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Clinical Outcomes in Patients with Gullain-Barre Syndrome with or without Respiratory Failure

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ABSTRACT

Objectives: To compare the demographic/clinical profile and outcomes in patients with Gullain-Barre syndrome (GBS) with or without mechanical ventilation and evaluate the association of various variables with patient outcomes.

Methodology: This comparative cross-sectional study was done at Polyclinic Hospital, Islamabad from January 2019 to June 2023 after ethical approval. Thirty seven GBS patients admitted in intensive care unit (ICU) were allocated into two groups with and without mechanical ventilation. The GBS Disability score was estimated at admission, 2 weeks, 1 month, 3 months and 6 months follow-up. The GBS disability scale is an extensively used scale to determine patient outcomes ranging from 0 to 6. A score <2 shows good functional outcomes, whereas a score ≥3 indicates poor outcome. The outcomes evaluated were in-hospital mortality and functional status.

Results: There was a significant difference in tracheostomy and treatment given between two groups. The GBS disability scores were significantly less in patients who were not ventilated than ventilated patients at presentation and follow-ups. In-hospital mortality occurred in 7(18.9%) of the patients. Out of 30 patients, 7(18.9%), 10(27%) and 13(35.1%) patients were able to run, walk without and with support, respectively. Patients without mechanical ventilation had significantly better outcomes than ventilated patients. Patients with greater duration of hospital stay, mechanical ventilation and higher GBS disability score at admission had poor outcomes.

Conclusion: The Gullain-Barre syndrome patients with or without mechanical ventilation vary significantly in tracheostomy and treatment given. The GBS disability scores were significantly less in patients who were not ventilated than ventilated patients at presentation and follow-ups. In-hospital mortality occurred in 18.9% of the patients and 35.14% of the patients had poor functional outcomes.

Keywords: Guillain-Barre syndrome; GBS; GBS Disability score

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Introduction

Guillain-Barre Syndrome (GBS) is a rapidly progressive ascending paralysis occurring in 1.1 out of 100,000 people annually.[1] The disease has a rapid progression reaching its peak in 2-4 weeks, this point being known as nadir.[2] The disease is common in younger and older adults. Acute flaccid paralysis is the most common disease presentation in children. The majority of the affected patients are males.[3] The syndrome is responsible for causing severe disability or mortality in 20% of the patients.[4]

The disease is triggered by a preceding infection that stimulates the immune system to damage the peripheral nerves. The preceding infection is mostly a respiratory or gastrointestinal tract infection.[4] The pathogens commonly

involved are Campylobacter jejuni, Mycoplasma pneumoniae, Epstein-Barr virus, Cytomegalovirus, Hepatitis E virus and Zikavirus. Influenza and Swine flu vaccines are also associated with GBS.[5] Patients with GBS present with progressive limb weakness which can also affect the autonomic system, respiratory system and cranial nerves.[3,6] One of the type of GBS is acute inflammatory demyelinating polyneuropathy (AIDP) in which there is demyelination of the peripheral nerves secondary to acute inflammation.[7] Other types are acute motor axonal neuropathy (AMAN) and acute motor sensory axonal neuropathy (AMSAN).[8] Another variant of GBS is Miller-Fisher syndrome (MFS), in which the patient presents with areflexia, ataxia and ophthalmoplegia.[9] The disease is diagnosed based on clinical manifestations, neurological, electrophysiological and cerebrospinal fluid (CSF) examination. Electrophysiological studies help to identify the specific type of disease.[5] Examination of CSF reveals elevated protein level with a normal white blood cell count, called albuminocytological dissociation.[6] The treatment of choice is plasma exchange (PE) and intravenous immunoglobulin (IVIG). Literature has reported that PE/IVIG administered within 2 weeks of disease onset fastens the recovery of patients.[10]

Respiratory failure occurs in up to 30% of the patients necessitating intensive care unit (ICU) care and mechanical ventilation.[2] Around 60% of the intubated patients develop complications such as sepsis, pneumonia, and pulmonary embolism.[11] Prior studies have demonstrated that patients who walk with support or are bedridden or labile blood pressure, cardiac arrhythmia or respiratory distress require critical care in the ICU as they have a high mortality rate.[12] A multidisciplinary approach is needed to manage these patients to prevent complications.[9]

Although Gullain-Barre syndrome is not very common, yet it is linked to substantial morbidity and mortality. The outcomes of the disease vary from patient to patient. Around 30% of the patients develop respiratory failure for which they need critical care & monitoring in ICUs and mechanical ventilation.[13] In a developing country like Pakistan, the facilities of ICU and mechanical ventilation are not available in most of the healthcare setups.[14] This also contributes to a major financial burden for the patients and healthcare systems. In addition, the treatment regime for GBS includes plasma exchange/immunoglobulins. The majority of the patients cannot afford immunoglobulins. This study was planned to determine the demographic/clinical profile and outcomes in patients with Gullain-Barre syndrome (GBS) with or without mechanical ventilation and evaluate the association of various variables with patient outcomes. The evaluation of prognostic factors will help in the risk stratification of patients and their management as high-risk patients in the future.

