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ORIGINAL ARTICLE

Clinical Presentations and Variants of Guillain-Barré Syndrome (GBS) among Patients in a Tertiary Care Hospital of Hazara Division, Pakistan

SAIMA GILLANI, MUHAMMAD JUNAID KHAN, MADIHA GUL, Armaghan Ali, Nasir Hussain Shah Kazmi, Shazia Sadaat

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Correspondence to:

Saima Gillani
Department of Pediatrics, Ayub Teaching Hospital, Abbottabad

E-mail: drsaimagillani@gmail.com

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ABSTRACT

Objective: To find out clinical presentations and GBS variants among patients in a Tertiary care Hospital of Hazara division.

Study design: A cross-sectional study.

Place and Duration: It was conducted in all units of Neurology, Medicine and Pediatrics Departments of Ayub Teaching Hospital, Abbottabad over duration of four years from 12.11.2017 till 14.01.2021.

Materials and Methods: By consecutive sampling techniques, patients diagnosed clinically with GBS according to diagnostic criteria and confirmed by electrodiagnostic studies were selected. Data and results of electrodiagnostic studies were recorded on a specified proforma. Due to patient refusal, a lumbar puncture couldn't be performed in most, hence was not included in the final analysis. Using SPSS version 16, descriptive test and chi-square test were applied for data analysis. *P-value* <0.05 was considered significant.

Results: From total of 51, 35(68.6%) were males, overall mean age was 37.8±18.891 years (min 10 and max 75 years). Among clinical presentation of GBS, motor weakness 33 (65.7%) and quadriplegia 29 (56.9%) appeared the most common. Electrodiagnostic studies recorded acute motor axonal neuropathy (AMAN) as more prevalent observed in 18 (35.3%) patients.

Conclusion: The clinical presentation and GBS variants of the Hazara population of Pakistan slightly differed from the available literature. Younger age groups were affected more, however, the predominance in males remains similar to current literature. Motor weakness and quadriplegia were most common presentations and AMAN was the most common variant.

Key Words: *Guillain-Barré syndrome (GBS); Variants; Motor weakness; Acute motor axonal neuropathy; Acute flaccid paralysis; Acute post infectious polyneuropathy, electrodiagnostic tests*

INTRODUCTION

GBS is an immune-mediated post-infectious polyneuropathy, affecting all age groups and has a male predominance. It is considered the most important differential of acute flaccid paralysis (AFP), presenting as progressive, relatively symmetrical weakness with decreased or absent myotatic reflexes. Symptoms may reach

maximum intensity within four weeks of onset, sometimes progressing very rapidly and affecting respiratory muscles to an extent requiring ventilator support and intensive care, other possible causes must be excluded.[1] In many cases GBS follows a preceding respiratory or gastrointestinal viral or bacterial infection that triggers an autoimmune response.[2,3] Early diagnosis and prompt action is required. Diagnostic criteria for GBS are a progressive weakness (ascending), areflexia, symmetrical presentation, only mild sensory involvement, possible cranial nerve involvement, and autonomic dysfunction in the absence of fever. Cerebrospinal fluid findings strongly supporting the diagnosis are an increase in CSF protein with a cell count <10 (albuminocytological dissociation). Electro-diagnostic studies i.e. Electromyography (EMG) and nerve conduction studies (NCS) showing conduction slowing, block, prolonged distal latency or F-wave latencies are evidence enough to support the clinical diagnostic criteria as well as to distinguish the GBS variants, and are observed in 80% cases. In cases with marked persistent asymmetry of weakness, a sensory level, early bowel/bladder dysfunction and marked CSF pleocytosis, an alternative cause for the neuropathy should be sought.[2,4] The many subtypes of GBS vary among countries, knowledge of subtypes is helpful in predicting prognosis as Miller Fisher syndrome (MFS) has better outcome whereas AMAN associated with axonal damage has worse prognosis.[5] Plasmapheresis and intravenous immunoglobulin (IVIG) are two important treatment options to hasten recovery and reduce complications.[6]

According to the National Institute of Neurological and Communicative Disorders and Stroke (NINCDS), there is an annual incidence in the range of 1–2 per 100,000 population.[7] Another study revealed an incidence of 0.4 to 2 per 100,000 with an estimated 100,000 patients worldwide contracting GBS.[8,9] Though studies covering GBS clinical presentations, variants and outcomes have been published from other hospitals in Pakistan, our study aims at presenting the clinical features and GBS variants from our area over a period of four years and comparing them with different age groups and gender.

