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CLINICAL PREDICTORS OF MECHANICAL VENTILATION IN GUILLAIN-BARRÉ SYNDROME (GBS)

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ABSTRACT

Introduction: Guillain-Barre' Syndrome is the most common cause of acute flaccid paralysis worldwide. One of the most serious complications is respiratory failure warranting mechanical ventilation which is required in about 30% of the patients. Various studies have been carried out to identify clinical factors which could help identify patients with impending respiratory failure and facilitate elective mechanical ventilation in these patients to reduce the associated mortality. **Material and methods:** 92 patients diagnosed with GBS were enrolled from February 6, 2013 to August 5, 2013 in department of Neurology, PIMS, Islamabad. Each patient was then be managed accordingly and monitored for therequirement of ventilatory support. Based on the need of Mechanical ventilation patients were divided in to 2 groups: ventilated (Group 1) and non-ventilated (Group 2) and presence of various clinical factors were assessed in both groups. **Results:** The mean age of patients was 33.83 ± 16.91 years with a male preponderance (68.48%). 31 (33.7%) patients of GBS needed mechanical ventilation.Patients requiring mechanical ventilation tended to have more severe disease evidenced by the presence of bulbar dysfunction (P=.000), autonomic dysfunction (P = .000), and upper limb paralysis (P = .010). The presence of a preceding gastrointestinal illness did not prove to be an independent predictor of mechanical ventilation on multivariate analysis. **Conclusion:** The course of patients with severe GBS leading to mechanical ventilation can, to some extent, be predicted on the basis of clinical factors. This study identifies bulbar dysfunction and dysautonomia as significant independent predictors of mechanical ventilation.

INTRODUCTION

Guillain-Barre' Syndrome (GBS) isthe most common cause of acute flaccid paralysis worldwide [1].It is an autoimmune, self-limiting disease triggered in most cases by a preceding respiratory tract infection or diarrheal illnessin 60% of the cases. The most frequent antecedent pathogens include Campylobacter jejuni, Cytomegalovirus, Epstein Bar virus and Mycoplasma pneumonia [1, 2]. It is thought that immune responses directed towards infective organisms cross react with neural tissues resulting in GBS [2].The incidence is variable between 0.4-1.7 cases per 100,000 persons per year and it occurs in all parts of the world in all seasons. It affects people of all ages and both genders [1].Diagnosis is descriptive made on the basis of clinical parameters, nerve conduction studies and the presence of protein cell dissociation on CSF analysis. There are two chief variants on the basis of electrodiagnostic studies - demyelinating and axonal. Guillain-Barre' Syndromeisa cause of significant disability and morbidity worldwide. Acute mortality in GBSis about 5% [3].One of the most serious complications is respiratory failure warranting mechanical ventilation. Worldwide various studies have been carried out to identify various clinical and electrodiagnostic markers which could help identify patients with impending respiratory failure and facilitate elective mechanical ventilation in these patients to reduce the associated mortality [3, 4]. The management of patients with Guillain-Barré syndrome (GBS) can be difficult because of the unpredictable course and potential for rapidly producing life-threatening respiratory failure necessitating shifting to an intensive care facility and mechanical ventilation. Many studies have identified factors that are associated with the need for ventilation. Bulbar dysfunction and facial palsy are thought to be important clinical factors leading to mechanical ventilation in patients of Guillain-Barre' Syndrome [3].Other factors include rapid disease progression, upper limb paralysis and autonomic dysfunction [5,6] reatment of GBS though challenging,is mainly supportive and is centered at the anticipation and prevention of various complications.Immunomodulation with Plasmapheresisand IV immunoglobulin (IVIG) help shorten the course of the disease [1, 2, 7, 8].Management of patients with respiratory dysfunction would be simplified and guidelines for the use of elective intubation and admission to the ICU could be developed if accurate predictors of respiratory failure could be identified early in the course of the disease. Mechanical ventilation, which is the final

consequence of several clinical factors, [3-6] is required in about 30% of patients of Guillain-Barre' Syndrome [9-10]. Although guidelines exist as to when to proceed with intubation, early indicators of subsequent progression to respiratory failure have not been established. The aim of this study is to determine the frequency of mechanical ventilation in GBS patients in our local clinical setting and to identify the clinical factors leading to respiratory failure,which would help in the early management of these patients and reduce the associated morbidity and mortality.

