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Clinical and Paraclinical Predictors of Mechanical Ventilation in Guillain Barré Syndrome

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Abstract

Background Guillain Barré syndrome (GBS) is an acute post infective autoimmune polyradiculo-neuropathy; it is the commonest polyneuropathy causing respiratory failure. A lot of studies suggested certain GBS clinical and preclinical features anticipate and predicate the neuromuscular respiratory failure and can accurately assess the progression to mechanical ventilation; bulbar muscles involvement, severity of weakness of upper and lower limbs, bilateral facial muscles involvement and autonomic nervous system involvement were the main features associated with progression to mechanical ventilation.

Objectives To assess demographic, clinical and para clinical features and their relation with the progression of GBS to respiratory failure.

Methods Clinical and paraclinical predictors of impending respiratory involvement and requirement for mechanical ventilation were studied in 40 GBS patients aged 12-57 years (28 males and 12 females).

Results Ten (6 female/4 male) patients (25%) were admitted to the intensive care unit and received mechanical ventilation. Younger age, female gender and rapid disease progression in first 3 days were associated with respiratory involvement and subsequent ventilation. Bulbar weakness, bilateral facial palsy, poor digit counting (<10/1 breath) were the strongest indicators of impending respiratory failure. In combination they were found in 90% of ventilated patients. Dense weakness (power grade ≤2), weak neck flexion and axonal electromyography also showed significant risk for mechanical ventilation. Other parameters (autonomic dysfunction, antecedent gastrointestinal and respiratory illness, earlier upper limbs weakness and pain) showed no statistical significance in our study

Conclusion Respiratory failure in the course of GBS can to some extent, predicted depending on clinical information. Respiratory failure was associated with younger age, female gender, rapid progressive weakness, bulbar weakness. Facial weakness. Dense weakness, weak neck flexion, poor digit count and axonal neuropathy.

Keywords Guillain Barre syndrome, respiratory failure, bulbar weakness, mechanical ventilation.

List of abbreviation: GBS = Guillain-Barré syndrome, ICU = intensive care unit, GI = gastrointestinal, EMG = electromyography

Introduction

Guillain-Barré syndrome (GBS) is a group of autoimmune syndromes consisting of segmental demyelination and acute axonal degenerating forms [(1)]. All GBS variants are rapidly evolving polyradiculoneuropathy preceded by a triggering event, most often an infection [(2)]. GBS generally manifests as progressive areflexic weakness with or without autonomic disturbances [(1)].

Its incidence rate is 4/ 100,000 per year worldwide [(3)]. The age range was from 2 months to 95 years [(4)], with most patients presenting

between 15-50 years age [4,5,6]. Pathophysiologically peripheral nerve focal demyelination leading to conduction slowing or conduction block was the most common pathophysiological feature; however there is a rare pathophysiologic type of axonal forms [6,7].

Respiratory failure was reported in 10-30% of GBS patients which may require respiratory support by Mechanical ventilation.

Respiratory failure caused by neuromuscular dysfunctions develops rapidly in very short period mandating immediate mechanical ventilation [8].

Respiratory failure in GBS is caused by weakness of the facial, oropharyngeal, and laryngeal muscles, also weakness of the muscles of inspiration (the diaphragm, intercostals, and accessory muscles) results in inadequate lung expansion and frequently decompensation occurs during night sleep when the diaphragm affects nearly all the work of breathing [9,10]. Nevertheless expiratory-muscle weakness prevents adequate cough and secretion clearance, increasing the risk of aspiration and pneumonia [10].

The purpose of this study is to identify the demographic, clinical and paraclinical features that may help in anticipating the progression of GBS to respiratory failure

Methods

Across sectional study of forty patients with acute paralysis attended the neurology ward or intensive care unit (ICU) in Neuroscience Teaching Hospital from January to May-2012, were collected. Forty patients were examined by neurologists and considered as GBS cases when fulfilled Asbury criteria [11-12]. They were 28 males and 12 females with an age range from 12-57 years (mean = 34 years). Ten out of the total number (6 female/4 male) patients were admitted to ICU and mechanically ventilated for respiratory failure.