MATERIAL AND METHODS

This cross-sectional was conducted in all units of neurology, medicine and pediatrics departments of Ayub Teaching Hospital over duration of four years from 12.11.2017 till 14.01.2021. After ethical approval, informed written consent was obtained from each patient. (In the case of children, consent from parents was obtained). By consecutive sampling techniques, patients who fulfilled the diagnostic criteria, mentioned earlier were diagnosed clinically with GBS and confirmed by electrodiagnostic studies (evidence of conduction slowing, block, prolonged distal latency or F-wave latencies) were selected. Data and results of electrodiagnostic studies were recorded on a specified proforma. On account of refusal to a lumbar puncture by most patients it couldn't be included in the final analysis. Using SPSS version 16, descriptive and chi-square tests were applied for data analysis. *P-value* <0.05 was considered significant. All those who had chronic inflammatory demyelinating polyneuropathy, diabetes, polio disease, cerebral palsy, neoplasia, hypothyroidism, renal failure, vasculitis, or history of intoxication, marked asymmetry at presentation or a well demarcated sensory level were excluded from the study. Majority of patients underwent 5 or 6 sessions of plasmapheresis (Plasmapheresis machine/unit Sichuan Nigale Biotech Co. Ltd model NGL XJC 2000 donated by PMWO to ATH) as treatment because IVIG is not available free of cost at our hospital and purchasing it is costly and out of reach for most patients.

RESULTS

Out of a total of 51, 35 (68.6%) were males with overall mean age of 37.8 ± 18.891 years (min 10 and max 75 years) table 1.

TABLE 1. Descriptive details of GBS patients. (n=51)

Patients' variables		Frequency	Percentage
Gender	Male	35	68.6
	Female	16	31.4
Total		**51**	**100.0**
Age group	10-29 Year	20	39.2
	30-49 Years	12	23.5
	50-75 Years	19	37.3
Total		**51**	**100.0**

Among symptoms and clinical presentation of GBS, motor weakness 33 (65.7%) and quadriplegia 29 (56.9%) appeared the most common. Electrodiagnostic finding ensued acute motor axonal neuropathy (AMAN) as more prevalent i.e., 18 (35.3%) table 2.

TABLE 2. Frequencies and percentages of different features and variants of GBS (n=51)

Features of GBS		Frequencies	Percentages
Symptoms of patient	Motor weakness	33	64.7
	Both sensory and motor weakness	17	33.3
	Facial weakness	01	2.0
Total		**51**	**100.0**
Clinical Presentation	Quadriplegia	29	56.8
	Upper limb weakness	01	2.0
	Lower limb weakness	16	31.4
	Facial palsy	01	2.0
	Diffused paralysis (widespread involvement: quadriplegia and associated central involvement of cranial nerves/bulbar/facial and /or respiratory involvement)	04	7.8
Total		**51**	**100.0**
Electrodiagnostic findings	AMAN	18	35.3
	AMSAN	15	29.4
	AIDP	9	17.6
	MFS	1	2.0
	MG	3	5.9
	Normal results	3	5.9
	Isaac syndrome	2	3.9
Total		**51**	**100.0**

AMAN = Acute motor axonal neuropathy, **AMSAN** = Acute motor-sensory axonal neuropathy, **AIDP** = Acute inflammatory demyelinating polyradiculoneuropathy, **MFS** = Miller fisher syndrome, **MS** =Myasthenia grevis

TABLE 3. Distribution of symptoms of GBS patients with gender and age group (n=51). p-value by chi-square test

Patients' variables		Symptoms of patient						Total		*p-value*
		Motor weakness		Both sensory and motor weakness		Facial weakness				
		n	%	n	%	n	%	n	%	
Gender	Male	21	41.18	13	25.49	01	1.96	35	68.62	0.516
	Female	12	23.5	04	7.8	0	0	16	31.37	
Total		**33**	**64.68**	**17**	**33.29**	**01**	**1.96**	**51**	**100.0**	
Age groups	10-29 Year	18	35.3	02	3.9	0	0	20	39.2	0.001*
	30-49 Years	09	17.6	02	3.9	01	1.96	12	23.5	
	50-75 Years	06	11.8	13	25.5	0	0	19	37.3	
Total		**33**	**64.7**	**17**	**33.3**	**01**	**1.96**	**51**	**100.0**	

n = frequency, **% =** percentage, **p-value* <0.05 i.e., significant

TABLE 4: Distribution of clinical presentations of GBS patients with gender and age group (n51). *p-value* by Chi-square test