Methodology

This comparative cross-sectional study was done at Polyclinic Hospital, Islamabad from January 2019 to June 2023 after ethical approval. Thirty seven GBS patients admitted in intensive care unit (ICU) were allocated into two groups with and without mechanical ventilation. The GBS Disability score was estimated at admission, 2 weeks, 1 month, 3 months and 6 months follow-up. Informed written consent was obtained from all the patients. The patients were diagnosed based on history and neurological examination. The demographic characteristics of the patients including age, gender and co-morbidities were noted. The history of any preceding infection such as gastrointestinal (GI) or respiratory tract infection, length of hospital stay and number of days to nadir were also taken. Nadir is the stage when the symptoms of the disease have reached their severity and then stabilized. Baseline investigations and cerebrospinal fluid (CSF) examination of all the patients were done for albuminocytological dissociation. Albuminocytological dissociation is the higher protein level in CSF without a rise in white blood cellscount. Other treatment parameters such as the need for mechanical ventilation and/or tracheostomy andPE/IVIG were also recorded. The GBS Disability score of each patient was estimated at admission, 2 weeks, 1 month, 3 months and 6 months follow-up. The GBS disability scale is an extensively used scale to determine the outcomes of patients with GBS. It ranges from 0 to 6. A score $\leq$2 shows good functional outcomes, whereas a score $\geq$3 indicates poor outcome.[15] The scoring of the GBS disability scale is given in Table I.

Table I: GBS Disability Scale Scoring & its Interpretation.[16]

0	Healthy
1	Minor symptoms but capable of running
2	Able to walk without support
3	Able to walk with support
4	Confined to bed
5	Need assisted ventilation
6	Dead

The demographic/clinical profile and outcomes was compared between the two groups. The outcomes evaluated were in-hospital mortality and functional status.

The functional status included the ability to run or able to walk with or without support. The relation of patient outcomes with demographic and clinical variables was determined.

The data was analyzed using the Statistical Package for the Social Sciences (SPSS) version 25. Frequency and percentage were used to represent qualitative data, whereas mean and standard deviation (SD) were used to represent quantitative ones. The study variables were compared between two groups using the Chi-square test for qualitative variables and independent T test for quantitative variables. The Chi-square test was used to determine the relationship between different variables and patient outcomes, with a significant p-value of ≤0.05.

Results

The age of the patients varied from 14 to 75 years with an average of 43.97±16.51 years. The highest proportion of the patients (54.1%) were <40 years old. Most of the patients were male (62.2%). Only 24.9% of the patients had co-morbidities. Out of 51.36% of patients with a precipitating infection, 27.03% had respiratory tract infection followed by gastrointestinal infection in 24.32% of the patients. The mean number of days to nadir was 9.05±1.87 days (Range: 6-12 days) and the mean length of hospital stay was 14.94±7.49 days (Range: 2-32 days). Only 21.6% of the patients were intubated and out of them, 10.8% of the patients underwent tracheostomy. Most of the patients (54.1%) had albuminocytological dissociation. All the patients received plasma exchange but 2 patients received intravenous immunoglobulins in addition to plasma exchange.

When the study variables were compared between the two groups, there was a significant difference in tracheostomy and treatment given. All 4 patients who underwent tracheostomy were on mechanical ventilation. Two patients on mechanical ventilation received both plasma exchange and immunoglobulins. The GBS disability scores were significantly less in patients who were not

Table II: Demographic and Clinical Profile of Qualitative Variables in Patients with or without Mechanical Ventilation.

