

Comparison of Cerebrospinal Fluid Protein Level with Clinical Severity and Electrophysiological Category in Patients with Guillain-Barre' Syndrome

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Abstract:

Background: Guillain-Barre' syndrome (GBS) is an acute onset polyneuropathy with variable presentation and severity. It is the most common cause of acute flaccid paralysis worldwide. The cerebrospinal fluid (CSF) analysis and electrophysiological study plays a pivotal role in diagnosis of GBS. **Objective:** This study aimed at finding a relation between CSF protein level with clinical severity and electrophysiological category of GBS patients. **Methods:** Sixty-three patients of GBS were diagnosed and enrolled as per Brighton collaboration criteria. Besides analyzing CSF and electrophysiological study various epidemiological and clinical parameters were also studied. Patients were sub-grouped into AIDP, axonal GBS including in-excitables forms incorporating both Acute Motor Axonal Neuropathy (AMAN) and Acute Motor Sensory Axonal Neuropathy (AMSAN), equivocal and normal categories by modified electrodiagnostic criteria of Rajabally. Clinical severity was assessed by Hughes functional grading scale and were classified into ambulatory group (Grade 1-3) and non-ambulatory group (Grade 4-6). **Results:** Axonal variety was found the most common subtype 36 (57.1%) followed by AIDP 24 (38.1%) elicited by electrophysiological criteria. Mean CSF protein was 102.10 ± 43.06 mg/dl. History of preceding illness was present in 65.1% subjects. Cranial nerve involvement was found in 36.5% patients and autonomic dysfunction in 23.8% patients. A disability score of 4 was found in 36.5% patients, followed by 3 in 34.9% and 2 in 27% and 1 in 1.6% patients. Ambulatory group represents 63.5% patients and 36.5% were in non-ambulatory group. Mean CSF protein found to be significantly higher in non-ambulatory group compared to ambulatory group ($p < 0.001$). AIDP showed higher CSF protein than axonal subtype ($p = 0.014$). **Conclusion:** This study demonstrates that higher level of CSF protein is associated with higher grade of clinical severity and also with demyelinating subtype.

Keywords: GBS, CSF protein level, Clinical severity, Electrophysiological category

Introduction

Guillain-Barre' syndrome (GBS) is an immune mediated disorder of peripheral nerves where autoantibodies are formed against healthy nerve

cells. It is characterized by acute onset ascending, symmetrical weakness of limbs with or without respiratory or bulbar involvement.¹ After eradication of poliomyelitis it is the most common cause of

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acute flaccid paralysis in Bangladesh^{2,3}. The incidence of GBS in Bangladesh is 1.5 to 2.5 per 100000 population in adults and 3.25 in children under 15 years.^{2,3} The overall prevalence of GBS in South-East Asian countries is 1.1 per 100000 population.⁴ In about two-third of the cases it is preceded by upper respiratory tract infection or diarrhea caused by *Campylobacter jejuni*.⁵ Clinical symptoms develop 1-3

weeks after the precipitating illness. Immune response involving both humoral and cell-mediated immunity is responsible in the pathogenesis of GBS.⁶ Progressive symmetrical weakness of muscles which reaches maximum severity within 4 weeks associated with areflexia or hyporeflexia is the clinical hallmark of the disease.⁷ Along with weakness of limbs other muscles like oropharyngeal, facial, respiratory and extraocular musculature may also be involved. Other presentation includes mild sensory impairment, pain in extremities and autonomic dysfunction.⁶

Diagnosis is mainly clinical which may be guided by rise in cerebrospinal fluid (CSF) protein despite normal cell count along with typical electrophysiological abnormalities.⁸ CSF protein is raised in 80% cases during the second week of illness.⁹ Elevation of CSF protein indicates increased intrathecal deposition of antibody, complements and products of active myelin breakdown due to inflammatory damage to the nerve roots.¹⁰ Elevated CSF protein may provide useful information about degree of blood nerve barrier disruption and the extent of radicular involvement. It also gives useful clues to differentiate demyelinating from axonal GBS variety.¹¹ According to electrophysiological abnormalities GBS can be differentiated into- acute inflammatory demyelinating polyradiculoneuropathy (AIDP), axonal GBS including inexcitable forms (incorporating both Acute motor axonal neuropathy and Acute motor sensory axonal neuropathy) and normal/equivocal pattern.¹² Axonal variety is reported as the predominant subtype of GBS in Bangladesh.¹³ Previous studies found that acute motor axonal neuropathy (AMAN) is characterized by axonal degeneration and it carries a poor outcome.^{14,15}

However some recent studies have suggested that patients with AMAN can also experience quick recovery.

