Clinical Profile and Outcomes of Guillain-Barre Syndrome: A Four-Year Retrospective Study at a Tertiary Hospital in the Philippines

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Abstract

Guillain-Barre syndrome (GBS) is the leading cause of acute neuromuscular weakness in the developed world. In this retrospective study, a total of 34 patients were identified and diagnosed with GBS from January 2016 to December 2019. The Brighton criteria was used to classify the certainty and diagnosis of GBS. The clinical profile and outcomes were then determined. GBS was seen in all age groups with a mean age at 47.9 with a slightly male predominance. The majority(47%) of patients had a history of respiratory infection although almost 30% had no known triggering event. The most common presenting symptom was ascending paralysis followed by complaints of cranial nerve involvement. Younger age and less severe disease presentation at onset correlate with a more favorable outcome. Patients who presented earlier after the triggering event were noted to have a faster rate of progression of symptoms and a worse outcome. The common GBS variants in this study according to nerve conduction studies were AMSAN and MFS. Methylprednisolone and IVIG were both effective with no statistical significance noted. The in-hospital mortality rate was at 3%. Majority of patients had a good functional outcome.

Keywords:Guillain-Barre Syndrome;IVIG

1. Introduction

Guillain-Barre syndrome (GBS) is the leading cause of acute neuromuscular weakness in the world[1]. It is an acute peripheral neuropathy which presents as rapidly developing ascending motor paralysis with associated autonomic dysfunction and/or cranial nerve palsies. The clinical diagnosis of GBS is made after cerebrospinal fluid (CSF) tests and electrodiagnostic studies such as EMG showing typical abnormalities.[5] Lumbar puncture often reveals an elevated CSF protein with a normal CSF white blood cell count known as albuminocytologic dissociation. This is present in 50 to 66 percent of patients with GBS in the first week after the onset of symptoms and ≥75 percent of patients in the third week.[6,7,8] A normal CSF protein is found in one-third to one-half of patients when tested earlier than one week after symptom onset. This does not exclude the diagnosis of GBS. [9] The mortality rate of GBS was 5-15%. A systematic literature review done by McGrogan last 2009 showed an estimated incidence of GBS worldwide to be between 1.1-1.8/100,000/year. Their review also showed an increase of incidence with age after 50 years from 1.7/100,000/year to 3.3/100,000/year[2]. A meta-analysis of studies by Sevjar last 2011 showed an increase in incidence by 20% for every 10-year increase in age, and the risk of GBS was higher for males than females[3]. However, data about the clinicoepidemiological profile and outcome of the patients from the Philippines are limited.

With limited resources in a developing country such as ours, identifying patients with GBS and knowing the factors associated with worse prognosis, can help in better utilization of our limited resources. To fulfill this need and to better manage our patients with GBS, a retrospective study among patients with GBS admitted to the Department of Neurology at a Tertiary Hospital in the Philippines to determine the clinic epidemiological profile and outcome of patients with GBS.

2. Methodology

This retrospective study was done at a tertiary hospital in the Philippines. All adult patients, 18 years of age and above, diagnosed with Guillain-Barre Syndrome from January 2016 to December 2019 were included in this study. Patients with mimics of GBS including those with previous trauma leading to paresis, history of neuromuscular weakness, poliomyelitis, periodic paralysis, transverse myelitis, and diphtheria and porphyria renal tubular acidosis were excluded from this study. Electronic records and handwritten case records were checked. The following data were then recorded: baseline vital signs, clinical profile and history, initial physical and neurologic examination, laboratory values if lumbar puncture was done, electrodiagnostic test results, treatment and outcomes. The Brighton criteria was used to classify the certainty and diagnosis of GBS. Level 1 showing the highest certainty and the level 4 the lowest. The severity of disease was assessed during admission using the Medical Research Council sum score, which includes power assessment of the deltoid, biceps, wrist extensor, iliopsoas, quadriceps, and tibialis anterior with maximum score of 60. Outcomes measured included a clinicoepidemiological profile of GBS patients, functional outcomes assessed by Hughes motor scale at the time of discharge and mortality. The Hughes motor scale ranges from 0 to 6 wherein O is asymptomatic, 1 is having mild signs or symptoms but able to run, 2 is able to walk without assistance for 5 meters, 3 is able to walk 5 meters with assistance, 4 is bedridden or chair-bound, 5 is requiring ventilator and 6 is death.

