Cohort Study

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Clinical characteristics and management outcomes of Guillain-Barré syndrome: eight-year experience at a tertiary center in jordan – a retrospective cohort study

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Background: Guillain-Barré syndrome (GBS) is a major cause of acute flaccid paralysis that is encountered in all geographical areas. Very limited data about this syndrome has been reported from the Arab countries. This study is the first one trying to describe the clinical features and management outcomes of GBS in the Jordanian population.

Methods: This retrospective study looks at adult patients admitted to a major tertiary referral hospital in the north of Jordan between 2013 and 2021.

Results: A total of 30 patients met the inclusion/exclusion criteria. Males were predominantly affected (70%) with a male-to-female ratio of 2.33. Acute inflammatory demyelinating polyradiculoneuropathy variant was encountered in 60% of cases, whereas axonal variants, namely, acute motor axonal neuropathy and acute motor axonal and sensory neuropathy variants were seen in about 23% of cases. ICU admission was reported in 37% of patients and 6.7% required mechanical ventilation. Most patients had a favorable outcome with a GBS disability score of three or better at out-patient follow-up visits.

Conclusion: Our cohort of patients showed a significant deviation in disease expression from that reported in other parts of the globe. This deviation was obvious in more prominent male predominance, frequencies of different GBS variants, and more favorable short-term morbidity/mortality outcomes. However, larger multicenter prospective studies are needed for confirmation of these results.

Keywords: Arab countries, epidemiology, Guillain-Barré syndrome, Jordan, variant

Introduction

Guillain-Barré syndrome (GBS) is a major cause of acute flaccid paralysis in most countries worldwide[1,2]. There is some heterogeneity in the clinical presentation in different parts of the world, and the prevalence of different variants of the syndrome is variable[1–3]. For example, acute inflammatory demyelinating polyradiculoneuropathy (AIDP) is the most common form in Europe and North America, whereas acute motor axonal neuropathy (AMAN) and acute motor axonal and sensory neuropathy (AMSAN) are much more common in Asia and South America[1,2]. Describing and characterizing the different phenotypes and outcomes of GBS in variable geographical areas are vital for a better understanding of the disease and its expected presentations. Reliable incidence figures are scarce in many parts of the world due to a lack of studies or case ascertainment, among other factors. Very few epidemiological studies examining GBS have been conducted in the Arab countries over the past few decades, particularly in the adult population[4–10]. A recent meta-analysis concluded that a significant shortage of data about GBS exists in the Arab world[11]. This is the first study to describe the clinical characteristics of GBS among Jordanians.

HIGHLIGHTS

- Our cohort showed few significant deviations from global cohorts.
- There was a higher male-to-female ratio.
- Patients had a more favorable morbidity/mortality outcomes.
- The incidence of main axonal variants was middling compared to global figures.

Methods

We performed a retrospective analysis looking at charts of patients admitted to a major tertiary referral hospital in the north of Jordan between 2013 and early 2021. The facility is one of three major referral hospitals in the north of Jordan, with a total

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Table 1

Cohort's demographics and GBS variants

Variables	Categories	*n* (%)	Male *n* (%)	Female *n* (%)
Age	50 or less	17 (56.7)	12 (70.6)	5 (29.4)
	Above 50	13 (43.3)	9 (69.2)	4 (30.8)
Seasons	Fall/Winter	16 (53.3)	11 (68.8)	5 (31.2)
	Spring/Summer	14 (46.7)	10 (71.4)	4 (28.6)
Triggers	URTI	7 (46.7)	7 (100)	0
	GIT infection	4 (26.7)	3 (75)	1 (25)
	Both URTI and GIT infection	2 (13.3)	1 (50)	1 (50)
	Covid 19	1 (6.7)	0	1 (100)
	Chickenpox	1 (6.7)	0	1 (100)
Duration between preceding infection and onset of GBS symptoms	1–7 days	6 (40)	5 (83.3)	1 (16.7)
	8–14 days	7 (46.7)	5 (71.4)	2 (28.6)
	15–21 days	1 (6.7)	1 (100)	0
	Current infection	1 (6.7)	0	1 (100)
Days from onset of symptoms to admission	1–7 days	19 (63.33)	15 (78.95)	4 (21.05)
	8–14 days	6 (20)	3 (50)	3 (50)
	>14 days	5 (16.67)	3 (60)	2 (40)
GBS variant	AIDP	18 (60)	13 (61.9)	5 (55.6)
	AMAN	5 (16.7)	3 (14.3)	2 (22.2)
	Miller-Fisher	3 (10)	2 (9.5)	1 (11.1)
	Facial Diplegia	1 (3.3)	1 (4.8)	0
	AMSAN	2 (6.7)	2 (9.5)	0
	Pure Sensory	1 (3.3)	0	1 (11.1)