Study Variable	Not Ventilated	Ventilated	Total	Chi-Square	p-value
Age Groups					
<40 years	14(37.84%)	6(16.22%)	20(54.1%)	3.787	0.151
41-59 years	10(27%)	0(0%)	10(27%)		
≥60 years	5(13.5%)	2(5.4%)	7(18.9%)		
Total	**29(78.4%)**	**8(21.6%)**	**37(100%)**		
Gender					
Male	16(43.24%)	7(18.92%)	23(62.2%)	2.786	0.095
Female	13(35.1%)	1(2.7%)	14(37.8%)		
Total	**29(78.4%)**	**8(21.6%)**	**37(100%)**		
Co-morbidities					
No-comorbidities	21(56.75%)	7(18.9%)	28(75.7%)		
Diabetes mellitus	3(8.1%)	0(0%)	3(8.1%)	3.070	0.381
Hypertension	4(10.8%)	0(0%)	4(10.8%)		
Both Diabetes & Hypertension	1(2.7%)	1(2.7%)	2(5.4%)		
Total	**29(78.4%)**	**8(21.6%)**	**37(100%)**		
Precipitating Factor					
Gastrointestinal infection	7(18.91%)	2(5.41%)	9(24.32%)	0.021	0.989
Respiratory tract infection	8(21.62%)	2(5.41%)	10(27.03%)		
No precipitating factor	14(37.84%)	4(10.81%)	18(48.65%)		
Total	**29(78.4%)**	**8(21.6%)**	**37(100%)**		
Tracheostomy					
Done	0(0%)	4(10.81%)	4(10.8%)		
Not Done	29(78.37%)	4(10.81%)	33(89.2%)	16.258	0.001*
Total	**29(78.4%)**	**8(21.6%)**	**37(100%)**		
Albuminocytological Dissociation					
Present	16(43.24%)	4(10.81%)	20(54.1%)		
Absent	13(35.13%)	4(10.81%)	17(45.9%)	0.068	0.795
Total	**29(78.4%)**	**8(21.6%)**	**37(100%)**		
Treatment Given					
Plasma Exchange	29(78.4%)	6(16.2%)	35(94.6%)	7.664	0.006*
Both Plasma Exchange & Immunoglobulins	0(0%)	2(5.4%)	2(5.4%)		
Total	**29(78.4%)**	**8(21.6%)**	**37(100%)**		

**Statistically Significant

ventilated than ventilated patients at presentation and follow-ups. These results are shown in Table II and Table III.

Table III: Demographic and Clinical Profile of Quantitative Variables in Patients with or without Mechanical Ventilation.

Study Variable	Not Ventilated	Ventilated	t-statistic	p-value
Age	42.52±16.26	49.25±17.40	-1.022	0.313
No of days to Nadir	9.21±1.91	8.50±1.69	0.945	0.32
Length of hospital stay (Days)	13.82±6.98	18.25±9.11	-1.48	0.26
GBS Disability Score				
At Presentation	3.61±0.49	5±0.0	-7.83	0.001*
At 2 Weeks	3.38±0.82	5±1.41	-4.19	0.004*
At 1 Month	2..90±0.97	4.75±1.75	-3.95	0.002*
At 3 Months	2.69±1.10	4.75±1.75	-4.08	0.01*
At 6 Months	2.41±1.26	4.75±1.75	-4.24	0.05*

**Statistically Significant

In-hospital mortality occurred in 7(18.9%) of the patients. Out of 30 patients, 7(18.9%), 10(27%) and 13(35.1%) patients were able to run, walk without and with support, respectively. There is a significant difference in outcomes between the two groups, with better outcomes in patients without mechanical ventilation (Chi-square statistic: 13.27, p-value: 0.004). The functional outcomes of the patients in both the groups are shown in Figure 1.

Patients with greater duration of hospital stay, mechanical ventilation and higher GBS disability score at admission had poor outcomes. The relation of different variables with the outcomes is tabulated in Table IV.

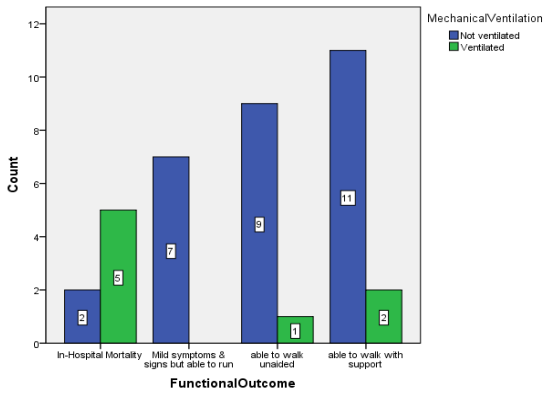

Figure 1: Outcomes of Patients at 6-Month Follow-up.