Patients with AMAN with electrophysiological evidence of axonal failure shares a similar prognosis with that of AIDP which can be explained by reversible conduction failure at nodes of Ranvier without secondary axonal degeneration.¹⁶ Few factors were found to be responsible for poor prognosis of the disease. These are – increasing age, preceding history of diarrhea, rapid onset of weakness, respiratory involvement, high grade on disability scale and persistently low CMAP amplitude.⁷ Disability can range from no or mild weakness with functional independence to patients requiring assisted ventilation or death.³ Increased disability score at onset was found to have poor short-term outcome.¹⁷ Several international studies correlating CSF protein level with severity and electrophysiological pattern in GBS patients have been done recently. It was found that higher level of CSF protein level is associated with demyelinating electrophysiological pattern compared to axonal one. Elevated level of CSF protein is also associated with a more severe form of the disease.^{11,20} This study aims to evaluate the relation between CSF protein level with clinical severity of GBS. It will also evaluate the relation of CSF protein level with electrophysiological category of GBS.

Materials and Methods

This is a cross sectional descriptive study, was done in the Department of Neurology, Mymensingh Medical College Hospital, Mymensingh from February, 2022 to January, 2024. Patients admitted with GBS was included in the study. A purposive type of non-probability sampling method was used and sample was collected on the basis of inclusion and exclusion criteria. The following working definition was used-

Brighton collaboration criteria (2011): All patients were diagnosed as per Brighton collaboration criteria level 1 & 2 of diagnostic certainty.

Normal Cerebrospinal fluid protein level: 15-45 mg/dl.

Modified electrodiagnostic criteria of Rajabally for Guillain-Barre' Syndrome: All patients were categorized into following subtypes on the basis of electrophysiological properties-

1. Normal.
2. Acute inflammatory demyelinating polyradiculoneuropathy (AIDP).
3. Axonal GBS including inexcitable forms.
4. Equivocal.

Hughes Clinical performance score

- | | |
|---|---|
| 0 | A healthy state. |
| 1 | Minor symptoms and capable of running. |
| 2 | Able to walk 10 m or more without assistance but unable to run. |
| 3 | Able to walk 10 m across an open space with help. |
| 4 | Bedridden or chair bound |
| 5 | Requiring ventilation for at least part of the day |
| 6 | Dead |

Results

This cross-sectional descriptive type study was done 63 patients of GBS. It was observed that majority respondents belonged to the age group 18-29. Mean age ($\pm$ SD) of the respondents was 41.24 ± 17.61 years. Majority of the patients were male (68.3%). More than half of the GBS cases (58.7%) hailed from rural areas. Regarding the history of previous illness; total 17(27.0%) patients were presented with preceding history of respiratory tract infection, 24 (38.1%) patients had preceding history of diarrhea, so there were 41 (65.1%) patients having history of preceding illness; and 22 (34.9%) had no preceding illness (Figure 1). The present study revealed that, most of the patients were having axonal variety 36 (57.1%), followed by AIDP 24 (38.1%) and equivocal pattern 3 (4.8%) (Figure 2). The mean CSF protein in non-ambulatory group (HFGS 4-6) was 130.78 ± 28.03 mg/dl compared to ambulatory group (HFGS 1-3) was 85.60 ± 41.73 mg/dl (Figure 3). We found that, mean CSF protein level was 117.17 ± 34.85 (mg/

dl) in AIDP, which was higher than axonal (96.56 ± 45.11) and equivocal (48.00 ± 14.93) findings in NCS (Table III).

