The Canadian Journal of Neurological Sciences (2023), **50**, 221–227
doi:10.1017/cjn.2022.19

Canadian Journal of Neurological Sciences
Journal Canadien des Sciences Neurologiques

Original Article

Predictors of Mechanical Ventilation in Guillain–Barré Syndrome with Axonal Subtypes

Anaclara Michel-Chávez[1], Erwin Chiquete[1], Alfonso Gulías-Herrero[2], Diego Luis Carrillo-Pérez[2,3], Antonio Olivas-Martínez[2], Julio Macías-Gallardo[4], José de Jesús Aceves-Buendía[1], Eduardo Ruiz-Ruiz[1], Tatiana Bliskunova[1], Jennefer Portillo-Valle[1], Rafael Cobilt-Catana[1], Jorge Alberto Ortiz-Quezada[1], Salvador Durán-Coyote[1], Elizabeth Rodríguez-Perea[1], Emmanuel Aguilar-Salas[1], Carlos Cantú-Brito[1], Guillermo García-Ramos[1] and Bruno Estañol[1,4]

[1]Department of Neurology and Psychiatry, Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Mexico City, Mexico, [2]Department of Internal Medicine, Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Mexico City, Mexico, [3]Tecnologico de Monterrey, Escuela de Medicina y Ciencias de la Salud, Monterrey, Nuevo León, Mexico and [4]Laboratory of Clinical Neurophysiology, Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Mexico City, Mexico

ABSTRACT: ***Background:*** The early clinical predictors of respiratory failure in Latin Americans with Guillain–Barré syndrome (GBS) have scarcely been studied. This is of particular importance since Latin America has a high frequency of axonal GBS variants that may imply a worse prognosis. ***Methods:*** We studied 86 Mexican patients with GBS admitted to the *Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán*, a referral center of Mexico City, to describe predictors of invasive mechanical ventilation (IMV). ***Results:*** The median age was 40 years (interquartile range: 26–53.5), with 60.5% men (male-to-female ratio: 1.53). Most patients (65%) had an infectious antecedent (40.6% gastrointestinal). At admission, 38% of patients had a Medical Research Council (MRC) sum score <30. Axonal subtypes predominated (60.5%), with acute motor axonal neuropathy being the most prevalent (34.9%), followed by acute inflammatory demyelinating polyneuropathy (32.6%), acute motor sensory axonal neuropathy (AMSAN) (25.6%), and Fisher syndrome (7%). Notably, 15.1% had onset in upper limbs, 75.6% dysautonomia, and 73.3% pain. In all, 86% received either IVIg (9.3%) or plasma exchange (74.4%). IMV was required in 39.5% patients (72.7% in AMSAN). A multivariate model without including published prognostic scores yielded the time since onset to admission <15 days, axonal variants, MRC sum score <30, and bulbar weakness as independent predictors of IMV. The model including grading scales yielded lower limbs onset, Erasmus GBS respiratory insufficiency score (EGRIS) >4, and dysautonomia as predictors. ***Conclusion:*** These results suggest that EGRIS is a good prognosticator of IMV in GBS patients with a predominance of axonal electrophysiological subtypes, but other early clinical data should also be considered.

