Mortality Outcome in Patients of Guillian Barre Syndrome. A single Center Study

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ABSTRACT

Introduction: The Guillian Barre syndrome (GBS) is characterised by acute areflexic paralysis with albumin-cytological dissociation. Study was undertaken to analyze the electrophysiological studies, clinical profile and outcome of GBS at our institute.

Material and Methods: This study was a hospital based descriptive and prospective study was conducted on patients admitted in the Medical intensive care unit. Patients with age more than 18 years, irrespective of their sex, diagnosed as GBS, fulfilling the criteria as modified by Asbury were included in the current study. Association between qualitative variables was assessed by Chi-Square test. Quantitative data was represented using mean ± SD, median.

Results: Out of 50 enrolled, 21 patients belonged to age 21 to 40. 33 pts were male and 17 pts were female, 7 patients expired. Two peak of occurrence of GBS was found in age one in age group 21 to 41years and another in age more than 51 years.13 patients had history of antecedent infection. 35 patients had albumin-cytological dissociation. As per the results of nerve conduction study, patients were categorized in the following 3 groups AMAN-24, AIDP-14 and ASMAN-12.

Conclusions: The independent predictors for the need of mechanical ventilation were history of breathlessness on admission, SBC of equal to or less than 10, upper or lower limb power of less than or equal to 2 (P valve <0.01). The predictors of poor outcome were presence of sepsis, need for mechanical ventilation, VAP, SBC of ≤ 10 and lower limb power ≤2.

Keywords: Nerve Conduction Study, Mechanical Ventilator

INTRODUCTION

The Guillian Barre syndrome (GBS) is characterised by acute areflexic paralysis with albumin-cytological dissociation. GBS is a heterogeneous condition with several variant forms. The incidence rates for GBS are 1-2 per 100,000 population.[1,2] While all age groups are affected the incidence increases by 20 percent with every 10 year increase in age group beyond first decade of life. Most patients need hospitalization and about 30 percent require a mechanical ventilatory support due to respiratory muscle paralysis.[3] The need for mechanical ventilation is associated with more rapid progression of disease, more severe weakness at the time of admission and the presence of facial or bulbar weakness during the first week of admission. Several subtypes of GBS are recognized and are classified according to the electro-diagnostic studies. The most common variant is acute inflammatory demyelinating polyneuropathy (AIDP). Additionally there are two axonal variants which are often clinically severe:- the acute motor axonal neuropathy (AMAN) and acute sensory motor axonal neuropathy (ASMAN).

Approximately 70 percent of cases of GBS occur after 1 to 3 weeks of an acute infectious episode usually respiratory or gastrointestinal. Cerebrospinal fluid (CSF) findings are characterised by ablumino-cytological dissociation i.e. elevated CSF protein without pleocytosis. Electrodiagnsotic (EDX) features are mild or absent in early stages of disease. In AIDP the earliest feature is prolonged F wave latencies, prolonged distal latencies and reduced amplitude of the compound muscle action potential. In cases with primary axonal pathology, the principle finding is reduced amplitude of the compound muscle action potential without conduction slowing or prolongation of distal latencies. In majority of patients of GBS the treatment should be initiated as soon after the diagnosis as possible. Either high dose intravenous immunoglobulin (IVIg) or plasmapheresis can be initiated as they are equally effective. A combination of two therapies is not significantly better than either alone. Glucocorticoids have not been found to be effective.

Approximately 85 percent of patients with GBS achieve a full functional recovery within several months to a year, with a mortality rate between 1-18 %.[4,5] Between 5 to 10 percent of patients with GBS have one or more relapses. In India the incidence of AIDP and AMAN are almost equal though AMAN is more common in younger patients.[6] In western countries, GBS is common in the 5th decade but in India it occurs more commonly at younger age.[7,8,9]

Very few studies have addressed the issue of the clinical predictors of the need of mechanical ventilaton and the outcome. Hence, we decided to undertake this study to analyze the electrophysiological studies, clinical profile and outcome of GBS at our institute.