3. Results

A total of 34 patients were identified and diagnosed with GBS from January 2016 to December 2019.

3.1. The certainty of diagnosis.

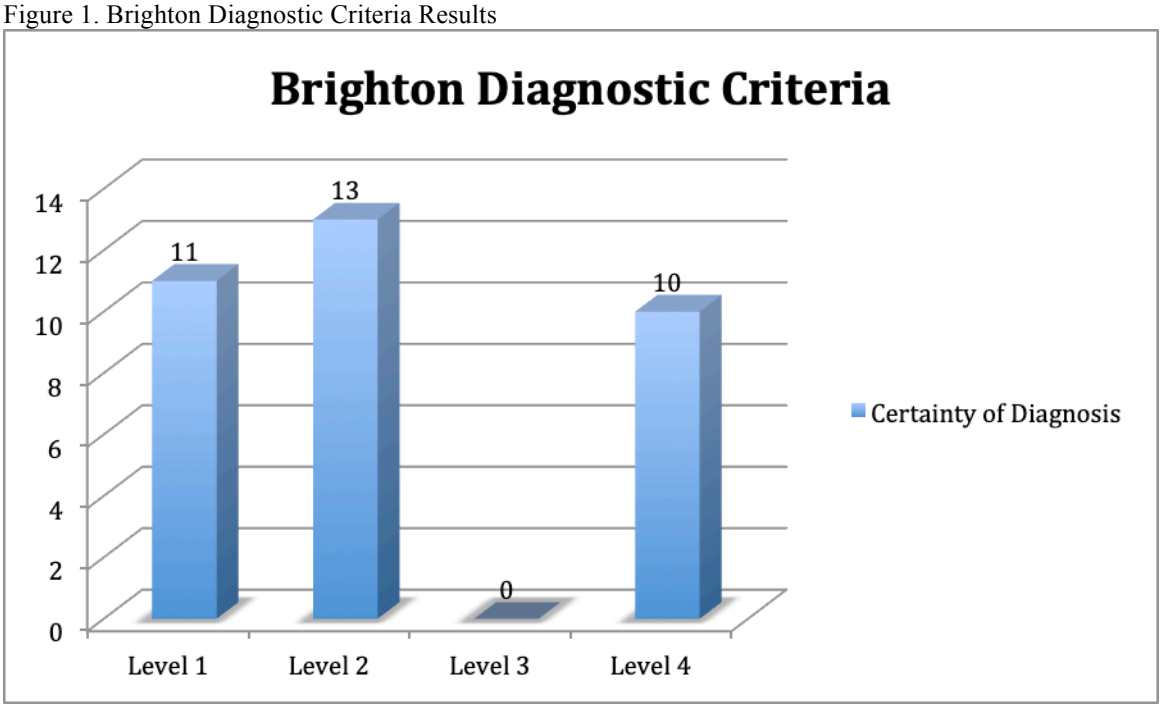
The certainty of diagnosis of GBS was based on the Brighton criteria. Below, a table of the criteria is shown. The majority 38% of the patients had a Brighton criteria level 2 certainty of diagnosis. 32% of the study population had level 1 diagnosis certainty and 29% of patients had a level 4 certainty of diagnosis. These patients with a level 4 certainty of diagnosis did not present with any motor weakness and all of these patients were classified under the Miller fisher variant.