Patients' variables		Clinical Presentation										Total		*p-values*
		Quadri-plegia		Upper limb weakness		Lower limb weakness		Facial palsy		Diffused paralysis				
		N	%	n	%	n	%	N	%	n	%	n	%	
Gender	Male	18	35.3	01	2.0	12	23.5	01	2.0	03	5.9	35	68.6	0.759
	Female	11	21.6	0	0	04	7.8	0	0	01	2.0	16	31.4	
Total		**29**	**56.9**	**01**	**2.0**	**16**	**31.3**	**01**	**2.0**	**04**	**7.9**	**51**	**100.0**	

Age groups	10-29 Year	8	15.7	01	2.0	09	17.6	0	0	02	3.9	20	39.2	
	30-49 Years	6	11.8	0	0	03	5.9	01	2.0	02	3.9	12	23.5	0.138
	50-75 Years	15	29.4	0	0	04	7.8	0	0	0	0	19	37.3	
Total		**29**	**56.9**	**01**	**2.0**	**16**	**31.4**	**01**	**2.0**	**04**	**7.8**	**51**	**100.0**	

n=frequency, **%**=percentage, ***P-value*** <0.05 i.e., significant

TABLE 5: Distribution of Electrodiagnostic findings of GBS patients with gender and age group (n51). p-value by chi-square test

Patients' variables		**Electrodiagnostics**														**Total**		***p-Value***
		AMAN		**AMSAN**		**AIDP**		**MFS**		**MS**		**Normal**		**ISAAC syn-drome**				
		n	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**N**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	
Gender	M	11	21.6	12	23.5	07	13.7	0	0	02	3.9	01	2.0	02	3.9	35	68.6	0.363
	F	07	13.7	03	5.9	02	3.9	01	2.0	01	2.0	02	3.9	0	0	16	31.4	
Total		18	35.3	15	29.4	09	17.6	01	2.0	03	5.9	03	5.9	02	3.9	51	100.0	
Age groups (Years)	10-29	11	21.6	02	3.9	04	7.8	0	0	01	2.0	01	2.0	01	2.0	20	39.2	0.008*
	30-49	04	7.8	01	2.0	02	3.9	01	2.0	02	3.9	02	3.9	0	0	12	23.5	
	50-75	03	5.9	12	23.5	03	0	0	0	0	0	0	0	01	2.0	19	37.3	
Total		18	35.3	15	29.4	09	17.6	01	2.0	03	5.9	03	5.9	02	3.9	51	100.0	

M = Male, **F** = Female, **n**=frequency, **%**=percentage, **AMAN** =Acute motor axonal neuropathy, **AMSAN**= Acute motor sensory axonal neuropathy, **AIDP**=Acute inflammatory demyelinating polyradiculoneuropathy, **MFS**=Miller fisher syndrome, **MS**=Myasthenia gravis, ***P-value*** <0.05 i.e., significant

Among males, 21 (41.18%) patients and the younger age group 18 (35.29%), motor weakness was found more in GBS patients with significant differences of age group p=0.001 (table 3). From the total, quadriplegic patients were found more in males 18 (35.29%) and older age group 15 (29.41%) table 4. Electrodiagnostic findings revealed that Acute motor-sensory axonal neuropathy (AMSAN) was highest among males (12=23.53%) and older patients (12=23.53%) however, only one Miller fisher syndrome (MFS) was found in each. A significant difference was noticed between age group and given Electrodiagnostic findings, p=0.008 (table 5).

Pattern of weakness	
Quadriparesis	66 (73.3)
Paraparesis	22 ((24.4)
Only upper limb weakness	2 (2.2)
Other symptoms	
Sensory	3 (3.3)
Dysphagia	6 (6.6)
Dysphonia	6 (6.6)
Diplopia	3 (3.3)
Ptosis	3 (3.3)
Bladder and below involvement	2 (2.2)
Cranial nerve (CN) involvement	
Present	23 (25.6

DISCUSSION

GBS involves the peripheral nerves mainly controlling motor function or those which transmit pain, touch and temperature sensation.[10] It's a rare condition and literature mostly reports cases with peculiar features.

