ----------

1.6 Date of admission

1.7 Date of inclusion into the study

1.8 Duration of symptoms at presentation: ---------- days

2. Clinical features (1 = Yes, 2= No)

2.1 Antecedent event

(0 = None, 1= URTI, 2 = LRTI, 3 = GI infection, 4 = Other infection, 5 = Vaccination, 6 = Others)

2.1.1 Duration between antecedent and symptom onset ----------

2.2 Time to nadir: ---------- days

2.2.1 Time to initiation of treatment

2.3 Symptoms and signs at nadir (1 = Yes, 2= No)

2.3.1 Backache ----------

2.3.2 Myalgia ----------

2.3.3 Distal paraesthesias ----------

2.3.4 Proximal lower limb weakness ----------

2.3.5 Distal lower limb weakness ----------

2.3.6 Proximal lower limb weakness ----------

2.3.7 Distal lower limb weakness ----------

2.3.8 Neck/ trunk weakness ----------

2.3.9 Facial weakness ----------

2.3.10 Bulbar weakness

2.3.11 Other cranial nerve weakness

2.3.12 If yes, specify

2.3.13 Respiratory weakness

2.3.14 Deep tendon reflexes
(0=Absent, 1=sluggish, 2=normal, 3=brisk)
2.3.15 If abnormal, specify
2.3.16 Sensory loss
2.3.17 Specify pattern of sensory loss
2.3.18 Ataxia
2.3.19Autonomic involvement
2.3.20 If yes, specify
2.3.21Bladder dysfunction
2.3.22 Specify
Time from onset of symptoms
Duration of symptoms

2.5 Disability at presentation(Hughes score) ----------

2.6 Disability at nadir ----------

2.7 Comorbidities ----------

3. Laboratory investigations (1= Abnormal, 2= Normal, 0 = Not done)

3.1 CSF study

3.1.1 Colour ----------

3.1.2 Total cell count ----------

3.1.3 Differential count ----------

3.1.4 RBCs ----------

3.1.5 Sugar/Blood sugar ----------

3.1.6 Protein ----------

3.2.7 Other relevant ----------

3.2 Serology

3.2.1 Antiganglioside antibodies ----------

3.2.2 If positive, specify ----------

3.3 Serum albumin ----------

3.4 Other relevant investigations

4. Treatment (1=Yes, 2 = No)

Date of initiation of definitive treatment

4.1 Large volume plasma exchange

If yes, dose and duration

Period of treatment

4.2 Intravenous immunoglobulin

If yes, dose and duration

Period of treatment

4.3 Small volume plasma exchange

If yes, dose and duration
Period of treatment
4.4 Steroid
If yes, dose and duration

Period of treatment
Reason for steroid initiation
Adverse effects to treatment
If yes, details
(Date, Adverse effect, Drug)

5. Disease course (1=Yes, 2=No)

5.1 Intensive care unit stay
If yes, period of stay
5.2 Reason for ICU care
5.3 Ventilation required
Duration of ventilation
5.4 Tracheostomy done
Duration of tracheostomy ---------- to ----------, ---------- days
5.5 Complications during hospital stay
5.5.1 Autonomic fluctuations
5.5.2 Bulbar dysfunction
5.5.3 Respiratory dysfunction
5.5.4 Infection
Details
5.5.5 Sepsis
Details
5.5.6 Deep vein thrombosis
5.5.7 Others (specify)

Clinical follow up

Date	At admission		At discharge		3 months	
	R	L	R	L	R	L
Facial muscles						
Palatal muscles						
Tongue muscles						
SBC						
Neck flexion						
Neck extension						
Shoulder flexion						
Shoulder extension						

Shoulder abduction						
Shoulder adduction						
Elbow flexion						
Elbow extension						
Wrist flexion						

Wrist extension						
Intrinsic muscles						
Trunk						
Hip flexion						
Hip extension						
Hip abduction						
Hip adduction						
Knee flexion						
Knee extension						
Ankle dorsiflexion						
Ankle plantar flexion						
Ankle eversion						
Ankle inversion						
Toe dorsiflexion						
Toe plantar flexion						

Deep tendon reflexes

Date	At admission		At discharge		3 months	
	R	L	R	L	R	L
Biceps jerk						
Supinator jerk						
Triceps jerk						
Knee jerk						
Ankle jerk						
Abdominal reflex						
Plantar response						

Other clinical

Date	At baseline	At discharge	3 months
Hughes grade			
Sensory			

Ataxia			
Bladder			
Autonomic			
Ventilation			
Tracheostomy			

6. Serial electrophysiology

Distal motor latency

Date	At baseline	At discharge	3 months
Right peroneal			
Left peroneal			
Right tibial			
Left tibial			
Right median			
Left median			
Right ulnar			
Left ulnar			
Right phrenic			
Left phrenic			
Right facial			
Left facial			

Nerve conduction velocity

Date	At baseline	At discharge	3 months
Right peroneal			
Left peroneal			

Right tibial			
Left tibial			
Right median			
Left median			
Right ulnar			
Left ulnar			

Distal CMAP amplitude

Date	At baseline	At discharge	3 months
Right peroneal			
Left peroneal			
Right tibial			
Left tibial			
Right median			
Left median			
Right ulnar			
Left ulnar			
Right phrenic			
Left phrenic			
Right facial			
Left facial			

Conduction block (If yes, distal/proximal CMAP and distal/ proximal CMAP duration)

Date	At baseline	At discharge	3 months

	CMAP amplitude	Duration	CMAP amplitude	Duration	CMAP amplitude	Duration
Right peroneal						
Left peroneal						
Right tibial						
Left tibial						
Right median						
Left median						

Right ulnar						
Left ulnar						

Sensory study

Date	At baseline		At discharge		3 months	
	SNAP amplitude	Peak latency	SNAP amplitude	Peak latency	SNAP amplitude	Peak latency
Right sural						
Left sural						
Right supf peroneal						
Left supf peroneal						
Right median						
Left median						
Right						

ulnar						
Left ulnar						

F wave latency

Date	At baseline	At discharge	3 months
Right peroneal			
Left peroneal			
Right tibial			
Left tibial			
Right median			

Left median			
Right ulnar			
Left ulnar			

H reflex latency

Date	At baseline	At discharge	3 months
Right tibial			
Left tibial			

Blink reflex

Date	At baseline			At discharge			3 months		
	R1	R2i	R2c	R1	R2i	R2c	R1	R2i	R2c
Right									
Left									

12. Final outcome

12.1 Date of final follow up ----------

Subtype at discharge

Subtype at follow up

12.2 Hughes grade at final follow up ----------

12.3 Any complications till 3 months ----------

12.4 Treatment at last follow up ----------

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