Time to peak disability was defined as time to intubation (patients who were ventilated), or time to the worst motor function (patients who were not ventilated) from onset of neuropathic symptoms [13].

The patients were divided into 3 groups:

1. Those who progressed to peak within 3 days (≤ 3 days).
2. Those who progressed to peak within 4-7 days.
3. Those who progressed to peak more than 7 days.

Regarding Antecedent infections, patients were divided into those with preceding GI illness (diarrhea, abdominal pain), respiratory illness (flu, cough) or those who had negative history of preceding infection.

The patients were studied in two steps; relation of all types of antecedent infection to ventilation and whether gastro-intestinal (GI) illness or respiratory illness is related to ventilation.

Each patient was examined for:

1. Bilateral facial weakness.
2. Bulbar weakness.
3. Weakness grade: weakness at presentation was graded according to medical research council scale for muscle power dense weakness was defined as grade 2 or less [14].
4. Distribution of limb weakness at presentation: upper limb weakness at presentation was taken as a parameter.
5. Autonomic dysfunction: was assessed according to Ewing method [15].
6. Weakness of neck flexion (patient fails to elevate the head against gravity or against resistance).
7. Digit count in one deep breath was taken as a rough estimate of vital capacity.

Digit count less than 10 (corresponds to vital capacity less than 1 L) was taken as a variable in prediction of mechanical ventilation [16]. The patients then were divided into 3 groups; those who count to less than 10, those who count between 10-15 and those who count to more than 15.

8. Presence of pain: whether dysasthesia or cramp muscle pain.

Electromyography (EMG) was done in whole non-ventilated patients, but only in 4 ventilated

patient. It could not be conducted in 6 ventilated patients as they were directly transferred to the ICU. It was performed after the first week of the disease. EMG study was done in the same neurophysiology clinic.

Cerebrospinal fluid examination was refused by most patients, including those admitted to the ICU. So it was canceled as a parameter. It was done in 5 patients only and was typical of albuminocytologic dissociation.

Statistical analysis

Characteristics between patients with GBS who received mechanical ventilation and those who did not were assessed using unpaired t-test with Welch correction for comparability. Fisher exact test and odd ratio for categorical variables by contingency table using Graph Pad in Stat 3 Software, Version 3.06 [17] was used to assess the p value. P value < 0.05 was regarded statistically significant to the prediction of ventilation.

Results

Twenty seven patients (68%) gave history of a preceding infection. Nine of them underwent ventilation. No statistical significance for the presence of a preceding infection to mechanical ventilation No statistical significant difference between antecedents GI or respiratory illness to ventilation.

Bilateral facial palsy (whether symmetrical or asymmetrical) was seen in 14 patients (35%), 9 of them (64.3%) needed ventilation ($P < 0.0001$) which indicates a considerable significance association of bilateral facial weakness with ventilation (Table 1).

Bulbar weakness was seen in 15 patients (38%). Mechanical ventilation was indicated in 10 of them (all ventilated patients). Therefore, bulbar weakness was a considerably significant predictor for mechanical ventilation ($P <0.0001$) (Table 1).

Dense weakness (power grade ≤ 2) at presentation was studied for the prediction of mechanical ventilation.

Eighteen patients (45%) had dense weakness at presentation. Eight of them (44%) were ventilated ($P = 0.02$, which is a statistically significant suggesting association of severe weakness with mechanical ventilation (Table 1).

Distribution of weakness at presentation was studied to predict the progression to mechanical ventilation.

Upper limbs weakness presented in 13 patients (32.5%); 5 of them needed ventilation ($P = 0.2$). Three patients gave history of simultaneous upper and lower limbs weakness; 2 of them were ventilated.