MATERIAL AND METHODS

The Study was carried out for a period of 18 months on 50

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How to cite this article: Rakesh Bhadade, Rosemarie deSouza, Parag Bawaskar. Mortality outcome in patients of guillian barre syndrome. a single center study. International Journal of Contemporary Medical Research 2019;6(6):F17-F21.

DOI: http://dx.doi.org/10.21276/ijcmr.2019.6.6.22

patients after receiving approval from the institutional ethics committee. This study was a hospital based descriptive and prospective study was conducted on patients admitted in the Medical intensive care unit at tertiary care teaching public hospital. Patients with age more than 18 years, irrespective of their sex, diagnosed as GBS, fulfilling the criteria as modified by Asbury were included in the current study.[10]Patients (pts) with hexacarbon abuse, abnormal porphyrin metabolism, recent diphtheria infection, lead intoxication, botulism, hysterical paralysis, and toxic neuropathy were excluded from the study.

50 patients of the GBS according to inclusion and exclusion criteria were included in our study. It was observed that, in previous three years the number of GBS pts in medical intensive care unit (MICU) were around 3 to 4 per month. Hence by convenient sampling the number of patients in 18 months would be around 54 to 72.But in our study we could get 50 cases during 18 months period.

Written informed valid consent was taken from each patient. Consent of legally accepted relatives was taken in patients who were intubated and on a mechanical ventilator. A participant re-consent was taken once patient was able to do so. The study was explained to the patient and their relatives in the language they best understood. The patient information sheet was provided to them. Patients were selected as per the inclusion and exclusion criteria and were enrolled from MICU. Demographic data including the age of patient, gender, address was noted. Detailed history with respect to the duration of onset of symptoms, rate of progression of weakness, severity of disease in terms of breathlessness on admission, history of autonomic nervous system involvement such as, alteration in bladder, bowel habits and presence of abnormal sweating, presence of sensory symptoms in the form of tingling sensation, pains and numbness was noted. History of cranial nerve involvement was recorded. Past history of infection such as upper respiratory tract infection (URTI), loose motions, history of vaccination and any recent surgery was enquired. Neurology examination as per case record sheet; power in all 4 limbs, cranial nerve examination, single breath count, sensory / motar examination was done. CSF analysis was done to look for albumin-cytological dissociation i.e. CSF protein of more than 45 mg and total cells less than 10/mm^3. Nerve conduction studies (NCS) were carried out in all the patients enrolled in the study. Based on electrophysiological abnormalities GBS was divided into AIDP, AMAN and AMSAN according to Ho et al criteria.[11] Patients were examined daily and a note was made of any complications that developed during their hospital stay, including duration of mechanical ventilation. The treatment received was documented and outcome in terms of survival or death was noted. Patients were followed up till discharge from the hospital. The Results and conclusion were drawn from the analysis of data.

STATISTICAL ANALYSIS

Qualitative data was represented in form of frequency and percentage. Association between qualitative variables was assessed by Chi-Square test, with Continuity Correction for all 2 X 2 tables and by Fisher's exact test for all 2 X 2 tables where Chi-Square test was not valid due to small counts. Continuity Correction was applied for all 2 X 2 tables after pooling of data. Quantitative data was represented using mean ± SD, median. Appropriate statistical software, including but not restricted to MS Excel, PSPP version 1.0.1 was used for statistical analysis. An alpha value (p-value) of $\leq$0.05 was used as the cut-off for statistical significance.

RESULTS

Out of 50 enrolled, 21 (42%) patients belonged to age 21 to 40. 33 pts were male and 17 pts were female, 7 (14%) patients expired. Two peak of occurrence of GBS was found in age one in age group 21 to 41years and another in age more than 51 years.13 (26%) patients had history of antecedent

