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Antecedent Infections and Hospital Outcomes in Demyelinating and Axonal type of Guillain-Barre Syndrome among adult Patients

Md. Zakirul Islam[1], Anjuman Ara[2], Syeda Marufa Hasan[3], Md. Abdullah Yusuf[4], Rezaul Karim[5], Md. Azharul Hoque[6], Quazi Deen Mohammad[7]

[1]Assistant Professor, Department of Medicine, Kurmitola General Hospital, Dhaka, Bangladesh; [2]Assistant Professor, Department of Gynaecology & Obstetrics, TMSS Medical College, Bogura, Bangladesh; [3]Associate Professor (C.C.), Department of Biochemistry, National Institute of Neurosciences & Hospital, Dhaka, Bangladesh; [4]Associate professor, Department of Microbiology, National Institute of Neurosciences & Hospital, Dhaka, Bangladesh; [5]Senior Consultant (Medicine), Department of Medicine, General Hospital Nilpharmary, Bangladesh; [6]Former Head & Professor of Neurology, Department of Neurology, National Institute of Neurosciences and Hospital, Dhaka, Bangladesh; [7]Director & Professor of Neurology, National Institute of Neurosciences & Hospital, Dhaka, Bangladesh

Abstract

Background: Many differences are observed with respect to hospital outcome among demyelinating and axonal type of Guillain-Barre Syndrome. **Objective:** Aims of this study was to compare the hospital outcome at discharge among demyelinating and axonal type of Guillain-Barre syndrome. **Methodology:** This prospective observational study was conducted from Oct, 2017 to September, 2018 at the National Institute of Neurosciences and Hospital, Dhaka, Bangladesh. All demyelinating and axonal variant of GBS, presented within 2 weeks were included in this study. The clinical parameters were taken for baseline analysis. Outcomes were measured at discharge by MRC score, length of hospital and ICU stay, recovery and death. **Results:** Out of 108 GBS cases 55 (50.9%) demyelinating & 53 (49.1%) were axonal subtype. Mean age; 40.20 ± 16.26 vs. 32.43 ± 14.93 years in demyelinating vs. axonal cases (p=0.011). Symptom onset and nadir of weakness are quicker in axonal than demyelinating cases (8.47±4.97 vs. 12.36±7.94) (p=0.017) and (6.7 ± 4.5 vs. 8.36 ± 4.59) (p=0.022)] days. Baseline MRC score were (18.04±9.85 vs 12.94±9.91) (p=0.009) demyelinating vs. axonal cases. At discharge, Mean MRC score, length of hospital stay, length of ICU stay were, (22.15±9.38 vs 17.39±9.46; p=0.013); (15.13±17.60 vs 23.58±23.55) days (p=0.038)} and (28.69±23.28 vs 37.0±20.01) days respectively. **Conclusion:** Hospital outcome of GBS patients is favorable to demyelinating subtype in respect of MRC score, length of hospital stay, length of ICU stay and also death and survivability.

Keywords: Guillain Barre syndrome; acute inflammatory demyelinating polyneuroradiculopathy; Acute Motor Axonal Polyneuroradiculopathy; hospital-outcomes

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Introduction

Guillain-Barre syndrome (GBS) is an acute immune mediated polyradiculo-neuropathy[1]. Electro-physiologically GBS are categorized as demyelinating, axonal subtype. More than two third of cases are associated with an antecedent events specially gastroenteritis and respiratory tract infection[2]. Acute motor axonal neuropathy variety of GBS are strongly associated with Campylobacter jejuni gastroenteritis[3]. Variations are observed in clinical presentation among the different subtypes.

Acute motor axonal neuropathy variety has a rapid evolution of clinical course and reaches to nadir very quickly and usually more severe than acute inflammatory demyelinating polyneuropathy[4].

Correspondence: Dr. Md. Zakirul Islam, Assistant Professor, Department of Medicine, Kurmitola General Hospital, Dhaka, Bangladesh; Email: zakir.doc@gmail.com; Cell no.: +8801748994027;
ORCID iD: https://orcid.org/0009-0002-9772-7152

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Diagnosis is based on typical clinical presentation along with CSF albuminocytological dissociation increase CSF protein in the absence of increase cell[5]. Nerve conduction study is done for classifying the subtyping. Other investigations includes serum electrolytes to exclude electrolyte imbalance. Definitive management of GBS is either with Plasmapheresis or IVIg therapy with equal efficacy[6]. Acute inflammatory demyelinating polyneuropathy is associated with rapid and usually complete clinical recovery while others have poorer outcome and has a longer clinical course[7]. The purpose of the present study was to compare the hospital outcome at discharge among demyelinating and axonal type of Guillain-Barre syndrome.

