GUILLAIN-BARRÉ SYNDROME; THE SEASONAL TRENDS IN A COHORT OF PAKISTANI POPULATION FROM SOUTHERN PUNJAB

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ABSTRACT

Objective: To report the seasonal trends of Guillain-Barré Syndrome in a cohort of Pakistani population from southern Punjab, Pakistan.

Study Design: A retrospective observational study.

Place and Duration of Study: Department of Physical Medicine & Rehabilitation, Combined Military Hospital Bahawalpur, from Jan 2016 to Oct 2018.

Methodology: One-hundred and fifty-two individuals fulfilling the electrophysiological criteria of Guillain-Barré Syndrome were included from the records of the department and subdivided into four main subtypes on the basis of electrodiagnostic studies including Acute Inflammatory Demyelinating Polyneuropathy, Acute Motor Axonal Neuropathy, Acute Motor and Sensory Axonal Neuropathy, and Miller Fisher Syndrome. The seasons were divided as: summer; May to August, autumn; September and October, winter; November to February, and spring; March and April. Demographic characteristics, type of Guillain-Barré Syndrome, and month and season of presentation were investigated. Data were analyzed with SPSS version 20.

Results: The sample (mean age: 39 ± 21 years) consisted of 114 (75%) males and 38 (25%) females. The highest reporting (63, 41.4%) was in winter followed by (53, 34.9%) summer (p<0.001). May was the peak reporting (n=24) month with January to follow (n=20) (p=0.002). Acute Inflammatory Demyelinating Polyneuropathy was the most frequent sub-type 88 (57.9%). Acute Inflammatory Demyelinating Polyneuropathy and Acute Motor Axonal Neuropathy were significantly more frequent in winter season (p<0.001 and p=0.008 respectively) while Acute Motor and Sensory Axonal Neuropathy was in summer season (p=0.01). Regarding the association with a particular month, Acute Inflammatory Demyelinating Polyneuropathy was significantly more common in May (p=0.025). Acute Motor Axonal Neuropathy and Acute Motor and Sensory Axonal Neuropathy could not find any association. Statistics for Miller-Fisher Syndrome were not computable.

Conclusion: Clustering of Guillain-Barré Syndrome cases was found in winter. Acute Inflammatory Demyelinating Polyneuropathy and Acute Motor Axonal Neuropathy were significantly more frequent in winter while Acute Motor and Sensory Axonal Neuropathy was in summer.

Keywords: Electrodiagnosis, Flaccid paralysis, Guillian-Barre Syndrome, Pakistan, Seasonal variation, Southern Punjab.

INTRODUCTION

Guillian- Barré Syndrome (GBS) is a rapidly progressive acute inflammatory acquired peripheral polyneuropathy characterized by symmetrical weakness and areflexia. It is one of the most frequent causes of acute onset ascending flaccid weakness since eradication of polio with an incidence of 1-2 per 100,000/year in most populations[1]. Nearly two-third cases of GBS have a 4-6 weeks' preceding history of infection. Gastrointestinal and respiratory infections are the two most common identified antecedent infections either of bacterial or viral origin. Campylobacter jejuni, Cytomegalovirus, Epstein Bar Virus, Mycoplasma, Hepatitis E Virus, and recently, Zika virus are frequently identified responsible organisms[2]. GBS presents clinically as symmetrical ascending weakness with areflexia, oculomotor weakness, and ataxia[3]. However, other rare clinical presentations of GBS have

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been reported in the Pakistani literature[4,5]. On the basis of neurophysiological properties, GBS is subdivided into four main subtypes including Acute Inflammatory Demyelinating Polyneuropathy (AIDP), Acute Motor Axonal Neuropathy (AMAN), Acute Motor and Sensory Axonal Neuropathy (AMSAN), and Miller Fisher Syndrome (MFS)[6].

Contradictory evidence exists for seasonal variation of GBS with some studies suggesting a winter trend[3], some reporting summer, spring or autumn peak[7-9], and others finding no significant variation[10]. Seasonal variations in GBS are likely to be dependent on the seasonality of underlying illness considered to cause cross-reactivity with molecular epitope on the peripheral nerves. The subtypes of GBS are also thought to follow some seasonal tendencies independent of each other.

In our clinical practice in Southern Punjab, we observed a clustering of GBS occurrence in certain months and seasons of the year. So, we carried out this retrospective study to know the seasonal reporting and monthly variation of GBS. We then ascertained the seasonal preferences of GBS sub-types as determined on electrodiagnosis (EDX) i.e. nerve conduction studies (NCS) and electromyography (EMG). This, in turn, has an implication for seasonal demand for EDX procedures, neurology, neuro-intensive care, and neuro-rehabilitation services.

METHODOLOGY

It was a retrospective observational study carried out from January 2016 to October 2018 in the department of Physical Medicine & Rehabilitation (PMR) at Combined Military Hospital (CMH) Bahawalpur, which is one of the only two referral setups for EDX facilities in Southern Punjab. PMR specialty is relatively new in Pakistan. There are only two PMR physicians for 3.0 million population of southern Punjab. So, patients reporting here for EDX represent the bulk of GBS patients in this region.