RÉSUMÉ : ***Facteurs prédictifs du recours à la ventilation mécanique dans des cas de syndrome de Guillain-Barré avec variants axonaux*** ***Contexte :*** Les facteurs prédictifs cliniques précoces de l'insuffisance respiratoire chez des patients latino-américains atteints du syndrome de Guillain-Barré (SGB) ont rarement été étudiés. Cela revêt pourtant une importance particulière dans la mesure où les populations latino-américaines présentent une fréquence élevée de variants axonaux du SGB qui peuvent sous-tendre un pronostic davantage défavorable. ***Méthodes :*** Nous nous sommes penchés sur 86 patients d'origine mexicaine atteints du SGB et admis à l'*Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán*, un centre médical spécialisé de la ville de Mexico, afin de décrire les facteurs prédictifs du recours à la ventilation mécanique invasive (VMI). ***Résultats :*** L'âge médian de ces patients était de 40 ans (EI : 26 – 53,5), 60,5 % d'entre eux étant des hommes (rapport hommes-femmes : 1,53). La plupart des patients, soit 65 %, donnaient à voir des antécédents de maladie infectieuse (40,6 % de nature gastro-intestinale). Au moment de leur admission, 38 % des patients avaient un score total au *Medical Research Council* (MRC) inférieur à 30. Les variants axonaux se sont avérés prédominants (60,5 %), celui de type NAMA (neuropathie axonale motrice aiguë) étant le plus courant (34,9 %). Il était suivi du type PIDA (polyneuropathie inflammatoire démyélinisante aiguë, 32,6 %), du type NAASM (neuropathie axonale aiguë sensitivomotrice, 25,6 %) et du syndrome de Fisher (7 %). De façon notable, 15,1 % des patients ont montré leurs premiers symptômes dans leurs membres supérieursÂ ; 75,6% d'entre eux des symptômes de dysautonomie et 73,3 % de la douleur. En tout, 86 % des patients ont bénéficié soit d'un traitement par immunoglobulines (IgIV 9,3 %) ou d'un échange plasmatique (EP 74,4 %). La VMI a été nécessaire chez 39,5 % des patients (72,7 % pour le variant NAASM). Un modèle multivarié n'incluant pas les scores pronostiques publiés a révélé que le temps écoulé depuis l'apparition des premiers symptômes jusqu'à l'admission (< 15 jours), les variants axonaux, le score total au MRC (< 30) et la faiblesse bulbaire étaient les facteurs prédictifs indépendants du recours à la VMI. Un modèle incluant des échelles de

Corresponding author: Erwin Chiquete, MD, PhD, Department of Neurology and Psychiatry, Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, 15 Vasco DE Quiroga, Mexico City, CDMX 14050, Mexico. Email: erwin.chiquetea@incmnsz.mx

Cite this article: Michel-Chávez A, Chiquete E, Gulías-Herrero A, Carrillo-Pérez DL, Olivas-Martínez A, Macías-Gallardo J, Aceves-Buendía JdJ, Ruiz-Ruiz E, Bliskunova T, Portillo-Valle J, Cobilt-Catana R, Ortiz-Quezada JA, Durán-Coyote S, Rodríguez-Perea E, Aguilar-Salas E, Cantú-Brito C, García-Ramos G, and Estañol B. (2023) Predictors of Mechanical Ventilation in Guillain–Barré Syndrome with Axonal Subtypes. *The Canadian Journal of Neurological Sciences* **50**: 221–227, https://doi.org/10.1017/cjn.2022.19

gradation a révélé comme facteurs prédictifs l'apparition de symptômes affectant les membres inférieurs, un score au *Erasmus GBS respiratory insufficiency* (ou «Â EGRISÂ ») supérieur à 4 ainsi que la dysautonomie. ***Conclusion :*** Ces résultats suggèrent en somme que l'EGRIS est un bon outil pronostique de la VMI chez les patients atteints de SGB pour qui on note une prédominance des variants électro-physiologiques axonaux. Cela dit, d'autres données cliniques obtenues à un stade précoce doivent également être prises en compte.

Keywords: Axonal; Guillain–Barré syndrome; Polyradiculoneuropathy; Predictors

(Received 15 November 2021; final revisions submitted 9 February 2022; date of acceptance 12 February 2022; First Published online 22 February 2022)

Introduction

Guillain–Barré syndrome (GBS) is the most frequent acute polyradiculoneuropathy and the first cause of acute flaccid paralysis worldwide.[1–4] It is characterized by varying degrees of limb and cranial nerve-innervated muscles weakness associated with decreased or absent muscle reflexes. Sensory and autonomic symptoms can also be present.[5,6] Incidence varies from 0.62 to 2.66 per 100,000 person-years, depending on the population and age group.[7] A 70% of all GBS cases have the antecedent of systemic infections, such as respiratory and gastrointestinal infections.[8–15]

The GBS neurophysiological spectrum includes acute inflammatory demyelinating polyneuropathy (AIDP), acute motor axonal neuropathy (AMAN), and acute motor sensory axonal neuropathy (AMSAN).[16,17] A less frequent variant is the Fisher syndrome (also known as the Miller Fisher syndrome) that is characterized by ataxia, areflexia, and ophthalmoplegia.[18]