Methodology

Study Settings and Population: This cross-sectional study was conducted from Oct, 2017 to September, 2018 in the department of clinical neurology at the National Institute of Neurosciences and Hospital, Dhaka, Bangladesh. The patients were selected according to the selection criteria and after confirmation by electrophysiological study.

Study Procedure: Details of the study that included nature, purposes and procedure of the study, type of investigations & their risk, definite treatment and their side effects and management were well briefed to the patient and their attendant. Written consent was taken from patient or their legal attendant. Details history and meticulous examination were performed to collect the data according to the variable of interest. All necessary investigations were done at an optimum time. Nerve conduction study and CSF were done after 1st week of onset of the disease in the respective department of the institute. All patients were regularly monitored especially respiratory function for diagnosis of early impending respiratory failure and managed them accordingly.

Statistical Analysis: The collected data were analyzed by using SPSS version 22.0. statistical significance were determined by using Pearson chi-square test for all categorical data and student 't' test for all continuous data and result were expressed by frequency and percent & mean with standard deviation respectively. P value of <0.05 was taken as statistically significant.

Ethical Consideration: All procedures of the present study were carried out in accordance with the principles for human investigations (i.e., Helsinki Declaration) and also with the ethical guidelines of the Institutional research ethics. Formal ethics approval was granted by the local ethics committee. Participants in the study were informed about the procedure and purpose of the study and confidentiality of information provided. All participants consented willingly to be a part of the study during the data collection periods. All data were collected anonymously and analysed using the coding system.

Results

Mean age of the study participant was 36.39 ± 16.03 years. About 73(67.6%) cases out of 108 cases were within 18 to 40 years of age (Table 1).

Table 1: Demographic Characteristics of the Study Participants

Age Group	Values
18 to 40 years	73(67.6%)
41 to 60 years	28(25.9%)
More than 60 years	7(6.5%)
Mean±SD	36.4±16.03

The nerve conduction study of the 108 cases of GBS patients in this study revealed that 55 (50.9%) cases were demyelinating and 53 (49.1%) cases were of axonal variety. In the axonal group only 2 cases were AMSAN and the remaining 51 cases of AMAN variety. The distribution is nearly equal in both group. Antecedent events were reported by 33(60.0%) of demyelinating and 43 (81.1%) of axonal cases which was statistically significant (p=0.014). Gastroenteritis was the commonest antecedent infection in both group; 22(40.0%) in demyelinating and 32(56.4%) in axonal cases and the difference was statistically significant (p=0.027). RTI was reported by 7(12.7%) demyelinating and 11(20.8%) axonal cases (Table 2).

Table 2: Comparison of Clinical Events among the Demyelinating and Axonal Subtype of GBS

Antecedent	GBS Type		P value
Events	Demyelinating	Axonal	
RTI	7(12.7%)	11(20.8%)	0.195
Gastroenteritis	22(40.0%)	32(60.4%)	0.027*
Other infections	4 (7.3%)	0 (0.0%)	0.064
Total	**33(60.0%)**	**43(81.1%)**	**0.014***

RTI: respiratory tract infection, *Pearson chi-square was done to see the level of significance; Multiple response analysis was perfomed

Time interval from antecedent events to symptoms onset was 8.47 ± 4.97 & 12.36 ± 7.94 days in axonal and demyelinating cases respectively. The difference was statistically significant (p=0.017). The interval from symptom onset to hospitalization was also significantly shorter in axonal cases; which was 4.70 ± 2.13 days, and in demyelinating cases 6.75 ± 5.30 days (p=0.009). Nadir of weakness developed rapidly in axonal than demyelinating cases which were 6.70 ± 2.57 days and 8.36 ± 4.59 days respectively (p=0.022).

Table 3: Different Variables of Study Population (Mean±SD)

Variables	GBS Type		P value
	Demyelinating	Axonal	
Event to Symptoms Onset	12.36±7.94	8.47±4.97	0.017**
Onset to Hospitalization	6.75±5.30	4.70±2.13	0.009**
Onset to Develop Nadir of Weakness	8.36±4.59	6.70±2.57	0.022**

At hospital discharge: mean MRC score were 22.15 (±9.38) and 17.39 (±9.46) among the demyelinating and axonal cases respectively (p=0.013). Length of hospital stay was shorter 15.13 (±17.60) days, in demyelinating and 23.58 (±23.55) days in axonal cases (*p=0.038). Mean duration of ICU stay were 28.69 (±23.28) days in demyelinating and 37.00 (±20.01) days in axonal cases, and was not significant statistically (p=0.298). Clinical improvement were noted among 36 (65.5%) cases and 30 (56.6%) cases of demyelinating and axonal GBS respectively. About 13 (23.6%) of the demyelinating and 17 (32.1%) of axonal cases were static. Moreover 4 (7.3%) of demyelinating and 2 (3.8%) of axonal cases deteriorated further. 2 of the demyelinating and 4 of the axonal cases died in the hospital (Table 4).