GBS, Guillain–Barré syndrome; GIT, Gastrointestinal tract; URTI, Upper respiratory tract infection.

catchment population of about two million people. We obtained ethical clearance and approval to conduct this study from the Institutional Review Board (IRB) and Human Research Ethics Committee. Patient's consent was not required as we did not collect patient's identifiers in accordance with the Declaration of Helsinki. The study was conducted in compliance with Strengthening The Reporting Of Cohort Studies in Surgery (STROCSS) statement. All patients aged sixteen and above who met the National Institute of Neurological Disorders and Stroke (NINDS) diagnostic criteria for GBS were included[12]. Patients with incomplete data or unsecured diagnoses were excluded. Data related to the cohort's demographics, disease clinical features, results of cerebrospinal fluid (CSF) analysis, findings of nerve conduction studies (NCS), treatment lines, and patients' outcomes were collected. NCS were performed by American Board-certified electromyographers using the parameters of the European Federation of Neurological Societies and the Peripheral Nerve Society (EFNS/PNS) for demyelination. Response to treatment was assessed using the GBS disability scale[13].

Statistical methodology

Descriptive statistics were used to represent and determine the sample patients' characteristics and the distribution of patients' data. Such descriptive statistics, as range, mean, SD, and median were used for continuous variables, and counts, percentages, and cross-tabulation were used for the categorical variables. A visual examination of the data using side-by-side box plots was also considered in the study. Inferential statistics were also used to assess associations and relationships between categorical variables and group comparisons between quantitative variables. The proportions test was used to determine whether there is a difference in the proportions for dichotomous variables. Cramer's V test of association was also used between nominal categorical variables when one or two of these variables have more than two levels. Quantitative data of more than two independent groups were analyzed using the nonparametric Kruskal–Wallis test. *P* values less than 0.05 were considered statistically significant. For the descriptive statistics part we used the available data for the described variables, whereas for inferential statistics we used the complete data for the variables under investigation (complete case analysis). All statistical analyses were performed using the statistical package SPSS 21.0 (SPSS Inc.).

Results

Cohort demographics and GBS variants

A total of 30 patients met the final inclusion criteria. Most cases occurred between 2015 and 2020, with a consistent 4–5 cases encountered per year. Summary statistics for cohort demographics and GBS variants are shown in Table 1. Males constituted 70% of the cohort (21 patients), and females the remaining 30% (9 patients). The mean age of the cohort was 46 years (range 16–70, SD 16.02). The most frequent GBS variant was AIDP (18 patients, 60%), followed by AMAN (5 patients, 16.67%) and Miller-Fisher syndrome (MFS) (3 patients, 10%). Additionally, two patients (6.67%) had AMSAN, while one (3.33%) had a pure sensory presentation, and one (3.33%) had a facial diplegia variant. Overall, no clear seasonal trends were noted since 16 patients (53.33%) were admitted in fall/winter seasons, and 14 patients (46.67%) were admitted in the spring-/summer seasons. Triggers preceding the onset of GBS were reported by fifteen patients (50%). The most common potential trigger was upper respiratory tract infection, which was reported