Clinical Profile	Number of Pts (N=50)	Mortality (N=07)	P-value
Male:Female	3:1	5:2	-
Upper limb power $\leq$ 2	49	7	0.001
Lower limb power $\leq$ 2	49	7	0.001
Sensory symptoms	18	0	-
Breathlessness on admission	18	7	0.04
Single breath count $\leq$ 10	08	5	0.01
Cranial nerve involvement	10	1	0.1
Need for mechanical ventilation	15	7	0.01
Sepsis	05	3	0.016
Ventilator associated pneumonia	08	5	0.01
Antecedent infection	13	2	0.17
Hypertension	09	5	0.71
Tachycardia (Heart rate >100)	08	3	0.17
Abnormal sweating	09	1	1.00
Duration of symptom $\leq$ 5 days	27	5	0.32
Albumino-cytological dissociation	35	3	-
Immunoglobulin	38	5	0.04
Plasma exchange	12	2	0.75

Table-1: Clinical Profile and Mortality Outcome of study population

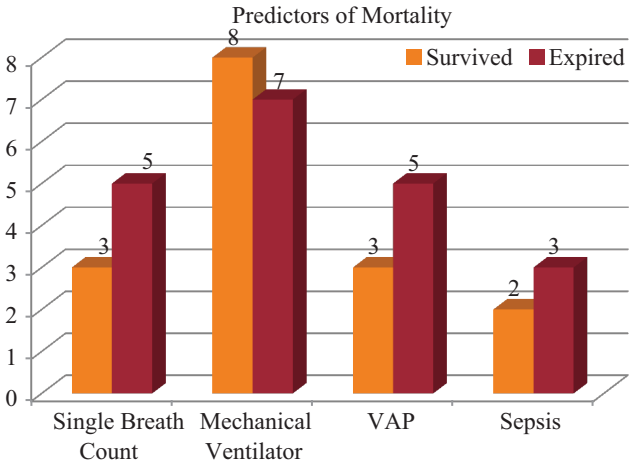

Figure-1: Predictors of mortality and poor outcome.

infection, out of 13 patients, 7 had loose motions, 5 had URTI and 1 patient had chicken pox in recent past. Peak occurrence of GBS, 22 pts was in monsoon i.e. from June to September. Nerve conduction study (NCS) was done in all 50 patients. As per the results of NCS, patients were categorized in the following 3 groups AMAN-24 (48%), AIDP-14 (28%) and ASMAN-12 (24%). 35 pts (70%) patients had albumin-cytological dissociation. [Table 1, Figure 1]

DISCUSSION

Our study included 50 patients of GBS. The youngest patient in our study was a 19 year old male and the oldest was an 86 year old female and the mean age of presentation was 40 years. Mean age of patients in a study done by Sudulagunta SR et al, which included 1166 patients was 42.8 years, and 35 % patients were above 50 years of age.[12] The ratio of male to female was approximately 2:1. Dhadke et al in a study done at Solapur found the male to female ratio of 1.5:1.[4] In our study, 22 (44%) of patients were admitted in between June – September month. Thus a monsoon predominance of occurrence of GBS was noted in our study. Kaur et al reported similar findings of peak incidence between Jun – July.[7]

In our study, 13 out of 50 i.e. 26% patients had a preceding illness. None of our patients had a recent history of either any vaccination or any surgery as a possible trigger for GBS.55% of the patients had a preceding illness in a study performed by Dhadke et al in which majority had URTI followed by loose motions.[4] An antecedent infection was present in 32.2 % of patients in a study done by Verma et al at Lucknow.[13] Our study found a lower incidence of an antecedent infection. The difference could be explained as a history of fever was not considered as antecedent event as other studies did. However, the most common preceding infection was loose motions, which was comparable to the finding in other studies.

Albumino-cytological dissociation in CSF was present in 35 (70 %) patients. In a study done by Dhadke, 65 % patients had albuminocytological dissociation which was comparable to our findings.[4] Hughes et al in their independent studies showed that 80% of the times there is albumin-cytological dissociation.[14] AMAN was the commonest variant of GBS in our study. In the north Indian study the distribution of GBS subtypes was AIDP in 86.3%, AMAN in 7.8%, and AMSAN in 6.7%. The distribution of GBS subtypes in the south Indian study was: AIDP in 85.2%, axonal variants in 10.6%, and 4.2% were unclassifiable.[15] AIDP was found to be the predominant variety of GBS in most of the studies done in India. In our study AMAN variety was the commonest. The difference in this finding could be explained by the difference in the age of patients included in other studies, as our study was limited to patients above 18 years of age and excluded the pediatric population and the difference in criteria used to classify GBS according to NCS.