MATERIALS AND METHODS

It was a prospective study carried out at the PIMS hospital, Islamabad from February 2013 to August, 2013. A consecutive series of 92 patients diagnosed with GBS admitted to the neurology department were studied. This study was an independent project of the department and was not funded by any pharmaceutical organization. Informed consent was obtained from all patients. All patients above the age of 13 years diagnosed as GBS were enrolled in the study. The diagnosis of GBS was made on the basis of clinical and typical electrodiagnosticfeatures, adapted from Asbury and Cornblath criteria [11].The clinical parameters includedpresence of all of the following on history and clinical examination: progressive weakness in both arms and both legs, development of symptoms in less than 4 weeks, relative symmetry of symptoms and areflexia. The electrodiagnosis of Guillain-Barre Syndrome wasmadeon the basis of Nerve Conduction Studies which includes thepresence of any one of the following: prolonged distal latencies in two or more nerves, slowing of Conduction Velocity in two or more nerves, decreased amplitude in two or more nerves, prolonged F response in one or more nerves or conduction blocks in one or more nerves. Key exclusion criteria included patients having a sensory level on clinical examination, pregnancy or four weeks post-partum, systemic illness other than GBS associated with neuropathy e.g.diabetes, chronic renal failure, hereditary neuropathies andtoxin exposure, hypokalemic periodic paralysis and presence of pulmonary comorbidity on history&/or chest X-ray (chronic obstructive airways disease, asthma, pulmonary fibrosis). All patients under went detailed history and neurological examination. Demographic data recorded included age, gender and antecedent event.Clinical features recorded included presence of facial weakness, upper limb paralysis (complete absence of movement in the upper limbs), autonomic dysfunction (unexplained blood pressure or heart rate fluctuations or significant bladder or bowel dysfunction), and bulbar dysfunction (dysarthria, dysphagia or impairment of the gag reflex). Each patient

was managed with specific treatment with plasma exchange and monitored for the requirement of ventilatory support. Patients were intubated if they had bulbar palsy, use of accessory muscles or arterial blood gases showing $pO2 <70$ mmHg or $pCO2 >45$mmHg. Based on the need of Mechanical ventilation patients were divided in to 2 groups: ventilated (Group 1) and non-ventilated (Group 2).

DATA COLLECTION & STATISTICAL ANALYSIS

Data was entered and analyzed using SPSS version 17. Mean and standard deviation were calculated for quantitative variables (age). Frequencies and percentages were calculated for qualitative variables (gender, antecedent illness, upper limb paralysis, autonomic dysfunction, bulbarinvolvement, facial weakness and mechanical ventilation). For the purpose of statistical tests, age was divided into three groups and assessed as a categorical variable. Chi-square/ Fisher-Exact test was used to compare the frequencies of clinical factors between the ventilated and non-ventilated patients. Predictors of ventilation were assessed using stepwise univariate logistic regression analysis. Predictors found to be significant in univariate analysis were further assessed via multivariate logistic regression. In both of these models, mechanical ventilation was the dependent variable and all others were independent variables. P < 0.05 was taken as statistically significant.

RESULTS

92 patients were included in the study. The demographic characteristics of the study population are summarized in Table I. The mean age of patients was 33.83 years with a standard deviation of 16.91 years (range 13 years- 75 years). There was a male preponderance and history of a preceding upper respiratory tract infection was the most frequent antecedent event reported.

