ORIGINAL ARTICLE

UNRAVELLING THE ANTECEDENT SYMPTOMS IN EARLY PRESENTATION OF GUILLAIN-BARRÉ SYNDROME: A COMPREHENSIVE EXPLORATION

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Background: Guillain-Barré Syndrome (GBS) is a autoimmune disease leading to ascending paralysis and areflexia. This condition often follows an infection or a triggering event, and understanding its preceding symptoms can help with early identification and treatment. Objective of this study was to explore the antecedent symptoms in Guillain-Barre syndrome, and to determine the most prevalent type of Guillain-Barré syndrome. **Methods:** This cross-sectional study was conducted at the Department of Neurology, Pakistan Institute of Medical Sciences (PIMS), Islamabad from May 2023 to Feb 2024. Qualitative and quantitative data was collected. Demographic details, CSF study, autonomic dysfunction, Erasmus Guillain-Barré Respiratory Insufficiency Score (EGRIS), preceding symptoms and duration was prospectively collected from 94 patients meeting the inclusion criteria and analysed on SPSS-23. Chi-square test of association was applied taking $p \leq 0.05$ as significant, and with a confidence interval of 95%. **Results:** The Nerve Conduction Studies (NCS) were normal in 22% patients while abnormal in 78% patients. Out of the total, 70% presented with preceding symptoms [(respiratory 43%), (diarrhoea 19%), (flu 8%)]. There was significant association ($p<0.05$)] between Nerve Conduction Studies (NCS) and GBS types. Whereas, no significant association was found between NCS and GBS preceding symptoms, duration of symptoms, CSF study, autonomic dysfunction, cranial nerve involvement, and EGRIS Score. **Conclusion:** Preceding symptoms were present in 70% of the cases of Guillain-Barré syndrome. Association of preceding symptoms with nerve conduction studies (NCS) facilitates timely intervention and optimizing patient management. In our study, AIDP was most prevalent type.

Keywords: Guillain-Barré syndrome, Nerve conduction study, Electrophysiological studies

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INTRODUCTION

The Guillain-Barré syndrome (GBS) is a group of clinical syndromes characterized by sudden onset of weakness and decreased reflexes due to an acute inflammatory polyradiculoneuropathy. The incidence of GBS is nearly 0.4–4/100,000 cases whereas its occurrence varies in diverse regions worldwide.[1] The typical characteristic of GBS is that of a demyelinating neuropathy with progressive weakening. GBS is divided in distinct subcategories including acute inflammatory demyelinating polyneuropathy (AIDP), acute motor axonal neuropathy (AMAN) and acute motor sensory axonal neuropathy (AMSAN), Miller Fischer syndrome and Bickerstaff encephalitis based on a spectrum of clinical symptoms and findings.[2]

The GBS diagnosis continues to rely mainly on the assessment of the subject's clinical condition and physical examination results.[2] Ascending paralysis with hyporeflexia are classic symptoms of GBS, making diagnosis relatively simple.[3] NCS and cerebrospinal fluid albumin-cytologic separation can be helpful indicators of this condition.[4] Accurate diagnosis of each variety requires electrophysiological testing; however, this can only be done if it is performed soon after the onset of symptoms.[5]

Gender differences in the prevalence of GBS have been observed, with a higher occurrence rate in males compared to females. Furthermore, the incidence of GBS tends to rise with advancing age, but individuals across all age categories can be susceptible to this condition.[6] Approximately 20% of individuals diagnosed with GBS experience respiratory failure, necessitating the use of mechanical ventilation.[7] The autonomic nervous system dysfunction leads to the development of arrhythmias of the heart and blood pressure instability. Individuals diagnosed with the conventional sensorimotor variant of GBS exhibit initial symptoms of distal paresthesias or sensory impairment, which are then accompanied or succeeded by a progressive weakening that initially, affects the lower extremities and subsequently extends to the upper limbs and cranial musculature. Majority of the patients exhibit diminished or non-existent reflexes upon initial assessment and nearly all patients experience this condition at its minimum grade.[8]

Dysautonomia is a prevalent condition characterized by manifestations such as instability in heart rate, blood pressure, pupillary failure response and impairment in bowel or bladder function. It is noted that before the onset of weakness, individuals with GBS may undergo intense and widespread pain or specific

impairments of cranial nerves.[8] Some cases exhibit a unique and persistent medical variation of GBS that diverges from the conventional manifestation characterized by sensory impairment and muscle weakness.[9] The diagnosis of GBS relies on a comprehensive evaluation of the patient's medical history, along with the analysis of neurological symptoms, electrophysiological findings, and cerebrospinal fluid (CSF) assessment. Individuals diagnosed with GBS commonly exhibit early symptoms of muscle weakness and sensory abnormalities in the lower extremities, which subsequently extend to the upper limbs and cranial muscles.[9] The presence of preceding symptoms is helpful in diagnosis of GBS.[10]

There is scarcity of data on association of prodromal symptoms and nerve conduction study findings. We explored the association between antecedent symptoms and nerve conduction studies, so that these symptoms may be recognised as red flag in susceptible individuals.