10 out of 50 (20%) patients had cranial nerve involvement. All the patients had bilateral facial nerve paralysis while one patient had bilateral sixth nerve paralysis. Study done by Dhadke et al found that 62.5 % of their patients had cranial nerve involvement, commonest being the facial nerve.[4] Bhargava et al found that 62.3% (38) patients had cranial nerve palsies, in that 25 had multiple cranial nerve palsies, and 13 had single type of nerve palsy, Facial nerve palsy was seen in 28 (46%), all had bilateral involvement except 3 patients who had unilateral palsy.[16] Thus occurrence of cranial nerve palsy was less common in our study population as compared to other studies. But the commonest cranial nerve palsy was facial nerve.

18 patients (36%) had a history of sensory symptoms in the form of parathesia, tingling, pain and numbness. All of these patients had sensory symptoms as one of the presenting complain along with weakness.70% patients had subjective sensory complaints in a study done by Bhargava et al.[16] Loeffel Rossi et al in 1997 reported that 75 % of patients the first neurological symptom was parathesia.[17] All of our patients presented with weakness in either lower or upper limb or both. 48 out of 50 (96%) patients had both upper and lower limb weakness as a presenting complain on admission. One patient presented with only upper limb (UL) weakness and one with only lower limb (LL) weakness. Dhadke et al in their study of 40 cases of GBS in 2013 in India observed that quadriparesis was the presenting complain in 97.5 % of patients.[4] Thus our study confirms this finding in which 96% had quadriparesis as the presenting feature.

44 out of 50 patients had absent deep tendon reflexes (DTR) while 6 patients had 1+ reflex. Adam and Victor have described incidence of absent or depressed reflexes in 90 % and 10 % cases respectively; there may be preservation of reflexes except ankle jerk which is lost in the initial phase of illness followed by loss of other reflexes later on.[18] The muscular weakness which is classical of GBS described as ascending and symmetrical with depressed and/ or absent DTR this pattern has been described in more than 90 % of cases of GBS in various studies Hadden et al.[19]

15 out of 50 (30%) patients required mechanical ventilation. The mean duration of mechanical ventilation was 15 days, and the mean age was 41.33 years. The longest duration of ventilator required was 40 days. Out of 15, 5 (33%) patients required mechanical ventilation for less than 10 days,6 (40%)

patients required for less than 20 days and 4 (26%) required for more than 20 days. In a study performed by John et al in 2014 in kerala, 18.2 percent required mechanical ventilation and the mean duration of ventilatory support was 17 days.[20] A study done in Pakistan included 92 patients.31 (33.7%) patients of GBS needed mechanical ventilation.[21] Thus the mean duration and number of patients requiring mechanical ventilation was comparable to other studies.

50 % of patient had an autonomic dysfunction. Tachycardia was present in 8 (16%) patients, hypertension in 9 (18%) patients and abnormal sweating in 9 (18%) patients. All three features were present only in 2 patients. 24 patients with GBS were prospectively evaluated by N.K Singh et al for the evidence of autonomic dysfunction which occurred in 16 (66.7%) patients. Sinus tachycardia (33.3%), bradycardia (8.3%), hypertension (33.3%), postural hypotension (35%), urinary sphincter disturbances (20.8%) and anhydrosis of lower limbs (12.5%) was noted.[22]