Table 2
Clinical features of patients

Clinical feature	Number of pts (%)
Lower extremity areflexia	22 (73.3)
Lower extremity weakness	20 (66.7)
Upper extremity weakness	16 (53.3)
Tetraparesis	16 (53.3)
Onset in lower extremity	16 (53.3)
Upper extremity hyporeflexia	14 (46.7)
Sensory deficit	14 (46.6)
Lower extremity hyporeflexia	4 (13.3)
Upper extremity areflexia	4 (13.3)
Ataxia	4 (13.3)
Autonomic features	3 (10)
Facial weakness	2 (6.7)
Ophthalmoplegia	2 (6.7)
Onset in upper extremity	1 (3.3)

by seven patients (23.33%), followed by gastrointestinal infection (four patients, 13.33%). Unfortunately, data regarding the pathogens involved in these potential triggers were not available. Interestingly, one patient who presented with MFS had an asymptomatic coronavirus disease of 2019 infection at the time of presentation. Most of the reported antecedent events (86%) happened less than 2 weeks of symptom onset. The majority of patients were admitted to the hospital within 2 weeks of symptom onset (see Table 1 for full details).

Regarding clinical presentations, sixteen patients (53%) had the onset of symptoms in the lower extremities. Areflexia of the lower extremities was the most common finding on the exam followed by lower extremity weakness (73.3 and 66.7%, respectively). The clinical findings are summarized in Table 2.

Investigations, treatment, and outcomes

Twenty-five patients had documented lumbar puncture results, of whom 22 (88%) had albuminocytologic dissociation, and three had normal CSF protein (Table 3). The mean CSF protein level was 104.2 mg/dl, with the highest levels seen in the AIDP variant (mean of 127.7 mg/dl, and highest level of 530 mg/dl). Twenty-five patients underwent NCS during their illness. These studies showed predominantly axonal changes in eight patients, predominantly demyelinating changes in seven patients, mixed changes in five patients, and normal NCS in four patients. One patient had his study performed at an outside facility, the results of which were unavailable (clinically diagnosed with an AIDP variant). In terms of hospital course, 11 patients (36.67%) were admitted to the ICU, and two patients (6.67%) were intubated. The total length of hospital stay was distributed as follows; 1–7 days (13 patients, 43.33%), 8–14 days (13 patients, 43.33%), more than 14 days (4 patients, 13.3%). The mean length of hospitalization was 9.25 days (SD 5.95). Intravenous immunoglobulin was the most frequently used treatment (28 patients, 93.32%), whereas one patient (3.33%) had plasma exchange, and one (3.33%) was observed clinically.

Treatment outcomes using the GBS disability scale were documented for all patients at hospital discharge and for 25 patients (83.33%) who presented for follow-up visits at variable intervals after discharge (mean duration between discharge and follow-up was 34.84 days 'SD 32.14'). These outcomes are

Table 3
Investigations, treatment, and outcome measures

Variables	Categories	*n* (%)
CSF protein (mg/dl)	45 and less	3 (12)
	More than 45	22 (88)
CSF WBC	0–5	23 (92)
	10	2 (8)
NCS	Predominantly Axonal	9 (36)
	Predominantly Demyelinating	7 (28)
	Mixed	5 (20)
	Normal	4 (16)
Treatment	IVIG	28 (93.3)
	Plasma exchange	1 (3.3)
	Observation	1 (3.3)
Length of hospital stay	1–7 days	13 (43.3)
	8–14 days	13 (43.3)
	>14 days	4 (13.3)
ICU admission	Yes	11 (36.7)
	No	19 (63.3)
Intubation	Yes	2 (6.7)
	No	28 (93.3)
Outcome at discharge (GBS disability score)	0 Healthy	0
	1 Minor symptoms and signs, able to run	5 (16.7)
	2 Able to walk 5 meters independently	4 (13.3)
	3 Able to walk 5 meters with a walker or support	7 (23.3)
	4 Bed or chair bound	14 (46.7)
	5 Requiring assisted ventilation for at least part of the day	0
	6 Death	0
Outcome on follow-up (GBS disability score)	0 Healthy	5 (20)
	1 Minor symptoms and signs, able to run	7 (28)
	2 Able to walk 5 meters independently	4 (16)
	3 Able to walk 5 meters with a walker or support	6 (24)
	4 Bed or chair bound	3 (12)
	5 Requiring assisted ventilation for at least part of the day	0
	6 Death	0
The interval between discharge and follow-up	3–29 days	15 (60)
	30 or more days	10 (40)

presented in Table 3. At the time of discharge, none of the patients had a GBS disability score of zero but 16 patients (53.33%) had a score of three or less. Nonetheless, at follow-up visits, the number of patients achieving these scores rose to five (16.66%) and 22 (73.33%), respectively. Unfortunately, five patients did not have follow-up data. This potentially makes follow-up scores an underrepresentation of the real ones as the missing patients may have improved with time.