Twenty-five patients (63%) were having autonomic dysfunction, 9 of them (36%) needed ventilation ($P = 0.06$). Twenty patients were having weak neck flexion; half of them were ventilated ($P = 0.0004$) (Table 1).

Patients were divided into 3 groups according to their ability to count in one deep breath. Ten patients (25%) could count to (<10) in one breath; Nine of them (90%) were ventilated ($P < 0.0001$). Pain was reported in 22 patients (55%). Only 4 of them (18.2%) needed ventilation ($P = 1.0$).

Six patients out of 34 patients in whom EMG was done; were having axonal pattern (18%), 3 of them (50%) needed ventilation ($P = 0.01$) showed that axonal pattern is a significant risk to mechanical ventilation (Table 1).

In this study, only 2 patients were having a previous attack of GBS. Both were female, having mild disease (able to walk), none of them needed ventilation.

Two females in the study were pregnant. One 14 years old, was in the last trimester and she did not need ventilation. The second pregnant female was 24 years old, was in the first trimester and needed ventilation within 2 days of the onset.

Table 1. Baseline Demographics and Clinical Features of Guillain-Barré syndrome Patients

Variables		Mechanical ventilation		*P* value
		Yes (N = 10)	Not (N = 30)	
Age (yr) mean (range)		18 (14-24)	27 (12-57)	0.0005
Gender (female/Male)		6/4	6/24	0.04
Time to peak disability (≤3)		7 (70%)	5 (17%)	0.003
Facial weakness		9 (90%)	5 (17%)	< 0.0001
Bulbar weakness		10 (100%)	5 (17%)	< 0.0001
Dense limbs weakness		8 (80%)	10 (33%)	0.02
Upper limb weakness		5 (50%)	8 (27%)	0.2
Autonomic dysfunction		9 (90%)	16 (53%)	0.06
Weak neck flexion		10 (100%)	10 (33%)	0.0004
Digit count < 10		9 (90%)	1 (3%)	< 0.0001
Pain		6 (60%)	16 (53%)	1.0
EMG (axonal)		3 (30%)	3 (10%)	0.01
Antecedent infection	GI illness	5 (50%)	9 (30%)	0.1
	URTI	4 (40%)	9 (30%)	
	Total	9 (90%)	18 (60%)	

GI = gastrointestinal, URTI = upper respiratory tract infection, Two tailed P value by unpaired t- test and Fisher exact test

A quarter of the patients received mechanical ventilation and (75%) did not. The youngest patient in the study was 12 years old and the oldest was 57 years. For ventilated patients, mean age was 18; and for non-ventilated it was 27 (Table 2).

Table 2. Relation of age to ventilation

Mechanical Ventilation	No.	Age (yr) mean±SD
Yes	10	18.00±3.71
No	30	27.06±11.39

P = 0.0005, 95% confidence interval (95%CI) = -16.543 to -1.590

Females were 30% (12/40) of the total number, and 60% (6/10) of ventilated patients were females. There was a significant association between female gender and respiratory failure (*P* = 0.04) (Table 3).

Progression to peak disability ranged between 1-15 days (mean was 5.4 days). Mean progression to peak disability for ventilated patients was 4.6 days, and for non-ventilated 5.7 days. Patients were divided into 3 groups regarding progression to peak disability (Table 4). Seventy percent of ventilated patients progressed to peak within 3 days. This study showed a statistical significance to rapid progression (≤3 days) for ventilation (*P* = 0.003) (Table 4).

Table 3.Gender and ventilation in Guillain-Barré syndrome patients

Gender	Mechanical ventilation		Total
	Yes	No	
Male	4 (10%)	24 (60%)	28 (70%)
Female	6 (15%)	6 (15%)	12 (30%)
Total	10 (25%)	30 (75%)	40 (100%)

P = 0.04, Odd ratio = 0.16, 95%CI = 0.03538 to 0.7851

Discussion

The results of this study suggest that the failure of neuromuscular respiratory function and progression to mechanical ventilation should be anticipated in GBS patients by assessing certain clinical and preclinical features.