Table 1. Brighton Diagnostic Criteria for GBS

Diagnostic Criteria	Level of Diagnostic Criteria			
Symptoms	1	2	3	4
Bilateral and flaccid weakness of limbs	+	+	+	+/-
Decreased or absent deep tendon reflexes in weak limbs	+	+	+	+/-
Monophasic course and time between onset-nadir 12h to 28days	+	+	+	+/-
CSF cell count <50/ul	+	+[a]	-	+/-
CSF protein concentration > normal value	+	+/-[a]	-	+/-
NCS findings consistent with one of the subtypes of GBS	+	+/-[a]	-	+/-
Absence of alternative diagnosis for weakness	+	+	+	+

+ present; - absent, +/- present or absent
NCS= nerve conduction studies
[a]If CSF was not collected or results not available, nerve electrophysiologic results must be consistent with the diagnosis of GBS

Figure 1. Brighton Diagnostic Criteria Results



3.2. The clinicoepidemiologic profile.

A. Sex

In this retrospective study, 34 patients, 58.8% (20) were male and 41.17%(14) were females.

Table 2. Sex of participants

Clinicoepidemiology study of Guillain-Barre Syndrome (N= 34)		
Variables	Value	Percentage
Gender		
Male	20	58.8
Female	14	41.17

B. Symptoms.

The most common presenting symptom was ascending paralysis (47%) followed by complaints of cranial nerve involvement (41%) and sensory disturbance at (11%). The most common symptoms seen in our patients are as follows: ascending paralysis (73%), cranial nerve involvement (47%), sensory disturbance (41%), respiratory failure (17%), dysphagia (5.8%) and bladder involvement (2.9%).

Table 3. Symptoms

Clinicoepidemiology study of Guillain-Barre Syndrome (N= 34)		
Variables	Value	Percentage
Clinical Profile – presenting symptom		
Ascending Paralysis	16	47.05
Cranial nerve involvement	14	41.17
Sensory disturbance	4	11.76
Respiratory failure	0	0
Dysphagia	0	0
Autonomic dysfunction	0	0
Bladder involvement	0	0
Symptoms		
Ascending Paralysis	25	73.52%
Cranial nerve involvement	16	47%
Sensory disturbance	14	41.17%
Respiratory failure	6	17.64%
Dysphagia	2	5.88%
Autonomic dysfunction	0	0
Bladder involvement	1	2.94%

C. Triggering Events.

The most common triggering event in this study was respiratory tract infection (47%) followed by diarrhea at 20% and surgery in 1 patient. However, 29% of these patients did not note any triggering event.

Table 4. Triggering events

Clinicoepidemiology study of Guillain-Barre Syndrome (N= 34)		
Variables	Value	Percentage
Antecedent Event		
Respiratory tract infection	16	47%
Surgery	1	2.9%
Recent vaccination	0	0
Diarrhea	7	20.5%
Urinary tract infection	0	0
Unidentified	10	29.4%

D. Severity of Involvement.

The most common complications noted in our patients were respiratory failure (17%) and autonomic dysfunction (12.9%). The mean Medical Research Council sum score, which assesses the motor power at the time of onset and severity of disease, was 53.47 $\pm$ 9.56.

E. Nerve Conduction Study Finding.

As shown below, the common GBS variants according to nerve conduction studies were AMSAN (38%), MFS (23%), AIDP (14%) and AMAN (8.8%). 5% of patients had unremarkable results and another 5% did not undergo the nerve conduction test.

Table 5. Nerve Conduction Study Findings

Clinicoepidemiology study of Guillain-Barre Syndrome (N= 34)		
Variables	Value	Percentage
NCV		
AIDP	5	14.7%
AMSAN	13	38%
AMAN	3	8.8%
MFS	8	23.5%
Not done	2	5.88%
Unremarkable results	2	5.88%

NCV: nerve conduction velocity, AIDP: acute inflammatory demyelinating polyneuropathy, AMSAN: acute motor sensory axonal neuropathy, AMAN: acute motor axonal neuropathy, MFS: Miller Fisher Syndrome

3.3. Treatment

The groups treated with immunoglobulin and methylprednisolone both showed improvements in terms of functions however these were not statistically significant. One patient refused treatment due to financial constraints but was noted with spontaneous improvement.