TABLE I: DEMOGRAPHIC FEATURES:

Age mean		33.83 ± 16.91 years
		(range 13-75 years)
Gender	Male	68.48% (n=63)
	Female	31.52% (n=29)
Antecedant illness	Diarrhea	18.5% (n=17)
	Upper respiratory tract illness	51.1% (n=47)
	Not identifiable	30.4% (n=28)

31 (33.7%) patients of GBS needed mechanical ventilation and 61 (66.3%) patients did not need mechanical ventilation. No significant differences were noted between those patients who received ventilation and those who did not for age and gender. Patients requiring mechanical ventilation tended to have more severe disease evidenced by the presence of bulbar dysfunction (P=.000), autonomic dysfunction (P = .000), and upper limb paralysis (P = .010). The presence of a preceding gastrointestinal illness was statistically significant in the ventilated group on univariate analysis. However, on multivariate analysis it did not prove to be an independent predictor of mechanical ventilation.

FIGURE I: DEMOGRAPHICS AND CLINICAL FEATURES OF THE VENTILATED AND NON-VENTILATED GROUPS
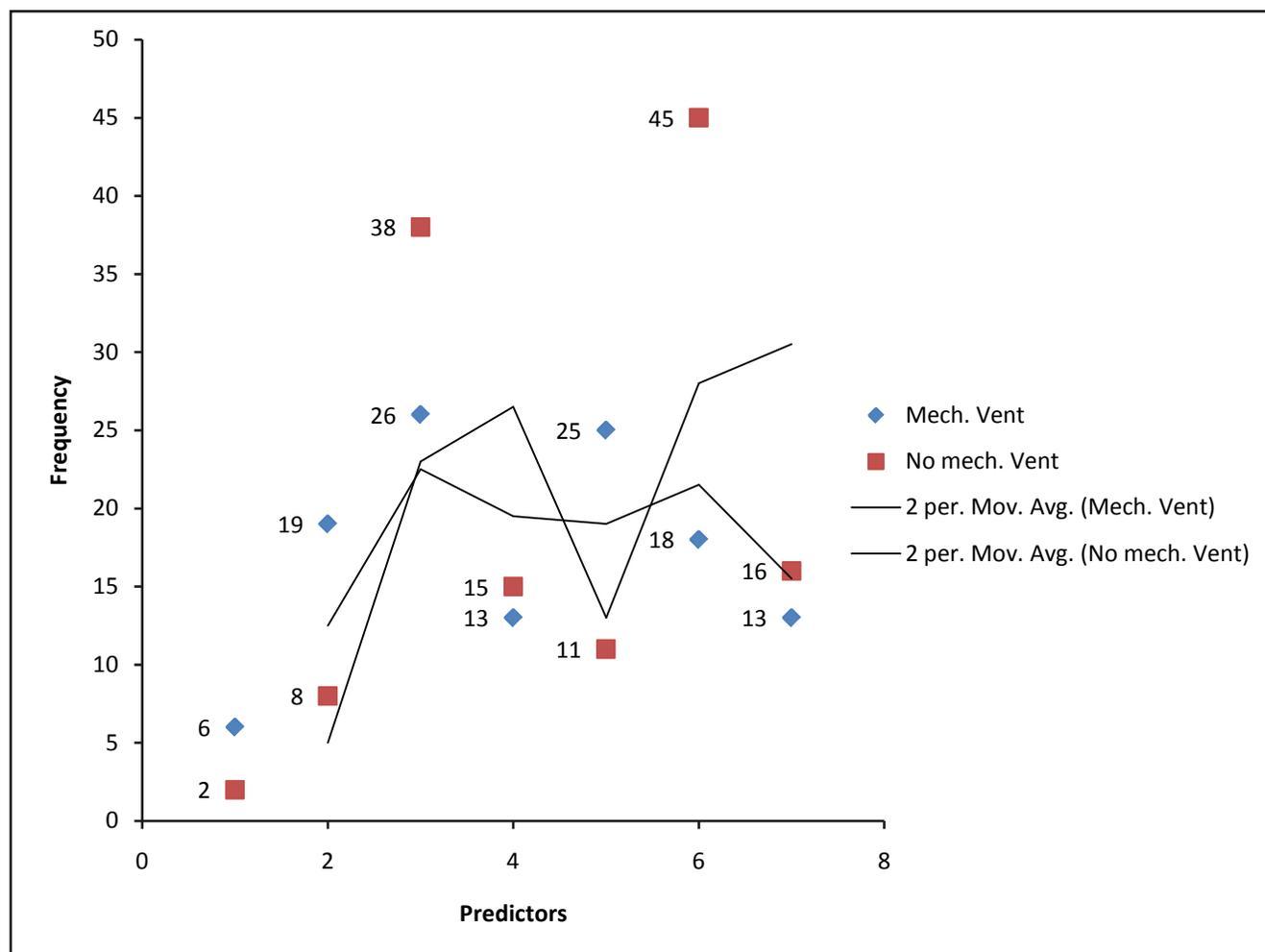
Predictors of mechanical ventilation in GBS.Figure 1: 1 = Upper limb paralysis, 2 = Dysautonomia, 3 = Antecedent illness, 4 = Facial palsy, 5 = Bulbar dysfunction, 6 = Male, 7 = Female.