The in-hospital case fatality rate (CFR) of GBS varies from 1.61% to 15%.[8–15,19,20,21] In Mexico the in-hospital GBS-associated CFR is nowadays deemed high.[8] The unpredictable clinical evolution and potential life-threatening complications often require admission to the intensive care unit. Respiratory failure requiring invasive mechanical ventilation (IMV) is a common ominous short-term complication with a reported incidence of about 20–35%.[16,22–27] Early prediction of IMV is important to enable clinicians tailoring supportive care and individualized treatment. To our knowledge, there is no published study dedicated to determining the predictors of IMV in a Latin American population.[28]

Methods

Patients and Study Design

The Research Ethics Committee approved this retrospective observational study. Signed informed consent was obtained from the patients upon hospitalization. We retrospectively reviewed all the existing medical records and neurophysiologic studies of adult patients admitted with a GBS diagnosis according to Asbury and Cornblath's diagnostic criteria[29] between January 1999 and March 2020 at the *Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán*, a tertiary referral hospital in Mexico City. Patients with other specific types of acute or chronic polyneuropathy (i.e., diabetic neuropathy, neuropathies associated with drugs or industrial substances, poliomyelitis, polyneuropathy associated with HIV infection, porphyria, and other), and without electrodiagnostic procedures performed or available were excluded. We also excluded cases with equivocal neurophysiological classification of GBS subtypes for whom no serial tests were performed to attain final subtyping. This was of particular importance given that one of the main interests of this study was to assess whether the axonal variants enable a poor short-term respiratory failure prognosis. Members of the Department of Neurology examined every patient and ascertained diagnosis. Electrophysiological diagnostic criteria were met in all cases.[16,29]

Data Collection

We collected information derived upon hospital arrival of GBS patients, as well as the clinical and paraclinical information that was obtained first in the following days after hospital arrival. Demographic and clinical features analyzed were age, sex, history of antecedent infections (e.g., upper respiratory tract infection and gastrointestinal infection), time from motor symptom onset to admission (the onset of GBS was defined as the occurrence of motor symptoms), onset of limb weakness, clinical severity assessed by the GBS disability score (scale ranging from 0 to 6, where 0 = healthy state and 6 = death),[30] the modified Erasmus GBS outcome score (mEGOS, scale ranging from 0 to 9, with higher scores meaning a worse functional prognosis) at hospital admission,[31] Erasmus GBS respiratory insufficiency score (EGRIS, scale ranging from 0 to 7, with higher scores meaning a worse respiratory failure prognosis),[32] Medical Research Council (MRC) sum score (scale ranging from 0 to 60, where 0 = tetraplegia and 60 = normal strength), presence of hyporeflexia or areflexia, cranial nerves involvement, inability to lift the head and/or bulbar dysfunction, sensitive symptoms such as neuropathic pain or paresthesias, autonomic dysfunction (fluctuating blood pressure, spontaneous severe bradycardia or spontaneous tachycardia), presence of protein-cytologic dissociation in cerebrospinal fluid (CSF) (defined as elevated protein in CSF without abnormal leukocytes count), total number of days for which ventilation support was needed, and hospital stay in days and outcome. Electrophysiological information was classified according to definitions of Hadden et al. as primary demyelinating, primary axonal, or equivocal.[16] Respiratory failure was defined as a need for IMV within the first 30 days of admission. We also registered for analysis the treatment with intravenous immunoglobulin (IVIg), plasma exchange (PLEX), or supportive management.