Table-I
Distribution of the study subjects by demographic profile (n=120)

Demographic profile	Frequency	Percentage
Age (years)		
18-29	21	33.3
30-39	8	12.7
40-49	9	14.3
50-59	13	20.7
60-69	6	9.5
>70	6	9.5
Mean±SD	41.24±17.61	
Gender		
Male	43	68.3
Female	20	31. /
Residence		
Rural	37	58.7
Urban	14	22.2
Suburban	12	19.1

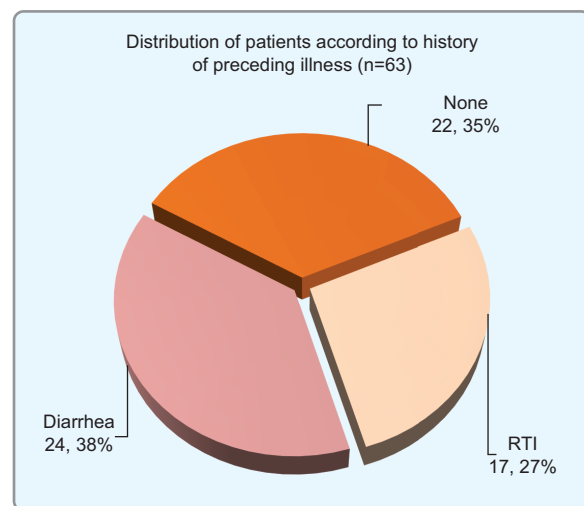


Figure 1: Pie chart showing pattern preceding illness in study population.

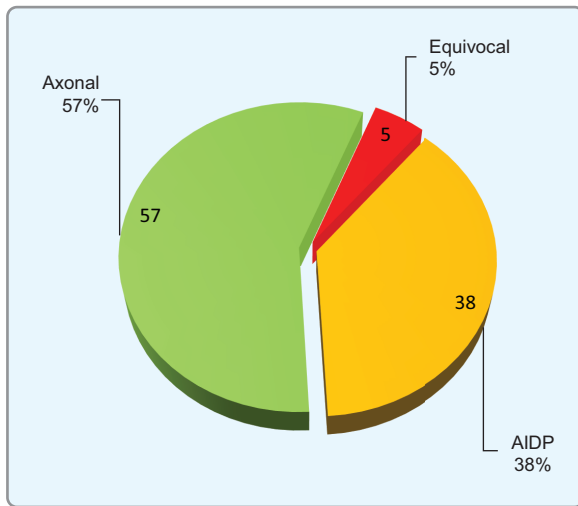


Figure 2: Pie chart showing electrophysiological subtypes of the studied GBS patients (n=63).

Table-II

Relation between Hughes functional grading scale (HFGS) range and mean CSF protein level among the studied GBS patients (n=63).

HFGS	N	Mean CSF protein level (mg/dl)±SD	P
Range			
Ambulatory group (1-3)	40	85.60±41.73	<0.001*
Non-ambulatory group (4-6)	23	130.78±28.03	

P value was obtained from unpaired student t-test.
*statistically significant.

Table-III

Relation between electrophysiological category and mean CSF protein level among the studied GBS patients (n=63).

Electrophysiological findings	Mean CSF protein level (mg/dl)±SD	P value
AIDP	117.17±34.85	0.014*
Axonal	96.56±45.11	
Equivocal	48.00±14.93	

P value was obtained from ANOVA test, *statistically significant

Discussion

The present study was a cross-sectional descriptive type of observational study involving 63 patients. In this study, mean age of the patients was 41.24 ± 17.61 years, ranging from 18 to 75 years. The majority of patients belonged to the age group of 18-29 years, comprising 21 patients (33.3%) followed by the 50-59 age group with 13 patients (20.7%). This could be attributed to the increased risk of acquiring infections, especially *Campylobacter jejuni*, in the younger age group. A large observational study conducted in Bangladesh found median age of GBS onset was 33 years with a range of 25-45 years.¹⁹ A hospital-based study conducted in Dhaka Medical College Hospital, Dhaka found majority of the patients belonged to age 18-25 years.¹⁴ These findings matches with the findings of the current study.