A sample size of 135 was calculated using World Health Organization sample size calculator while using 95% confidence level, absolute precision of 7% and of anticipated population proportion of 21.9%[11]. We explored record of the department and retrospectively sampled the patients with an EDX diagnosis of GBS. Electrodiagnostic criteria of Hadden *et al*[12] for GBS was followed for the diagnosis in our department. The criteria also classifies GBS into its subtypes that have a different pattern of clinical recovery. Patients with history of diabetes mellitus, porphyria, delayed milestones, cerebral palsies, and stroke were excluded. All EDX studies had been done with Nicolet Viasys EMG System using Viking Quest Master Software V. 9.00 (Natus Medical Incorporated, WI, USA). The studies were carried out within four weeks of the onset of weakness.

The data were analyzed with Statistical Package for Social Sciences v 20.0 (IBM Corp., Armonk, NY, USA). Demographic details including age, gender, residential area, month of referral, season, referring physician, and subtypes of GBS were documented in terms of frequencies and percentages. The seasons were divided as: Summer: May to August, autumn: September and October, winter: November to February, and spring: March and April. In order to compare the frequency of GBS in different seasons and months, we used the chi-square goodness-of-fit test. All tests for statistical significance had a level of significance set at ≤0.05.

RESULTS

Out of 152 cases, who were finally included after exploring the departmental record, 114 (75%) were males and 38 (25%) were females. Age at onset of the disease varied from one year to 86 years with a mean age of 39 ± 21 years. Majority 55 (36.2%) belonged to Bahawalpur with Lodhran and Yazman to fall at second place 10 (6.6%) each.

AIDP was the most frequent sub-type of GBS 88 (57.9%) followed by AMSAN 33 (21.7%), AMAN 30 (19.7%), and MFS 1 (0.7%). Neurophysicians sent the maximal referrals for EDX 83 (54.6%), followed by internal medicine specialists 48 (31.6%), pediatricians 17 (11.2%), neurosur-

geons 3 (2%), and orthopedic surgeons 1 (0.7%). The highest reporting was in winter season 63 (41.4%) followed by the summer season 53 (34.9%) (p<0.001) (table-I). Although disease was found throughout the year, the month of May had the highest frequency 24 (15.8%) followed by the month of Jan 20 (13.2%) (p=0.002) (table-II).

Table-I: Variation of Guillian- Barré Syndrome in reference to season.

Seasons	n (%)	χ2	Df	*p*-value
Winter	63 (41.4)	44.74	3	<0.001
Spring	23 (15.1)			
Summer	53 (34.9)			
Autumn	13 (18.6)			

Table-II: Distribution of Guillian- Barré Syndrome cases in different months (p=0.001).

Months	n (%)	χ2	df	*p*-value
Jan	20 (13.2)	29.9	11	0.002
Feb	12 (7.9)			
Mar	8 (5.3)			
Apr	15 (9.9)			
May	24 (15.8)			
Jun	5 (3.3)			
Jul	16 (10.5)			
Aug	7 (4.6)			
Sep	8 (5.3)			
Oct	7 (4.6)			
Nov	16 (10.5)			
Dec	14 (9.2)			

AIDP and AMAN were significantly more frequent in winter season (p<0.001 and p=0.008 respectively) while AMSAN was significantly more common in summer season (p=0.01) (table-III). Statistics for MFS were not computable. Regarding the association with a particular month, AIDP was significantly more common in May (p=0.025). AMAN and AMSAN could not find a particular predilection (p=0.178 and p=0.166 respectively) (table-IV). Statistics for MFS were not computable here as well.

DISCUSSION

Seasonal variation in occurrence of GBS is not consistent and considered attributable to distinct geographical and racial distribution. With analysis of nearly three-year' data, we found seasonal and monthly clustering in GBS cases i.e. we came across maximum cases in winter season though new cases were observed throughout the year. In earlier Pakistani studies, Abbas *et al*[3] observed winter as the trending season for GBS. Ali *et al*[8] and Chand *et al*[13] noted summer while Yaqoob *et al*[14] documented increased reporting in the spring season. This difference is probably due to geographic and climatic variation in residing areas of the studied population. A logical explanation of GBS winter trend appears to be higher frequency of upper respiratory tract infection and flu-like symptoms in winter.

A definite seasonal trend has been reported in other parts of the world as well. Winter season was reported from Denmark, France, UK, and Australia[15-18], autumn from Iran and Sweden[9,19], summer from India and China[7,20], and spring from Chile and Taiwan[21,22]. In contrast, no significant seasonal tendency was reported from Finland and Japan[10,23]. Hence the review of all these studies indicates that it is hard to define any specific trend of seasonal variations for GBS patients because the climate conditions are strikingly different even in the same country. So, the study with larger cohort size and maximum time

Table-III: Distribution of different entities of Guillian- Barré Syndrome based on the seasons.