Table 6. Treatment

Treatment	Value	Percentage	disability scale before treatment	disability scale after treatment	P value
Immunoglobulin	30	88.23%	2.36+ 1.21	1.96 + 1.4	0.241
Methylprednisolone	3	8.8%	1.66 + 1.15	1.33 + 0.57	0.687
None	1	2.9%	3	1	

3.4. Outcome of the Study Population

Among the 34 patients with GBS, 97% (33 out of 34) of the patients survived. The in-hospital mortality rate of patients with GBS in this study was 3% (1 out of 34).

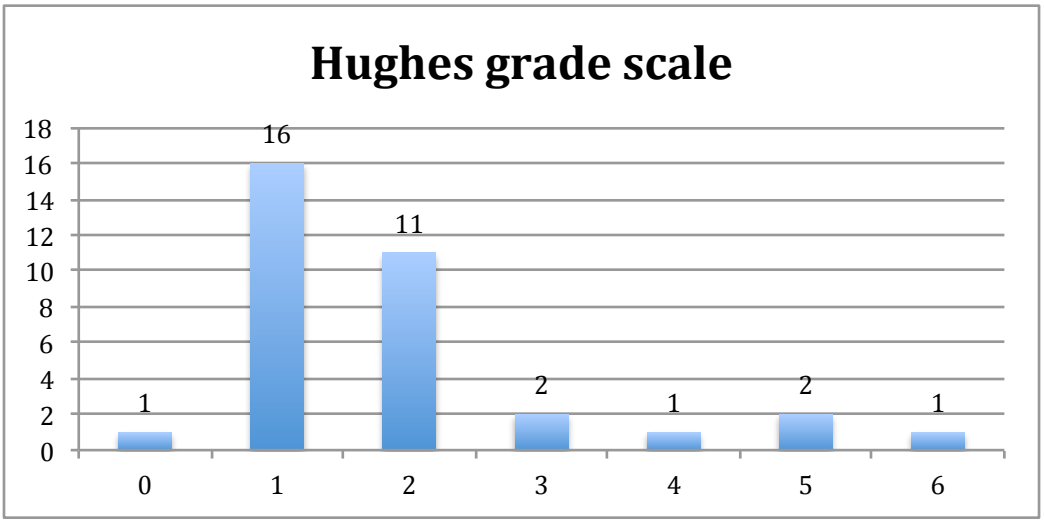
Patients were also classified under the Hughes grade scale for assessing functional motor deficits. The majority of patients had mild signs or symptoms and using the Hughes motor scale were able to run (47% - 16 out of 34), followed by patients who were able to walk unaided for 5 meters at 32% (11 out of 34). Figure 2 shows the hughes grade scale of all patients at discharge.

Table 7. Hughes motor scale

0	Healthy
1	Minor symptoms of neuropathy but capable of running
2	Able to walk without support (5m open space but incapable of manual work/ running
3	Able to walk with a stick, support (5m across an open space)

4	Confined to bed or chair bound
5	Requiring assisted ventilation (for any part of the day or night)
6	Death

Figure 2. Hughes grade scale of patients during discharge.