Discussion

Worldwide, the most frequent cause of ascending muscle paralysis is Gullain-Barre syndrome. The majority of the patients recover by treatment with immunotherapy but disability and death also occur in a considerable proportion of patients. The patients of GBS in low-income countries have limited access to immunotherapy treatment. It is the need of time to ensure the provision of treatment to all GBS patients and establish efficient disease-modifying therapies to decrease the severity of nerve injury.[17]

In our study, patients had a mean age of 43.97±16.51 years. The mean age was 37 years in two studies.[18,19] and 36 years in another study.[20] However, the average age was less (17 years) in a study.[21] The patients had an average age of 52 years in a study by Sung et al.[22] and 56 years in two other studies.[2,23] Most of the patients (54.1%) were

Table IV: Association of Patient Outcomes with Demographic Variables.

Variable	Patient Outcomes				Total	Chi-Square Statistic	p-value
	In-Hospital Mortality	No Symptoms but able to run	Able to walk unaided	Able to walk with support			
Age Groups							
< 40 years	3	5	5	7	**20**	4.82	0.567
41-59 years	1	1	4	4	**10**		
≥ 60 years	3	1	1	2	**7**		
Total	**7**	**7**	**10**	**13**	**37**		
Gender							
Male	6	5	4	8	**23**	3.997	0.262
Female	1	2	6	5	**14**		
Total	**7**	**7**	**10**	**13**	**37**		
Co-morbidities							
No co-morbidity	5	6	7	10	**28**		
DM	0	1	1	1	**3**		
HTN	1	0	2	1	**4**	4.89	0.84
Both DM & HTN	1	0	0	1	**2**		
Total	**7**	**7**	**10**	**13**	**37**		

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Table V: Association of Patient Outcomes with Clinical Variables.

Variable	Patient Outcomes				Total	Chi-Square	p-value
	In-Hospital Mortality	No Symptoms but able to run	Able to walk unaided	Able to walk with support			
No precipitating factor	3	4	5	6	**18**	4.32	0.63
GI infection	3	0	3	3	**9**		
RTI	1	3	2	4	**10**		
Total	**7**	**7**	**10**	**13**	**37**		
No of Days to Nadir							
1-7 days	3	2	3	3	**11**	0.85	0.83
8-14 days	4	5	7	10	**26**		
Total	**7**	**7**	**10**	**13**	**37**		
Length of Hospital Stay							
1-10 days	**0**	**2**	**8**	**3**	**13**	18.015	0.035**
11-20 days	**3**	**3**	**2**	**5**	**13**		
21-30 days	**3**	**2**	**0**	**5**	**10**		
>30 days	**1**	**0**	**0**	**0**	**1**		
Total	**7**	**7**	**10**	**13**	**37**		
GBS Disability Score at Presentation							
3	0	3	6	3	**12**	17.49	0.008**
4	2	4	3	8	**17**		
5	5	0	1	2	**8**		
Total	**7**	**7**	**10**	**13**	**37**		
Mechanical Ventilation							
Not ventilated	2	7	9	11	**29**	13.27	0.004**
Ventilated	5	0	1	2	**8**		
Total	**7**	**7**	**10**	**13**	**37**		
Tracheostomy							
Not Done	6	7	9	11	**33**	1.22	0.74
Done	1	0	1	2	**4**		
Total	**7**	**7**	**10**	**13**	**37**		
Albuminocytological Dissociation							
Present	3	3	8	6	**20**	3.74	0.29
Absent	4	4	2	7	**17**		
Total	**7**	**7**	**10**	**13**	**37**		
Treatment Given							
Plasma exchange	7	7	10	11	**35**	3.90	0.27
Both PE & IVIG	0	0	0	2	**2**		
Total	**7**	**7**	**10**	**13**	**37**		

<40 years old followed by 27% in the 41-59 years group. Similarly, 54.8% were <40 years old and 32.3% were in the 41-59 years age group.[18] Most of the patients were male (62.2%) in our study. Literature has also reported male predominance in GBS syndrome. Sixty to eighty percent of the patients were males in other studies.[2, 15,19,20,23,] Only 24.9% of the patients had co-morbidities in our study, with HTN in 10.8%, DM in 8.1% and both in 5.4% of the patients. Khedr et al. also reported co-morbidities in 22.6% of GBS patients. Among these, 11.3% of patient had both diabetes & hypertension, 8.1% had HTN alone and 3.2% had only diabetes.[18]