Statistical Analysis

Categorical data are presented as relative frequencies in the form of proportions, while continuous data are presented as means with standard deviations (SD) or medians with their respective interquartile ranges (IQR), depending on the distribution. The Kolmogorov–Smirnov test was performed to assess the equality of continuous probability distributions. Pearson chi-square or Fisher exact tests are used to compare proportions in nominal variables. To compare the distribution of quantitative variables between two groups, Student *t* test or Mann–Whitney *U* test was performed in parametric and non-parametric variables, respectively. To find independent predictors of respiratory failure with need for IMV, multivariate analyses were constructed using the forward stepwise logistic regression models. A selection step

https://doi.org/10.1017/cjn.2022.19 Published online by Cambridge University Press

Table 1: Characteristics of the population hospitalized with Guillain–Barré syndrome

Characteristics	All patients ($n = 86$)	Men ($n = 52$)	Women ($n = 34$)	p value
Age, median (IQR), years	40 (26–53.5)	40 (23–52)	40 (27.7–60)	0.754
History of infection, *n* (%)	53 (61.6)	34 (65.4)	19 (55.9)	0.376
Upper respiratory infection	23 (26.7)	17 (32.7)	6 (17.6)	0.123
Gastrointestinal infection	27 (31.4)	17 (32.7)	10 (29.4)	0.749
Onset of weakness, *n* (%)				
Lower limbs	13 (15.1)	5 (9.6)	8 (23.5)	0.078
Upper limbs	66 (76.7)	42 (80.8)	24 (70.6)	0.275
MRC sum score at admission, median (IQR)	33 (12–42)	36 (13–48)	30 (12–42)	0.015
mEGOS score at admission, median (IQR)	6 (3–7)	4 (3–7)	6 (3–7)	0.510
EGRIS score at admission, median (IQR)	4 (3–5)	3.5 (2–5)	4 (3–5)	0.092
GBS disability score at admission, median (IQR)	4 (4–5)	4 (4–5)	4 (4–5)	0.945
Time from onset to admission, median (IQR), days	5.5 (2–9.25)	6 (3–7.5)	4 (2–14.75)	0.508
Clinical features, *n* (%)				
Paresthesias	42 (48.8)	27 (51.9)	15 (44.1)	0.479
Pain	63 (73.3)	38 (73.1)	25 (73.5)	0.963
Autonomic dysfunction	65 (75.6)	37 (71.2)	28 (82.4)	0.237
Any cranial nerves involved	27 (31.4)	18 (34.6)	9 (26.5)	0.426
Facial palsy	18 (20.9)	12 (23.1)	6 (17.6)	0.545
Bulbar weakness	12 (14.0)	5 (9.6)	7 (20.6)	0.151
CSF protein-cytologic dissociation, *n* (%)	61 (72.6)	39 (76.5)	22 (66.7)	0.039
Neurophysiological subtype *n* (%)				
Axonal subtypes	52 (60.5)	28 (53.8)	24 (70.6)	0.121
AMAN	30 (34.9)	18 (34.6)	12 (35.3)	0.949
AMSAN	22 (25.6)	10 (19.2)	12 (35.3)	0.095
AIDP	28 (32.6)	20 (38.5)	8 (23.5)	0.149
Miller Fisher	6 (7.0)	4 (7.7)	2 (5.9)	0.747
IMV, *n* (%)	34 (39.5)	20 (38.5)	14 (41.2)	0,801
ICU stay, median (IQR), days	4.5 (0–46)	4.5 (0–44.5)	4.5 (0–51.75)	0.825
Hospital stay, median (IQR), days	20.5 (13–53.5)	20 (12.5–49)	21.5 (13–63.5)	0.824
In-hospital case fatality rate, *n* (%)	12 (14)	6 (11.5)	6 (17.6)	0.424

AIDP = acute inflammatory demyelinating polyneuropathy; AMAN = acute motor axonal neuropathy; AMSAN = acute motor sensory axonal neuropathy; CSF = cerebrospinal fluid; EGRIS = Erasmus GBS respiratory insufficiency score; IMV = invasive mechanical ventilation; ICU = intensive care unit; IQR = interquartile range; mEGOS = modified Erasmus Guillain–Barré syndrome outcome score; MRC = Medical Research Council.

process was performed with a p set at <0.1 in bivariate analyses. Adjusted odds ratios (OR) with 95% CIs are provided. We calculated corrected OR to approximate to the actual relative risks, with the equation proposed by Zhang and Yu[33] as follows: Corrected OR = Multivariate OR/[(1 − Incidence of the outcome in the non-exposed group) + (Incidence of the outcome in the nonexposed group * multivariate OR)]. The fitness of the model was assessed with the Hosmer–Lemeshow goodness-of-fit test, which was considered as reliable if $p > 0.2$. All p values are calculated two-sided and considered significant when $p < 0.05$. SPSS version 24.0 for iOS (IBM Inc., USA) was used for all calculations.