METHODOLOGY

This cross-sectional study was carried out at the Neurology Unit of Pakistan Institute of Medical Sciences (PIMS), Islamabad, from May 2023 to Feb 2024 after obtaining approval from the Ethical Review Board of Shaheed Zulfiqar Ali Bhutto Medical University (SZABMU). Study was approved by Advanced Studies and Research Board (AS & RB) of SZABMU. Sample size of 94 was calculated using WHO sample size calculator. Both male and female patients provisionally diagnosed with GBS with the age range of 13–65 years were included for this study by using non-probability consecutive sampling technique after taking written informed consent. All the patients who presented to Outpatient and Emergency Departments with acute flaccid paralysis in above age ranges were screened for GBS. The patients with diabetes mellitus, renal impairment, peripheral nerve disease, and myopathy were excluded from the study. Patients were broadly divided into two groups, i.e., Group A comprised of patients with normal NCS and Group B of patients with abnormal NCS.

After recording patients' demographic details and physical examination suspected GBS cases underwent NCS evaluation by the neurologist. Patients were grouped into above mentioned demyelinating or axonal variants of GBS as per the electrodiagnostic criteria.[11] Parameters like preceding symptoms, GBS Type, GBS symptoms duration, autonomic dysfunction and EGRIS Score, CSF routine examination for protein cell dissociation were recorded. CSF study was mostly done in those patients who were either having normal NCS or were admitted in intensive care unit directly due to autonomic dysfunction. All observations were recorded on a self pre-designed proforma.

The data were analysed on SPSS-23. Mean±SD were determined for numerical data. Frequency and percentages were determined for categorical data such as gender, Nerve Conduction Study, preceding symptoms, CSF study, GBS Type, GBS symptoms duration, Autonomic dysfunction, and EGRIS Score. Chi-square test of association was applied taking $p \leq 0.05$ as significant and with a confidence interval of 95%.

RESULTS

There were 50 (53.2%) males and 44 (46.8%) females in this study. The mean age of the patients was 39.77±16.43 years.

CSF Study was performed in 40 patients in whom 38.3% showed protein cell dissociation, and 4.3% showed normal study, while in 57.4% patients CSF study was not performed. Out of 94 cases in our study 33.0% patients had autonomic dysfunction whereas 67.0% showed no autonomic dysfunction. On EGRIS score low risk was seen in 54.3% patients, 28.7% showed intermediate risk, and 17.0% showed high risk. (Table-1).

Our patients were divided into two groups on the basis of nerve conduction study. One group with normal nerve conduction studies and second group with abnormal nerve conduction studies; and then did association with GBS symptoms, duration, types, autonomic dysfunctions, CSF study and EGRIS scoring and found that nerve conduction studies were showing significant association with GBS types only.

The preceding symptoms of GBS in which 8 (8.5%) patients presented with flu, 40 (42.6%) with respiratory symptoms, 18 (19.1%) with diarrhoea, and 28 (29.8%) patients had no preceding symptoms. The cases presented within 3 days were 15 (16.0%), in 3–5 days were 2 (26.6%), and 54 (57.4%) presented in 6–7 days. Patients presented with AIDP were 30 (32.0%), with AMAN were 25 (26.6%), with AMSAN were 18 (19.1%), and 21 (22.3%) had normal nerve conduction study. (Table-2).

Table-1: CSF findings, autonomic dysfunction and EGRIS score in patients with Guillain-Barré Syndrome (n=94)

Characteristics	Frequency	Percentage
CSF Study		
Protein: Cell dissociation (Present)	36	38.3
Protein: Cell dissociation (Absent)	4	4.3
Not Performed	54	57.4
Autonomic dysfunction		
Yes	31	33.0
No	63	67.0
EGRIS score		
Low Risk	51	54.3
Intermediate Risk	27	28.7
High Risk	16	17.0

Table-2: Association of GBS characteristics with Nerve Conduction Studies (n=94) [n (%)]