Guillian- Barré Syndrome Entity	Winter n (%)	Spring n (%)	Summer n (%)	Autum n (%)	χ2	*p*-value
Acute Inflammatory Demyelinating Polyneuropathy	36 (40.9)	13 (14.8)	32 (36.4)	7 (8)	27.36	<0.001
Acute Motor Axonal Neuropathy	15 (50)	6 (20)	7 (23.3)	2 (6.7)	11.87	0.008
Acute Motor and Sensory Axonal Neuropathy	12 (36.4)	4 (12.1)	14 (42.4)	3 (9.1)	11.24	0.01
Miller Fisher Syndrome	-	-	-	1 (100)		-

span may only serve as reference study for that area of the world.

Our study reported maximum cases in May (n=24) and January (n=20). Occurrence of GBS from January to May accounted for more than 50% cases with January and May having a peak with over 20 cases per month. Ali *et al*[8] reported maximum cases in June. Abbas *et al* and Sipila *et al*[3,10] received bulk of the cases in January and February. Momen and colleagues noticed maximum number of cases in December[9]. Levison *et al*[14] in a Danish study, observed maximum number of cases in December and January, while Wu *et al*[19] in a Chinese study, described peak GBS incidence in July and August.

Table-IV: Distribution of different entities of Guillian- Barré Syndrome based on the months.

Guillian-Barré Syndrome Entity	Jan n (%)	Feb n (%)	Mar n (%)	Apr n (%)	May n (%)	Jun n (%)	Jul n (%)	Aug n (%)	Sep n (%)	Oct n (%)	Nov n (%)	Dec n (%)	$\chi 2$	*p*-value
Acute Inflammatory Demyelinating Polyneuropathy	11 (12.5)	7 (8)	5 (5.7)	8 (9.1)	16 (18.2)	2 (2.3)	9 (10.2)	4 (4.5)	4 (4.5)	5 (5.7)	7 (8)	10 (11.4)	21.91	0.025
Acute Motor Axonal Neuropathy	8 (26.7)	2 (6.7)	1 (3.3)	5 (16.7)	3 (10)	2 (6.7)	2 (6.7)	-	2 (6.7)	-	2 (6.7)	3 (10)	12.67	0.178
Acute Motor and Sensory Axonal Neuropathy	1 (3)	3 (9.1)	2 (6.1)	2 (6.1)	5 (15.2)	1 (3)	5 (15.2)	3 (9.1)	2 (6.1)	1 (3)	7 (21.2)	1 (3)	15.36	0.166
Miller Fisher Syndrome	-	-	-	-	-	-	-	-	-	1 (100)	-	-		-

AIDP was the most frequent sub-type of GBS in our study. Other Pakistani studies have also observed AIDP as the most common variant[8,13]. Most other studies from India, China, UK, and Australia have reported AIDP as the most frequent form of GBS[7,17,18,21]. On the contrary, one recent study from Pakistan, one from Ethiopia, and one from Bangladesh showed opposite results with AMAN to be the most common variety[11,24,25]. The difference could be partly accounted for variations in the environmental factors, pathogenic mechanisms, genetic susceptibility, and other triggering factors such as different infections operating in different populations[25]. Here, it may be noted that the EDX features evolve over time and may be misleading in early stages of the disease[25]. Serial recordings are, therefore, may be recommended.

In this study, we found that AIDP and AMAN were significantly more frequent in winter season, while AMSAN was in summer

season. Regarding monthly distribution, AIDP found a significant association with the month of May. This association of AIDP appears to be different from the seasonal findings. This probably resulted from statistical mis-interpretation as the total cases in other months of summer and winter seasons were less for AIDP. Thus a reliable conclusion regarding a particular month could not be drawn. MFS did not find any association with a particular season or month. While reviewing the literature, Webb *et al*[17] reported all types of GBS to be more frequent in winter season. Shrivastava *et al*[7] found AIDP more common in spring and AMAN more common in summer seasons. The higher frequency of admissions in the winter season was associated with a higher incidence of patients reporting a respiratory prodromal illness[17].

Seasonal variation in GBS is particularly important for our understanding of the likely pathogenesis of the disease. This may have public health implications in the future for identifying prodromal infections that could be prevented to reduce the incidence of GBS in specific regions. It also has some potential implications for provision of tertiary neurological and rehabilitation services, particularly in regions with a high incidence of summer GBS due to AMAN, which can result in longer admissions and greater bed occupancy, particularly in neuro intensive care.

There are few limitations to this study. First, it was a retrospective study based on notes review. This may contribute to as certainment or under-reporting error. Second, in our study, Close tridum jejuni serology and anti-ganglio side antibodies were not systematically performed, and therefore these were not addressed in our study. Finally, we had only one case for MFS, thus conclusion based on this small number of patients could not be drawn.

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CONCLUSION

The clustering of GBS cases were found in winter season and in the month of May in our cohort. AIDP and AMAN were significantly more frequent in winter season, while AMSAN was significantly more frequent in summer season.

CONFLICT OF INTEREST

This study has no conflict of interest to be declared by any author.

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