As elucidated in Table 7, the patients with unfavourable outcome presented earlier than favourable outcome group with a significant difference (151 hours vs 14hours, P value: <0.001). The MRC sum score of favourable outcome patients was 55.56 and that of unfavourable outcome patients was 37.75 which was also significantly different. The vital signs of both groups are not significantly different. The length of stay of unfavourable outcome group is more than that of favourable outcome group, but is not statistically significant (31 daysvs. 14 days, P value: 0.164)

Table 7. Outcomes of population

Variables	Total participants Mean ± SD	Favourable outcome (n=30) Mean ± SD	Unfavourable outcome (n=4) Mean ± SD	P value
Age	47.9 (±16.62)	43.9 ± 17.4	69.25 ± 8.73	0.002
Time	151.26 ± 100.3	151.46 ± 95.95	14 ± 11.54	<0.001
MRC score	53.47 ± 9.56	55.56 ± 8.03	37.75 ± 2.87	<0.001
SBP	129.73 + 16.97	124.8 + 27.21	129.25 + 12.73	0.598
DBP	80.7 +9.9	81.16 + 9.72	94.25 + 19.01	0.263
Temperature	36.8 + 0.81	36.83 + 0.8	36.77 + 0.5	0.844
Pulse rate	78.97 + 18.42	76.9 + 17.67	94.25 + 19.01	0.165
SpO2	97.23 + 1.81	97.36 + 1.79	96.25 + 1.89	0.33
Length of hospital stay	16.2 + 13.44	14.4 ± 11.64	31 ± 18.16	0.164

Abbreviations. MRC: Medical Research Council, SBP: systolic blood pressure, DBP: diastolic blood pressure, SpO2: oxygen saturation, SD: standard deviation. #: including patients who were expired or went on leave against medical advice.

4. Discussion

4.1 Certainty of Diagnosis

The certainty of diagnosis of GBS was based on the Brighton criteria. The majority 38% of these patients had a Brighton criteria level 2 certainty of diagnosis. 32% of the study population had a level 1 diagnosis certainty and 29% of patients had a level 4 certainty of diagnosis. These patients with a level 4 certainty of diagnosis did not present with any motor weakness and all of these patients were classified under the Miller fisher variant.

4.2 Variation with Age, Gender, Season

In this study, among the 34 patients identified, the youngest patient presented at the age of 23 and the oldest at 77 with a mean age at 47.9. In the favorable outcome group, a younger age was observed and was shown to be statistically significant than the unfavorable outcome group, which shows a younger age at presentation has better outcomes. The cases were evenly distributed in age groups of 10 years. This result is similar to a previous 7 year retrospective study done by Evangelista et al from 1981-1987 at the same institution where cases were also distributed in all age groups equally. This however is not the same with most reports. Hughes at al states that age distribution of GBS is bimodal, with peaks in young adults and the elderly with the highest incidence in the elderly and stating a hypothesis that normal immune suppressor mechanisms fail in old age.

Among these patients, 58.8% (20) were male and 41.17%(14) were females. In the same study done by Evangelista et al from 1981-1987 at the same institution, the results showed that males were affected 2:1. Our study still shows that more males are affected at a ratio of 4:3. This was also previously cited by Hughes et al that although unusual for an autoimmune disease, higher incidence rates have been reported in males than females for GBS.

A seasonal variation of GBS incidence was also entertained. No studies have reported significant differences in levels of onset of GBS between seasons. In this study, incidence of GBS was also evenly distributed throughout the year. This is consistent with a hypothesis of Hughes et al stating that a lack of a seasonal association may be due to the fact that the most frequent antecedent infections, respiratory and enteric infections, have an opposite seasonality.

4.3. Clinical profile of GBS

The most common presenting symptom was ascending paralysis (47%) followed by complaints of cranial nerve involvement (41%) and sensory disturbance at (11%). The most common symptoms seen in our patients are as follows: ascending paralysis (73%), cranial nerve involvement (47%), sensory disturbance (41%), respiratory failure (17%), dysphagia (5.8%) and bladder involvement (2.9%). These results vary from most reports as majority, almost 74-90% of their populations would have presenting symptoms of weakness[18,19]. Sensory disturbance complaints of these patients were described as numbness, tingling, allodynia and pins and needles sensation, sometimes occurring with no sensory deficits.