Out of 51.36% of patients with a precipitating infection in our study, 27.03% had arespiratory tract infection followed by gastrointestinal infection in 24.32% of the patients. In another study, 30.6% of the patients had no infection, 48.4% had a respiratory infection and 21% had GI infection.[18] In another study, 80% patient had respiratory and 15% had GI infections.[20] In contrast, in another study, GI infection was predominantly present in 45.8% of the patients and 20.8% of patients had respiratory tract infection.[22] The mean number of days to nadir was 9.05$\pm$1.87 days in our study. The average duration to nadir was 3.32±1.64 days in a study by Khedr et al. and 10±7 days in another study by Martic et al.[18,23] Our results showed the mean length of hospital stay 14.94$\pm$7.49 days. Similarly, the hospital stay duration was 17.5$\pm$37 days in a study by Shangab et al.[15] The duration was only 6.7 and 4.3 days in other studies.[20,24] Another study reported the mean hospital duration of 26 days in GBS patients.[23]

Our study revealed that most of the patients (54.1%) had albuminocytological dissociation on CSF examination. Albuminocytological dissociation was present in 39.1%, 57.1% and 62% of the GBS patients in other studies.[18,19,24] In our study, only 21.6% of the patients were intubated and

out of them, 10.8% of the patients underwent tracheostomy. Similarly, in most of the studies, 20-30% of the GBS patients were put on mechanical ventilation.[15,20,22,24,25] In a study by Bhaggat et al., 16.1% of patients were intubated and Khedr et al. reported mechanical ventilation in only 8.1% of the GBS patients.[21,18] In our study, all the patients received PE and only 5.4% of patients received IVIG in addition to PE. In another study, 50% of patients received PE, 20% of patients received IVIG and 30% were given both.[20] In other studies, 50-60% of the patients received IVIG.[15,23] In a study by Asmat et al., 78.3% of the patients were treated with IVIG.[24]

Our study showed that in-hospital mortality occurred in 18.9% of the patients. Other studies revealed that in-hospital mortality occurred in 6.45% and 7.9% of the patients.[21,25] Mortality was reported in only 3.1% of patients in another study.[15] Our results revealed good functional outcomes in 45.95% of the patients and poor outcomes in 35.14% of the patients. Poor functional outcomes were reported in 39%, 30.1% and 10.5%, respectively in the studies by Martic et al., Shangab et al. and Asmat et al.[15,23,24] In our study, there was a significant difference in outcomes between the two groups, with better outcomes in patients without mechanical ventilation (p-value: 0.004). Siddiqui et al. reported better outcomes in patients without mechanical ventilation as compared to ventilated patients.[25] In our study, patients with greater duration of hospital stay, mechanical ventilation and higher GBS disability score at admission had poor outcomes. Other studies found a link between length of hospital stay and poor outcomes.[15,25] Bhaggat et al. reported an insignificant association between the two.[21] Other studies also showed a significant association between higher GBS scores at presentation and poor outcomes.[15,22,23] Siddique et al. reported that greater muscle weakness at presentation is linked with poor patient outcomes.[25] A significant association was seen between mechanical ventilation and poor outcomes in other studies.[15,19,22] Khedr et al. demonstrated a significant association of older age, co-morbidity, preceding infection and albuminocytological dissociation with poor patient outcomes.[18]

Conclusion

The Gullain-Barre syndrome patients with or without mechanical ventilation vary significantly in tracheostomy and treatment given. The GBS disability scores were significantly less in patients who were not ventilated than ventilated patients at presentation and follow-ups. In-hospital mortality occurred in 18.9% of the patients and 35.14% of the patients had poor functional outcomes. Patients without mechanical ventilation had significantly better outcomes than ventilated patients. Longer length of hospital stay (p-value=0.035), mechanical ventilation (p-value=0.004), and higher GBS disability score at presentation (p-value=0.008) were the predictors of poor outcomes.

Limitations

- The study enrolled all GBS patients presenting in the ICU within 4.5 years of duration. However, the sample size was less. Further multicenter studies should be carried out with a larger sample size.
- Electrophysiological studies are important to accurately diagnose GBS. So, it should be done in all GBS patients. The definitive diagnosis of GBS type was not made. So, its association with the prognosis of patients was not assessed. Further studies should be done with electrophysiological studies and identifying the types of GBS.
- Cranial neuropathy is common in GBS associated with poor prognosis. However it was not assessed in our study. The incidence of cranial neuropathy in GBS should be assessed in future research and its role as a prognostic factor should also be evaluated.
- Due to financial constraints, IVIG was administered in only 2 patients. So, the prognosis of patients with reference to plasma exchange/IVIG cannot be reliably assessed. Future research should be conducted with a larger number of patients receiving IVIG

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