Fig 1 shows the percentages of most common clinical presentations of GBS as mentioned in other sources.[11,12]

Clinical features	**Findings, n(%)**
Presenting symptoms	
Motor symptoms	87 (96.6)
Other symptoms	3 (3.3)

Our study presents 51 cases of GBS with clinical features and its variants in the Pakistani context. The most striking results ensued GBS affecting more males, younger patients, with motor weakness and AMAN variant of GBS as most common. GBS is generally considered the disease of adults and affects males more.[1,8]

The male-to-female ratio in our study group was 2.1:1, supporting other studies that report a male predominance.[13,14] One study aimed at identifying differences between male and female GBS patients in gene expression profiles of peripheral

leukocytes demonstrated gender stratification and differences among genders in the genome-wide gene expression of GBS patients.[13] This male predominance is also reported in another large scale study~~ies~~.[14]

Although considered as mainly affecting adults, some studies mentioned that GBS affects all age groups.[15,16] Our study contradicts the incidence in adults as 35% cases were present in the age group of 10 to 30 years. The mean age of GBS patients in the current study was 37.8 ± 18.891 years which is very close to a study conducted in Iran i.e., 42.78 ± 21.34 years.[17] Moreover, studies from North America and Europe report that the incidence of GBS increases with age.[1] This is even supported by a study done in Italy in which the lowest rate of GBS occurred in patients with age less than 35 years of age.[18] This observation is different from the current study in which the commonest affected were from a younger age group.

In the current study, 64.7% of patients had symptoms of Motor weakness. Yuqin YE discussed 26 patients with GBS from Northeast China and all of them had motor weakness.[19] Italian study reported 95% cases of GBS with muscle weakness as the second most common clinical presentation.[18] A study done in India also had the majority of cases with pure motor loss in 62.2% of GBS~~.~~ patients.[20] Their result is very close to the current study. A study by Nasiri J et al reporting a male predominance observed distal lower limb weakness (92.11%), as the most common clinical presentation followed closely by reduced deep tendon reflex (DTR) (82.46%) and neuropathic pain (75.44%). They also observed a low mortality in GBS patients with 92.9% of patients recovering completely.[21]

On Electrodiagnostic~~s~~, we observed AMAN was the most common variant (35.3% cases) followed by AMSAN in 29.4%. This is very close to a study conducted in Iran in which the highest frequency pertained to AMSAN with 93 cases (24%).[17] Similarly, Kalita J et al from India had 73.8% AIDP cases as more prevalent. [20] However, the second most common variant in both studies was AMAN (7%~~)~~ and 13.4%) respectively. Although this differs from our results yet depicts the commonest variation similar to our study.

Peric et al. from Serbia found AIDP as the most common variant of GBS in 65% of patients which is very high in accordance with our study i.e. 17.6%. In the present study, only 1 case of MFS was found whereas, 10 (3%) are reported by Peric et al.[22] Seen twice as common in males, MFS was first recognized by James Collier in 1932 as a separate clinical triad of ophthalmoplegia, ataxia, and areflexia. It was later reported in 1956 by Charles Miller Fisher as a limited variant of GBS as combination of ophthalmoplegia, ataxia, and areflexia without any weakness and subsequently named after him.[23] In western countries, GBS cases have 5 to 10% cases of MFS with more commonality in Asia i.e. Japan, 25%. [24] Regarding other variants of GBS, a study from Turkey resulted in 79.1% of cases of AIDP as the most common variant. In the same study, the second and third most common subtype of GBS was AMSAN (8.5%) and AMAN (7.8%) respectively.[25] In the Pakistani context, a study conducted on 1 to 12 years children, AIPD was found in 39.1% followed by AMSAN 26% and AMAN as 17.4%.[26] These data, however, support the available literature but contradicts the results of the current study.

GBS is generally associated with low mortality and in our study group as well, no mortality occurred. A study from India reported mortality as 12.1%,[27] though mortality of GBS patients varies widely i.e. between 1-18%. Most common causes of death are pneumonia, sepsis, adult respiratory distress syndrome (ARDS) with autonomic dysfunction or pulmonary embolism being less common.[25,28]

CONCLUSION

The clinical presentation and GBS variants of the Hazara population of Pakistan differed slightly from the available literature such as occurrence in the younger age group and more cases of AMAN and AMSAN variants of GBS with clinical presentation of motor dysfunction. However, the predominance in males remains similar to current literature. There were limitations to our study such as the smaller sample size and patient refusal to lumbar puncture. These as well as the outcome of treatments plasmapheresis and IVIG can be considered in future studies and data from other

hospitals of KP can be collected for future projects with larger sample sizes.

Conflicts of interest: There were None.

Authors affiliation

Saima Gillani, Muhammad Junaid Khan, Armaghan Ali, Prof. Nasir Hussain Shah Kazmi, Shazia Sadaat
Department of Pediatric Medicine, Ayub Medical College, Abborrtabad

Madiha Gul,
Department of Obstetrics and gynecology, PIMA Hospital, Mansehra

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