The most common triggering event in this study was respiratory tract infection (47%) followed by diarrhea at 20% and surgery in 1 patient. However, 29% of these patients did not note any triggering event. These findings are consistent with the current literature. In one patient, the only antecedent event recalled was hysterectomy and bilateral salphingoophorectomy for prolonged menstrual bleeding. There have been reports on incidence of GBS after surgery at 5% and 9.5% , however, these patients had undergone cardiovascular, gastrointestinal, or neurosurgical procedures.[10-17] She also received blood transfusion which ahs been identified as an anteceding event in some literature but has not been proven.

The most common complications noted in our patients were respiratory failure (17%) and autonomic dysfunction (12.9%). The mean Medical Research Council sum score, which assesses the motor power at the time of onset and severity of disease, was 53.47 $\pm$ 9.56. These findings note that most of our patients sought consult even with mild complaints of weakness. They were treated promptly as well which could have

explained that only a small percentage had complications.

4.4 Clinical Variants of GBS

As shown below, the common GBS variants according to nerve conduction studies were AMSAN (38%), MFS (23%), AIDP (14%) and AMAN (8.8%). 5% of patients had unremarkable results and another 5% did not undergo the nerve conduction test. Those who did not undergo the electrophysiologic tests were treated as GBS due to clinical findings of a Miller Fisher variant. In most of the literature, AMAN is the more common variant seen along with AIDP although there was one study reporting majority of their population had a MFS variant. In North America and Europe, around 5% of patients with GBS have the axonal subtypes. Central and South America, Japan and China have axonal subtypes that account for 30–47% of cases and Miller-Fisher syndrome has been found to account for around 5% of cases of GBS.[20]

4.5 Treatment

Both groups treated with immunoglobulin and methylprednisolone both showed improvement in functioning however these were not statistically significant. One patient refused treatment due to financial constraints but was noted with spontaneous improvement. All patients were treated within 1-3 days after admission.

4.6 Outcome

Among the 34 patients with GBS, 97% (33 out of 34) of the patients survived. The in-hospital mortality rate of patients with GBS in this study was 3% (1 out of 34). Although this patient initially presented with a mild weakness, he already had several comorbidities, which could have attributed to his condition. He also had an intracerebral hemorrhage and coronary artery disease. Although this study was conducted in a developing country, the results show a low mortality rate than the current literature. This could be attributed to patients seeking consult earlier and the disease diagnosed without delay, which allowed prompt treatment.

Patients were also classified under the Hughes grade scale for assessing functional motor deficits. The majority at 47% of patients had mild signs or symptoms and using the Hughes motor scale were able to run followed by 32% of patients who were able to walk unaided for 5 meters. Only 8.8% of the population was discharged with poor functionality. They are the ones under those with unfavorable outcome. These patients with unfavourable outcome presented earlier than the favourable outcome group with a statistically significant difference noted(151 hours vs 14hours, P value: <0.001). The MRC sum score of favourable outcome patients was 55.56 and that of unfavourable outcome patients was 37.75 which was also significantly different. They presented with a more severe weakness at onset. The vital signs of both groups are not significantly different. The length of stay of unfavourable outcome group is more than that of favourable outcome group, but is not statistically significant (31 days vs. 14 days, P value: 0.164).

5. Conclusion

GBS was seen in all age groups in this study with a slightly male predominance. The majority of patients had a history of respiratory infection although almost 30% had no known triggering event. The most common presenting symptom was ascending paralysis followed by complaints of cranial nerve involvement. Younger age and less severe disease presentation at onset correlates with a more favorable outcome. Patients who presented earlier after the triggering event were noted to have a faster rate of progression of symptoms and a worse outcome. The common GBS variants in this study according to nerve conduction studies were AMSAN and MFS. Methylprednisolone and IVIG were both effective with no statistically significance noted in both groups. The in-hospital mortality rate was at 3%. Majority of patients had a good functional outcome.

6. References

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