Characteristics	Nerve conduction studies		*p*
	Normal n=21	Abnormal n=73	
GBS Symptoms			
Flu	0 (0.0)	8 (11.0)	0.46
Respiratory	10 (47.6)	30 (41.1)	
Diarrhoea	4 (19.0)	14 (19.2)	
None	7 (33.3)	21 (28.8)	
GBS Duration			
≤3 days	6 (28.6)	9 (12.3)	0.15
3–5 days	6 (28.6)	19 (26.0)	
6–7 days	9 (42.9)	45 (61.6)	
GBS Types			
AIDP	0 (0.0)	30 (41.11)	**0.0001***
AMAN	0 (0.0)	25 (34.2)	
AMSAN	0 (0.0)	18 (24.7)	
None	21 (100.0)	0 (0.0)	
Autonomic dysfunction			
Present	4 (19.0)	27 (37.0)	0.12
Absent	17 (81.0)	46 (63.0)	
EGRIS Score			
0–2 Low Risk	15 (71.4)	36 (49.3)	0.19
3–4 Intermediate Risk	4 (19.0)	23 (31.5)	
5–7 High Risk	2 (9.5)	14 (19.2)	

*Significant

DISCUSSION

In our study, the age range of the patients spanned from 13 to 65 years. The average age of patients diagnosed with Guillain-Barré Syndrome was found to be 39.77±16.42 years a figure that closely aligns with the results of a previous study conducted in Pakistan where the mean age was recorded as 36.58 years. While it is true that GBS can affect individuals of either gender, it is commonly observed in males.[12,13] Our findings are quite in line with the previous work.

Majority of patients showed respiratory symptoms (42.6%) followed by diarrhoea (19.1%) and flu (8.5%), comparable to a study conducted in Bangladesh by Doets AY *et al*[14] showing 14% cases of flu, 35% cases of respiratory tract infection, 27% with diarrhoea and 25% with no preceding symptoms. We considered only those patients who presented within 7 days of presenting symptoms. It was observed that 16.0% cases presented in 3 days, 26.6% cases presented in 3–5 days, and 57.4% cases presented in 6–7 days after their symptoms started. Our findings are consistent with the findings by Alkahtani *et al*[15] who showed that 62.2% cases presented within relevant time period.

Regarding the type of GBS we found that AIDP was more prevalent variant of GBS followed by AMAN and AMSAN variant, while 22.3% patients had normal NCS. A study conducted by Iqbal R *et al*[16] showed that most prevalent variant of GBS in Pakistan is AIDP (47.27%) followed by AMAN (35.45%) and AMSAN variant (15.45%). The incidence of AIDP and AMAN was higher, and incidence of AMSAN was lower than our study. Another study[17] showed prevalent of AIDP as 66% which is quite higher than our study.

We also followed CSF study of patients presenting with early GBS. CSF was done in 40 patients who either had normal NCS on presentation or who were critical enough to go for NCS, and 90.0% cases showed protein cell dissociation. This means CSF study with protein cell dissociation is quite helpful for early diagnosis of GBS even if NCS is normal. Hegen H *et al*[18] found that 74% of their cases showed protein cell dissociation. Another study[19] showed 83% cases with CSF study showing protein cell dissociation. A study conducted in India[20] showed that 81% patients were having protein cell dissociation.

It was found that 33.0% of our patients had autonomic dysfunction and 67.0% showed no autonomic dysfunction. Our results are comparable to another study conducted in Pakistan[21] which showed 41.53% cases with autonomic dysfunction which was higher than our study. Another study[22] showed 31% cases with autonomic dysfunction which were nearly similar to our study. The above mentioned studies focused mainly on severity of GBS and its outcome but they employed the identical methods of data collection an analysis.

We applied EGRIS score to monitor patients if there is any need of early mechanical ventilation. Majority (54.3%) of our patients were at low risk, and the rest (45.7%) were having EGRIS score ≥3 which was less than a recent study conduct in Pakistan[23] in which 75.4% cases were having EGRIS score ≥3. Yao *et al*[24] showed an average EGRIS 2.5 as in our study.

Upon association of nerve conduction studies with duration of GBS, we observed that abnormality of NCS gradually increased with the increasing duration of GBS. However, we could not find any significant association of NCS with GBS symptoms duration, preceding symptoms, or infection in CSF study, autonomic dysfunction, or EGRIS score. This is in contrast to findings by Khedr *et al*[25] who showed higher severity with higher scores in axonal variants.

CONCLUSION

Preceding symptoms were present in 70% of the cases of Guillain-Barré Syndrome. Association of preceding symptoms with nerve conduction studies facilitates timely intervention and optimizing patient management. AIDP was the most prevalent type.

RECOMMENDATIONS

It was a single centre study. Similar studies may be conducted at multiple centres to further explore the diagnostic options along with electrophysiological parameters for diagnosis of GBS.

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SSS: Conceived and designed the analysis, contributed data and analysis tools, performed analysis, reviewed manuscript

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