Peak of age in whole patients was in the second decade (45%). Seven ventilated patients (70%) were in the second decade and 3 patients (30%)

in the third decade. Younger age is strongly related to the risk of ventilation in the present study.

Table 4. Three groups of patients regarding progression to peak disability

Progression (days)	Mechanical ventilation		Total
	Yes	No	
≤ 3	7	5	12
4 -7	1	18	19
> 7	2	7	9
Total	10	30	40

P = 0.003, Odd ratio = 11.66, 95% CI =2.220 to 61.303

Although males were more than females in whole patients by 2.6:1 ratio (consistent with other studies) [11], ventilated females were more than ventilated males by 3:2 ratio and statistical study showed a significant correlation between female gender and ventilation.

The above 2 findings (age and gender) were not fit with Lawn et al study, which showed no significant difference between those patients who received ventilation and those who did not for age and gender [11]. Lawn et al studied 114 patients of different ages and relatively equal number of patients to both genders, admitted to ICU over 20 years, whereas the present study assessed the patients over 4 months with age between second and third decade and relative male predominance.

Progress to peak disability within 3 days was a significant prognostic factor for respiratory failure and subsequent ventilation. Seven out of the ten patients who were ventilated (70%) were progressed to peak disability within 3days. The association between rapid progression and the likelihood of mechanical ventilation was also noticed in Lawn, et al study [11]. This feature might be a predictor of the fulminant course of the disease.

According to the present study, history of antecedent infection showed no association with the mechanical ventilation, and there is also no significance association with antecedent GI illness or to respiratory illness as a risk factor for ventilation. This is in agreement with Lawn et al study [11] and Al-Zaidi study [18]. Some previous reports considered antecedent GI illness as a bad prognostic point [11].

Autonomic dysfunction was identified in a high proportion of patients who subsequently received mechanical ventilation (90%) but this did not reach statistical significance. This finding is in agreement with Lawn et al study [11], but against Al-Tamimi study [12] who found a significant correlation between autonomic dysfunction and subsequent mechanical ventilation [20]. The present study and Lawn, et al study depend on Ewing criteria (appendix III) to define autonomic dysfunction; while Al-Tamimi study [12] (on autonomic dysfunction in GBS) depend on development of any clinical sign of autonomic dysfunction.

Weakness of neck flexion was reported by many studies [11], our study also found a strong indicator for the likelihood of subsequent ventilation. This could be related to the fact that neck flexion has the same root innervations as the diaphragm [6].

The present study showed no relation between pain and the subsequent need of ventilation. Axonal pattern EMG was seen in 3 of 4 ventilated patients and 3 of 30 non-ventilated patients. It was a highly significant predictor of mechanical ventilation. Lawn et al found that axonal EMG was associated with an adverse outcome, but not specifically in predicting ventilation [11].

One of two pregnant ladies with GBS in our study developed respiratory failure and received mechanical ventilation. They had progressed to respiratory impairment within 2 days with early development of bulbar and facial weakness. This may point to fulminant course of GBS in pregnant women [19,20]. This requires a separate study to estimate the risk of ventilation in pregnant women with GBS.

Two patients in our study had a previous attack of GBS years ago. They comprise (5%) of whole

patients in the study, which may approximate the percent of GBS recurrence in most reports [3]. In conclusion, while inherently unpredictable, the course of patients with GBS can, to some extent, be predicted on the basis of clinical information and simple bedside tests of respiratory function. These data may be used in the decision regarding admission to the intensive care unit, preparation for elective intubation, and possible mechanical ventilation.

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Author Contribution
Author ZAKI NOAH HASAN designed the study, performed in statistical analysis, wrote the protocol and wrote the first draft of manuscript, managed the analysis of the study and managed the literature search. Author Sajid Ibrahim wrote and revised the first and the final draft of manuscript . The third and fourth authors collect the patients for the study and read and approved the final manuscript.

Conflict of Interest
Authors have declared no conflict of interests.

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