GBS variants and some related attributes

The results of contingency tables for GBS variants versus gender and season are shown in Table 4. Using Cramer's V test, a significant association was detected between the three most common GBS variants (AIDP, AMAN, and Miller-Fisher) and the season (fall/winter and spring/summer) (P-value = 0.033). Two-thirds of

Table 4

Association between the most common GBS variants versus sex and season

	GBS variants			
Attribute	**AIDP *n***	**AMAN *n***	**Miller-fisher *n***	***P***
Sex				
Male	13 (72.22%) (72.22%)	3 (16.67%) (60%)	2 (11.11%) (66.67%)	0.867
Female	5 (62.5%) (27.78%)	2 (25%) (40%)	1 (12.5%) (33.33%)	
P-Value	**0.048**	0.500	0.500	
Season				
Fall/Winter	12 (93.31%) (66.67%)	1 (7.69%) (20%)	— —	**0.033**
Spring/Summer	6 (46.15%) (33.33%)	4 (30.77%) (80%)	3 (23.08%) —	
P-Value	0.119	0.187	—	

bold values are significant *P*-values.

the AIDP cases occurred in the fall/winter seasons, while 80% of AMAN and all MFS cases occurred in the spring/summer seasons. No significant association was found between the three most common GBS variants and gender (*P*-value = 0.867). The most common variant of GBS for both males and females was the AIDP variant. However, there was a significant difference in the proportion of male cases (72.22%) relative to female cases (27.78%) for this variant compared to the proportions in other variants (*P*-value = 0.048).

NCS outcome and age of onset

A side-by-side boxplot of the age of onset for NCS outcome is shown in Figure 1, which shows a remarkable difference between the box plots for the four NCS outcome categories in a slightly nonoverlapping pattern. A Kruskal–Wallis H test showed that there was a statistically significant difference in the age of onset between the different NCS categories (H = 10.39, *P*-value = 0.016), with a mean rank age of onset of 12.2 for axonal, 7.3 for demyelinating, 20.9 for mixed and 15 for normal. The highest age of onset was found among mixed cases, while the smallest was found among axonal cases (see Table 5 for full details).

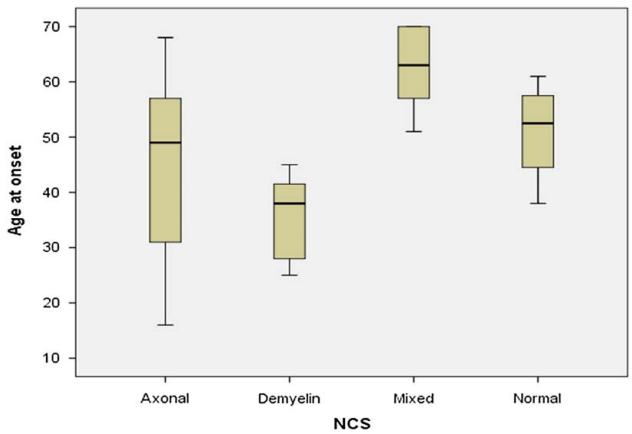

Figure 1. Side-by-side boxplot of age at onset for NCS outcome.

Table 5

Summary statistics for the age of onset of NCS outcome

NCS	*n*	Minimum	Maximum	Mean (SD)	Median	Average rank
Axonal	9	16	68	49 (18.356)	49	12.2
Demyelinating	7	25	45	38 (8.281)	38	7.3
Mixed	5	51	70	63 (8.289)	63	20.9
Normal	4	38	61	52.5 (9.626)	52	15
Total	25	16	70	47 (16.022)	47	13

Discussion

This is the first study examining the clinical features and outcomes of GBS in the Jordanian population. The syndrome is primarily a monophasic illness that is believed to be caused by an autoimmune process targeting peripheral nerves[14]. Different variants of the disease exist with variable frequencies in different geographical areas[1].