The mortality of patients with GBS has varied widely with rates between 1-18%. Death results from pneumonia, sepsis, adult respiratory distress syndrome (ARDS) and less frequently due to autonomic dysfunction or pulmonary embolism. In a retrospective study done from data of 1984 to 2007 mortality was found to be 12.1%.[5] In another Indian series from NIMHANS, patients with severe GBS, all requiring mechanical ventilation, had a mortality rate of (10.4%).Thus mortality rate in our patients was comparable to other studies. Out of 7 patients who died in our study, all had developed VAP, 3 of them had sepsis, 1 died of acute coronary syndrome and 1 had aspiration pneumonitis. Out of 43 patients who survived, only 2 of them had developed VAP while one had deep vein thrombosis. In total 9 (18%) patients developed VAP during hospital stay, 5 (10%) had sepsis, 2 (4%) had pressure-sores, 1 (2%) had acute kidney injury and urinary tract infection.VAP was the most frequent complication (56%) in a study done by Ali MI et al.[21]

8 out of 8 (100%) patients who had SBC of less than or equal to 10 required mechanical ventilation (P value < 0.01). 11 out of 21 patients (52%) and 12 out of 25 (48%) who had upper limb and lower limb power of less than or equal to 2 respectively required mechanical ventilation (P value <0.01). 12 out of 18 (67%) patients who required mechanical ventilation had history of breathlessness on admission (P value <0.01). SBC of ≤ 10, upper or lower limb power of ≤ 2 and history of breathlessness, were independent predictors for the need of mechanical ventilation and were statistically significant with a P value of<0.05. 2 out of 10 patients (20%) who required mechanical ventilation had cranial nerve paralysis (P valve 0.702), 6 out of 13 patients (46%) had a history of an antecedent infection (P value 0.17), 4 out of 8 patients (50%) had a heart rate more than 100 (P valve 0.17), 3 out of 9 patients (33%) had abnormal sweating (P valve 1.0), and 2 out of 9 patients (22%) who required mechanical ventilation had hypertension (P value 0.71). Thus the presence of cranial nerve involvement, history of an antecedent infection and presence of autonomic dysfunction were not associated with the need for mechanical ventilation. Paul et al concluded that factors independently associated with the need for mechanical ventilation included simultaneous motor weakness in UL and LL as the initial symptom (P=0.02) and UL power <3 at nadir.[23] Another study revealed that shorter interval from onset to admission ($p<0.05$), facial nerve palsy ($p<0.01$), glossopharyngeal and vagal nerve deficits ($p<0.01$) and lower Medical Research Council score at nadir ($p<0.01$) were risk factors for mechanical ventilation.[24] Time taken to reach maximum deficit, neck weakness, bulbar weakness, facial weakness, single breath count (SBC), forced vital capacity, and phrenic nerve latency predicted the need for mechanical ventilation in a study done in 2014.[25] Thus single breath count of less than or equal to 10, a need for mechanical ventilation, the presence of VAP, sepsis and LL power of ≤ 2 were associated with a poor outcome i.e. death.

Deaths resulting from GBS are nowadays uncommon, because of advances in all the aspects of intensive care. Patients requiring mechanical ventilation may have higher mortality rates.[26] Death in GBS usually results from pneumonia, sepsis, adult respiratory distress syndrome, and less frequently, from autonomic instability or pulmonary embolism; most of these patients are on ventilatory support.[27] In a study done by Alshekhlee A concluded that predictors of mortality in GBS included older age, composite comorbidity index, cardiac complications, and sepsis.[28]

CONCLUSION

GBS is now considered a heterogeneous disorder with both demyelinational and axonal variants. The independent predictors for the need of mechanical ventilation were history of breathlessness on admission, SBC of equal to or less than 10, upper or lower limb power of less than or equal to 2 (P valve <0.01).The predictors of poor outcome were presence of sepsis, need for mechanical ventilation, VAP, SBC of ≤ 10 and lower limb power ≤ 2. Thus, from the inference of the current study, to reduce the mortality we recommend avoiding unnecessary prolonged hospitalization, whenever possible considering noninvasive ventilation and starting an early and appropriate weaning protocol. Also identifying risk factors for VAP and meticulous preventive measures in high risk groups are must along with adequate staffing and strict hospital infection control policy.

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Source of Support: Nil; **Conflict of Interest:** None

Submitted: 26-04-2019; **Accepted:** 28-05-2019; **Published:** 18-06-2019