Bulbar dysfunction and dysautonomia were found to be multivariately predictive of mechanical ventilation as shown in table no 2. Corresponding 95% confidence intervals are also shown in table no 2. The other factors were not of any significance in this regard on multivariate analysis.

TABLE II: MULTIVARIATE PREDICTORS OF MECHANICAL VENTILATION:

Predictor	Frequency & percentage	95% confidence interval	P
Bulbar dysfunction Yes No	 25 & 80.6% 6 & 19.4%	 4.997-355.351	.000
Dysautonomia Yes No	 19 & 61.3% 12 & 38.7%	 8.000-521.420	.001

DISCUSSION

Guillain-Barré Syndrome is the leading cause of acute paralysis in industrialized countries. About one quarter of patients have respiratory failure requiring intensive care unit (ICU) admission and invasive mechanical ventilation[1]. Progressive weakness of both the inspiratory and the expiratory muscles is the mechanism leading to respiratory failure. Aspiration pneumonia and atelectasis are common consequences of the bulbar muscle weakness and ineffective cough [5-12]. The classical signs of respiratory distress occur too late to serve as guidelines for management, and measurements of vital capacity and static respiratory pressures are useful to determine the best times for starting and stopping mechanical ventilation. However, this facility is not available in most neurology wards of the developing world. Several clinical factors present at admission and during the ICU stay are known to predict a need for invasive mechanical ventilation. They include rapidly progressive motor weakness, upper limb paralysis, neck weakness, bulbar muscle weakness, facial nerve involvement and autonomic dysfunction [6, 13, 14] The results of our study suggest that a decline in respiratory function and progression to mechanical ventilation should be anticipated in patients with severe GBS who have bulbar dysfunction or dysautonomia. The presence of upper limb weakness and antecedent gastrointestinal illness were also associated with an increased likelihood of mechanical ventilation on univariate analysis. However, they did not independently predict the need for mechanical ventilation on multivariate analysis. This may be due to the confounding effect of the other variables. Facial palsy was identified in a higher proportion of patients who subsequently received mechanical ventilation, but this did not reach statistical significance. Patient-dependent factors such as age and gender did not predict the progression to mechanical ventilation In our study male preponderance was seen. 68.48%

patients were male and 31.52% patients were female. These results are comparable to other studies. Nachamkin et al reported a slight male predominance (M:F = 1.3:1) in the Mexican population[15]. A similar gender distribution was noted in a Turkish study [16]. The mean age of our study population was 33.83 ± 16.91 years. In a study conducted by Azim A et al on eighty six patients results showed that the mean age of patients was 32.4 (± 18.12) years [17].Majority (82%) of their patients were male. In another study which was conducted byAreeyapinan P et al it was reported that 26 patients were male and 29 patients were female [18]. The mean age of patients in this study was 43 +/- 17 years. In a study conducted by Yuan CL et al on 49 cases of typical GBS a non-specific age distribution was noted [19]. History of a preceding upper respiratory tract infection was the most frequent antecedent event reported in this study in 51.1% of the cases. Yuan CL et alhad reported Upper respiratory tract infection (URI, 53%) as the most common antecedent event, followed, in descending order, by gastrointestinal symptoms (10%), skin lesions (6%) and ear infections (2%), in their study (19).The presence of history of a gastrointestinal illness as one of the antecedent illnesses was significantly associated with patients who required mechanical ventilation on univariate analysis. This again is in harmony with the results of earlier studies (3). In our study population, 33.7% patient required mechanical ventilation. These results are also comparable to other international studies. Durand MC et al included 154 patients with Guillain-Barré syndrome in their study and 34 (22%) patients were subsequently ventilated (20).In a study by Lawn et al 60 patients out of 114 received mechanical ventilation (6)Paul et al in their study discussed that 39% of the patients required mechanical ventilation (3). Mechanical ventilation in GBS is the final consequence of several clinical factors. This study identified bulbar weakness and autonomic dysfunction as independent predictors of mechanical ventilation. These results are