Table 4: Comparison of Clinical Outcome at Hospital Discharge Between Demyelinating and Axonal Subtype of GBS

Clinical outcome	GBS Type		P value
At discharge	Demyelinating	Axonal	
Mean MRC Score (n=102)	22.15 (±9.38)	17.39 (±9.46)	0.013*
Length of Hospital Stay (n=108)	15.13 (±17.60)	23.58 (±23.55)	0.038*
Length of ICU Stay (n=35)	28.69 (±23.28)	37.00 (±20.01)	0.298*
Hospital outcome			
• Static	13 (23.6%)	17 (32.1%)	
• Improved	36 (65.5%)	30 (56.6%)	0.498**
• Deteriorated	4 (7.3%)	2 (3.8%)	
• Death	2 (3.6%)	4(7.5%)	

ICU: Critical care unit. mMRC: Modified Medical Research Council.*Independent sample T test was performed to determine the level of significance. **Pearson chi-square test was performed to determine the level of significance. P value less than 0.05 was considered as significant.

Discussion

The main focus of this study is to observe the differences in various clinical parameters as well as the differences of clinical and electrophysiological outcome at 12 weeks of demyelinating and axonal variety of GBS. The study includes 50.9% demyelinating and 49.1% axonal subtypes of GBS. Previous study[8] has demonstrated that there is a marked variation of GBS worldwide with respect to clinical pattern, severity, electrophysiological subtypes and outcome. The predominant electrophysiological subtype is demyelinating throughout the world- 55% in Europe-America, 45% in Asia and in Bangladesh 40% cases[8]. Axonal GBS is reported in 3.0% to 17.0% in Europe[9], 23 to 65% in Asia[10] and up to 67% in Bangladesh[11]. The result of this study is consistent with that of other studies.

The mean age of participant is 40.20 ± 16.26 years and 32.43 ± 14.93 years among the demyelinating and axonal subtypes respectively. All over the world frequency of GBS increases with age. Similar age distribution was reported previously[12]. In Bangladesh, patients are younger than other parts of the world which is supported by a previous study[11] where mean age was 21 years, lower than the present study probably due to the inclusions of pediatric group of patients. In this study axonal patients are younger than demyelinating one which is also supported by previous study[8].

Antecedent events are present in 76 (70.4%) cases in this study. This observation is consistent with that of many previous studies where an antecedent events were present in 40.0% to 76.0% of cases[13]. Axonal cases are mostly related to gastroenteritis[11]. In this series 43(81.1%) of axonal subtype is associated with gastroenteritis as an antecedent event and 33(60.0%) demyelinating cases are also linked to gastroenteritis as a preceding event. Earlier observation[11] has documented gastroenteritis as predominant antecedent event (50.0%) in Bangladesh. However, URTI is the main antecedent event in Europe or America which is about 38.0% and in Asia 51.0% where AIDP is the predominant subtype of GBS probably because of less exposure to *Campylobacter jejuni* infection. In a study from China it has been explored that URTI is more linked to demyelinating GBS however, result of the present study differs from that result[14].

There are significant differences between demyelinating and axonal subtype of GBS with respect to onset of symptoms, hospitalization and nadir of weakness. The present study has revealed, following an antecedent event; onset of symptom is rapid in axonal cases than demyelinating one; 8.47± 4.97 vs. 12.36± 7.94 days and a quick hospitalization: 4.70± 2.13 vs. 6.75± 5.30 days in axonal vs. demyelinating subtype of GBS. In contrast to demyelinating cases Nadir of weakness also develops more rapidly in axonal cases; 6.70± 2.57 Vs. 8.36± 4.59 days. All the findings of the present study are consistent with the results of the previous studies[8,14].

In this study autonomic features are present in 26 (47.3%) demyelinating cases and 29 (54.7%) axonal cases. Previous study[15] has found autonomic deficits in 55.26% of GBS cases which is consistent with this study 55.9%. No previous study has been found comparing the autonomic involvement in demyelinating and axonal subtype in adult population. However, in a pediatric study[15] has revealed 12.6% and 15.2% of autonomic disturbance in demyelinating and axonal GBS respectively. Age and geographical variation of the population may be the possible explanation of this difference. Tachyarrhythmia is the commonest autonomic features which is present 18(32.7%) of demyelinating and 24(45.3%) of axonal cases. Sweating is reported by 12(21.8%) vs. 12(22.6%) and Excessive salivation is found 10(18.2%) versus 18(34.0%) of demyelinating vs. axonal cases. Fluctuating BP is noted 10(18.2%) demyelinating and 10(18.9%) axonal cases. Only one patient (axonal) has urinary incontinence in this study.