In the present study, the male to female ratio was found to be 2.15:1, which is slightly higher than previously observed ratio of 1.80:1.¹⁹ International GBS Outcome study found 60% of the affected GBS patients were male.¹⁸ This might imply a higher susceptibility of males to various infections in this region. We observed that 37(58.7%) patients came from a rural background, whereas 12(19.1%) from suburban background. This can be explained by the fact that the majority of patients visiting Mymensingh Medical College Hospital were from rural backgrounds. This observation might also suggest that inadequate hygiene practices in rural areas are contributing to the higher incidence of infections.

The current study also found that 41 (65.1%) patients had a history of preceding illness, a finding consistent with previous study.⁶ Among them 24 (38.1%) patients had a history of diarrhea and 17 (27%) patients had a history of respiratory tract infection. This finding is compatible with the previous study.¹⁹ International GBS Outcome study (IGOS) which is a large multi-centered prospective observational cohort study also found diarrhea as the predominant preceding illness in Bangladesh (36%) whereas respiratory tract infection was the predominant preceding illness in Europe/America (38%) and other Asian countries

(51%).²⁰ This study also found that RTI is the preceding illness in 41.7% of the AIDP patients and 13.9% of the axonal GBS patients. On the other hand, diarrhea was found as a preceding illness in

52.8% of the axonal GBS patients and 20.8% of the AIDP patients. This finding matches with the findings observed previously.²

In this study mean CSF protein of the patients was 102.10 ± 43.06 . Additionally, albumin-cytological dissociation was detected in 88.9% of the patients in the current study. This finding is consistent with the findings of few previous studies.^{13,19} Although, Kalita reported albumin-cytological dissociation in 68% of patients.¹⁵ A large multicentered prospective observational cohort study, utilizing data from the international GBS outcome study (IGOS), revealed albumin-cytological dissociation in 70% of patients.¹⁸

In the present study, 36 patients (57.1%) had the axonal variety of GBS, followed by 24 patients (38.1%) with AIDP, and 3 patients (4.8%) exhibited an equivocal pattern. A large prospective study conducted in Bangladesh also reported similar findings.¹³ Other studies from Bangladesh, also found comparable results.^{14,19,21} However, the study utilizing data from IGOS, revealed that 55% of patients had the demyelinating subtype compared to only 9% with the axonal variety.¹⁸ This could be attributed to the majority of patients in IGOS being from Europe. From previous study it was found that demyelinating subtype is more common in Europe/America and other Asian countries except Bangladesh and axonal subtype is more prevalent in Bangladesh.²⁰ Studies conducted in India and Northern China also reported similar results.^{17,22} Conversely, a study from Southwest China, showed AIDP as the most common subtype of GBS.²³

In our study, the mean CSF protein measured was 117.17 ± 34.85 mg/dL in AIDP subtype, which is higher than axonal (96.56 ± 45.11 mg/dL) and equivocal pattern (48.00 ± 14.93 mg/dL). These differences were statistically significant ($p < 0.014$). This finding aligns with several other studies.^{18,11,8} However, it contradicts the findings of few, who showed no significant relation between mean CSF protein and the electrophysiological category of GBS.^{24,25} Additionally, another reported higher mean CSF protein levels in the axonal subtype compared to the AIDP subtype of GBS.¹⁴ This discrepancy may be attributed to the smaller number of patients in the demyelinating subtype of GBS in their study. The higher CSF protein levels observed in the AIDP subtype of GBS may result

from the disruption of the blood-nerve barrier, release of breakdown products of myelin, and greater intrathecal antibody synthesis in the proximal nerve root region.

Conclusion

The study demonstrates a significant relation between elevated CSF protein level and both the clinical severity and electrophysiological category in patients with Guillain-Barré Syndrome (GBS). This finding indicates that CSF protein level could be a useful biomarker for evaluating disease severity and distinguishing between demyelinating and axonal variants in GBS.

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