pretty much in keeping with the results of earlier studies. In the study conducted by Areeyapinan P et al bulbar paresis as the presenting symptom was the only clinical prognostic factor that significantly determined airway compromised and subsequently respiratory failure (18).In a study conducted by Netto AB et al showed that 273 GBS patients were managed with ventilatorysupport (21). Out of 273 patients with ventilatory support, bulbar palsy was present in 186 (68.1%), sensory involvement in 88 (32.2%) and symptomatic autonomic dysfunction in 72 (26.4%) patients. Sundar U et al in their study compared the clinical data in the ventilated and non-ventilated groups, early peak disability, autonomic dysfunction and bulbar weakness predicted the onset of respiratory paralysis (22).Age, gender, neck or bifacial weakness, upper limb paralysis, or preceding infection did not influence the development of neuromuscular respiratory weakness. On comparison of data in ventilated and non-ventilated groups, time to peak disability was significantly shorter in the ventilated group (33 hours) as compared to non-ventilated group (6 days). The presence of bulbar palsy (18/28 in ventilated vs. 2/18 in non-ventilated) and autonomic dysfunction (14/28 ventilated vs. 1/18 non-ventilated) were significantly commoner in the ventilated group. Lawn ND et al showed that progression to mechanical ventilation was highly likely to occur in those patients with rapid disease progression, bulbar dysfunction, bilateral facial weakness, or dysautonomia (6). Bulbar Palsy and Facial Palsy are thought to be clinical factors leading to mechanical ventilation in patients of Guillain-Barre' Syndrome, with frequencies of 92.5% and 98% respectively in ventilated patients against frequencies of 28.2% and 57.6% in non-ventilated patients (3). In the study conducted by AzimA et al Autonomic dysfunction was present in 35% of patients (17).In a study conducted by Yakoob MY et al83 showed that most patients developed GBS within one month of the preceding infection. Cranial nerve abnormalities (30/34, 88.2%), autonomic dysfunction (21/34, 61.8%) and respiratory failure requiring intubation (19/34, 55.9%) were also common (23). In our study, several limitations need to be recognized. The study was conducted at a single tertiary care center, and the severity of illness and complication rates may be different than what would be expected in a population based cohort. The duration of this study was just six months. The observational nature of the study and possible multiple confounding factors do not allow us to infer a cause and effect relationship between potential risk factors and outcomes.Further studies with large number of patients and longer duration are required to further evaluate the significance of these clinical factors in predicting mechanical ventilation. Bedside spirometer is not routinely available in most hospitals of the developing world; therefore assessment of vital capacity was not taken as a clinical variable in this study.

CONCLUSION

The course of patients with severe GBS leading to respiratory compromise and mechanical ventilation can, to some extent, be predicted on the basis of clinical factors. This study identifies bulbar dysfunction and dysautonomia as significant independent predictors of mechanical ventilation. This clinical information may be used in the decisions regarding admission to the intensive care unit and preparation for elective intubation.The presence of these factors alone or in combination may not necessitate immediate support with mechanical ventilation but may be used in the decision to admit the patient to the ICU and prepare for elective intubation which would help in the early management of these patients and reduce the associated morbidity and mortality.

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