In this study, we performed a retrospective chart review of patients diagnosed with GBS between 2013 and early 2021 at a major tertiary referral center in the north of Jordan. Seventy percent of the patients were males, resulting in a male-to-female ratio of 2.33, which is higher than reported in the west and many Arab countries[1,6,8,11]. A very recent multicenter study from neighboring Saudi Arabia that included 156 patients with GBS reported a male-to-female ratio of 1.6:1[9]. However, higher ratios have also been reported in a few other studies from Saudi Arabia, Iraq, and Kuwait[4,5,10]. In our cohort, the AIDP variant affected 60% of cases, whereas the main axonal variants (AMAN and AMSAN) were seen in about 23% of cases. Thus, the frequency of axonal variants in our population is higher than that encountered in the western world, which is about 5%, yet not as frequent as being reported in the far east, central, and south America, where it ranges from 30–47%[2]. The predominant finding on the exam was lower extremity areflexia followed by lower extremity weakness seen in 73.3 and 66.7%, respectively, which is in harmony with figures from other studies globally[1]. In our cohort, most patients (88%) who underwent CSF examination had albuminocytologic dissociation, which represents a higher percentage than that reported in cohorts elsewhere[1,9,15]. However, this higher percentage may be related to differences in the timing of CSF examination relative to disease onset among different cohorts.

Most patients were treated with intravenous immunoglobulin, which seems to be the most widely used therapy worldwide[1]. About 37% (11/30) of patients were admitted to the ICU, of which two patients underwent intubation. This represents an intubation percentage of 6.67compared to 26.3% reported in a recent study from Saudi Arabia[9]. No mortalities were reported in our cohort. The low number of cases requiring intubation and the lack of mortalities represent a better morbidity/mortality outcome, which may be related to earlier treatment initiation and/or less severe disease course in our population. The GBS disability score at hospital discharge was three or less in 53% of all patients. This percentage increased to 73% for the 25 patients who presented at follow-up. Five patients had missing follow-up data, and follow-up periods were not standardized. However, looking back at these five patients, we noticed that four of them had a score of three or less at hospital discharge, to begin with

(two patients had a score of 1, and two patients had a score of 3). Therefore, adding these patients, as they are very unlikely to worsen after discharge, it is reasonable to conclude that the actual percentage of patients with a disability score of three or less at follow-up approaches 86.6% (26/30). This outcome score is significantly better than that reported elsewhere[1].

This study has a few limitations; it is a retrospective analysis, which restricts control over variables and the accuracy of the data included, it has a small number of patients that limits the ability to make generalizations, not all patients underwent all investigations and not all of them had an out-patient follow-up. Moreover, long-term outcomes are not available. Several patients were excluded due to not meeting the National Institute of Neurological Disorders and Stroke diagnostic criteria or due to incomplete data (for example, two patients were discharged after one day of admission; one was against medical advice, and another was due to insurance reasons).

Conclusion

Our cohort of patients showed some significant deviation in disease expression from that reported in other parts of the globe. This deviation was obvious in the prominent male predominance, frequencies of different GBS variants, and more favorable acute morbidity/mortality outcomes. However, it is not clear whether this represents a milder disease course in our population or a study limitation effect, as many other factors can be responsible for this discrepancy. Larger prospective studies are needed to better characterize the disease's clinical spectrum, which should help better understand the overall picture.

Ethical approval

We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines. The study was approved by the Institutional Review Board (IRB) of Jordan University of Science and Technology and by the Human Research Ethics Committee of King Abdullah University Hospital and conformed to the Declaration of Helsinki.

Consent

NA (not required; no patient's identifiers collected).

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None.

Author contribution

K.A.-H.: (corresponding author) conceptualization, data curation, formal analysis, writing – review and editing; S.A.: data curation, writing – review and editing; M.M.S.: data curation, formal analysis, software validation, writing – review and editing; A.Y.: conceptualization, writing – review and editing; B.A.: conceptualization, writing – review and editing; M.A.Q.: conceptualization, writing – review and editing; R.K.: writing – review and editing; S.E.: formal analysis; K.E.-S.: conceptualization, writing – review and editing.

Conflict of interest disclosure

None of the authors have any conflict of interest or financial disclosures related to this study.

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Data sharing is not applicable to this article.

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