Mean MRC score is found 18.04 (±9.85) Vs. 12.94 (±9.91) in demyelinating vs. axonal cases (p=0.009). Mean disability score is 3.67 (±.94) Vs. 4.08 (±0.87) in demyelinating vs. axonal cases (p=0.023). Lower mean MRC score and higher mean disability score were also observed in axonal subtype than demyelinating one in an earlier study[13]. Mild GBS is found in 8 (14.5%) Vs. 3 (5.7%) cases and severe GBS cases are found in 47 (85.5%) versus 50 (94.3%) in demyelinating vs. axonal respectively. Previous study[14] revealed similar higher percentage of severe disease in axonal than demyelinating subtype of GBS.

Recent searching has not been found any adult study comparing outcome at hospital discharge. This study compare different parameters at hospital discharge mean MRC sum score differ significantly between the subtype; 22.15±9.38 versus 17.39±9.46 among demyelinating versus axonal subtype (p=0.013). Mean length of hospital stay is also significantly shorter in demyelinating, 15.13±17.60 versus 23.58±23.55 days in axonal cases (p=0.038). However, previous study14 has not found any difference in this aspect. A pediatric study[16] comparing AIDP and AMAN also has not found any difference in this issue. Mean duration of ICU stay in this study are 28.69±23.28 versus 37.0±20.01 days in demyelinating vs. axonal cases (p=0.298). Clinical improvement has been observed in 36(65.5%) and 30(56.6%) cases of demyelinating and axonal GBS respectively. About 13(23.6%) of the demyelinating and 17(32.1%) of axonal cases have remained static. Moreover, further deterioration has been observed in 4(7.3%) demyelinating and 2(3.8%) of axonal cases.

Significant difference in outcome at 12 weeks has been observed in this study among the demyelinating and axonal subtype of GBS, good outcome was observed among 27(57.4%) of demyelinating and 17(37.0%) of axonal GBS cases (p=0.038). The difference of mean disability score between the two groups at 12 weeks in this study is also significant which are in 1.66±1.83 versus 2.65±1.84 between the two groups. Both the above findings are supported by another study[16]. In the present study 42.6% of demyelinating and 52.7% of axonal cases have been remained in poor outcome group including all death cases. Axonal subtype has a slower and poorer outcome[11]. The mean MRC score at 12 week is also significantly comparable among demyelinating and axonal subtype which is 35.02 ± 6.89 vs. 30.98 ±8.75 (p=0.022) and the result is consistent with a previous study[17]. Death from GBS was reported as 2.0% to 13.0% cases[9,11,13] and it is higher in low income countries[17]. In this study total of 9 (8.3%) death has been occurred during the whole study period. High death rate was found in previous Bangladeshi study[18] which was 12% during a 6 month follow up period. Reduction of death rate is due to increased awareness of the people to seek urgent medical attention as well as improvement of ICU support. Among the total 9 deaths in this study; 4 (7.3%) cases were demyelinating and 5 (9.4%) cases were of axonal (p=0.476).

Conclusion

This study compares the clinical profile as well as short term outcome between demyelinating and axonal subtypes of GBS among the adult population. As per search, this is the first ever comparative study among demyelinating and axonal variety of GBS on adult population in Bangladesh. The present study reveals

both subtypes exist almost in equal frequencies. About two-third of the cases are associated with a preceding event. These two variant differs in many aspects of clinical parameter such as age, antecedent events, speed of onset, time to hospitalization, time to nadir of weakness, facial palsy, mean MRC score & mean disability score at nadir and at discharge. Differences are also observed in outcome at 12 weeks. Prognosis is more favorable in demyelinating subtype than axonal with respect to MRC, disability and electrophysiological parameters at the end of the study period.

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Conflict Of Interest
The authors have no conflicts of interest to disclose

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Authors' contributions
Islam MZ, Ara A, Hasan SM conceived and designed the study, analyzed the data, interpreted the results, and wrote up the draft manuscript. Hasan SM, Yusuf MA, Karim R contributed to the analysis of the data, interpretation of the results and critically reviewing the manuscript. Karim R, Hoque MA, Mohammad QD involved in the manuscript review and editing. All authors read and approved the final manuscript.

Data Availability
Any inquiries regarding supporting data availability of this study should be directed to the corresponding author and are available from the corresponding author on reasonable request.

Ethics Approval and Consent to Participate
Ethical approval for the study was obtained from the Institutional Review Board. As this was a retrospective study the written informed consent was not obtained from all study participants. All methods were performed in accordance with the relevant guidelines and regulations.

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