Results

After excluding cases with no neurophysiological tests performed or available ($n = 4$), patients with equivocal neurophysiological classification ($n = 7$), or incomplete clinical information ($n = 3$), a total of 86 adult patients were analyzed (Table 1). The mean age at diagnosis was 42.5 ± 19.8 years (median: 40, IQR: 26–53.5 years), with a male preponderance (60.5%, male-to-female ratio: 1.53). Most patients (65%) had a clear infectious antecedent preceding the onset of the weakness within the last 2 weeks, being the most frequent a gastrointestinal infection (34% of the total or 40.6% among patients with preceding infection).

At admission, 38% of patients had a MRC sum score <30 (32.7% vs. 47.1%, in men and women, respectively $p = 0.180$), with a higher median score among women, compared with men. GBS disability score >3 at hospital arrival occurred in 77.9% of patients, with mEGOS >6 in 62.8%, EGRIS >4 in 34.9%, and a MRC sum score <30 in 38.4%. The median (IQR) time elapsed since symptoms onset to hospital admission was 5.5 (2–9.5) days, from onset to CSF analysis 7 (5–12) days, and from onset to

https://doi.org/10.1017/cjn.2022.19 Published online by Cambridge University Press

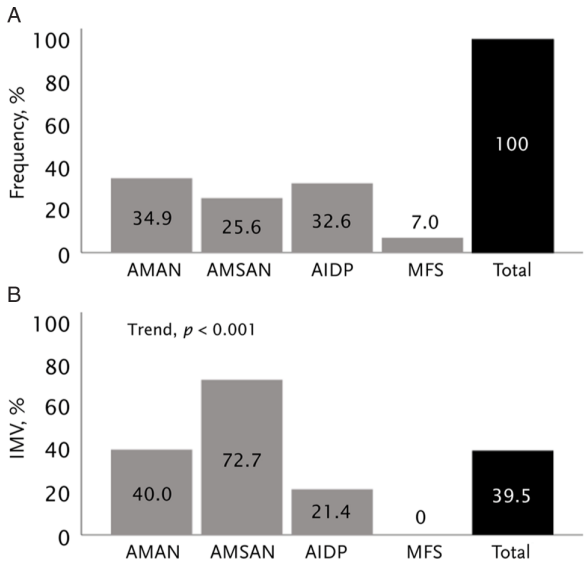

Figure 1: Relative frequency of electrophysiological subtypes among the 86 patients with Guillain–Barré syndrome (A). Rate of invasive mechanical ventilation according to electrophysiological subtypes (B). AIDP = acute inflammatory demyelinating polyneuropathy; AMAN = acute motor axonal neuropathy; AMSAN = acute motor sensory axonal neuropathy; MFS = Miller Fisher syndrome.

neurophysiological assessment 12 (7–12) days. There was a predominance (60.5%) of axonal GBS subtypes (i.e., AMAN/AMSAN), with AMAN being the most prevalent (34.9%). Notably, 15.1% of patients had a GBS onset in upper limbs. There was also a high frequency of dysautonomia (75.6%) and pain (73.3%).

In all, 74 (86%) received either IVIg (9.3%) or PLEX (74.4%). The median (IQR) time from onset to treatment was 11 (6–14) days. A total of 34 (39.5%) patients developed respiratory failure and received IMV, with a median (IQR) duration of 48.5 (31.75–89) days. Even when AMAN was the most frequent GBS variant, patients with AMSAN had the highest relative frequency of IMV (Figure 1).

The median (IQR) total hospital stay was 20.5 (13–53.5) days, with an in-hospital CFR of 14% ($n = 12$), 9.3% of these deaths due to sepsis or septic shock. In bivariate analyses to select potential variables associated with the occurrence of respiratory failure and the need for IMV, MRC sum score, mEGOS, EGRIS, GBS disability score, onset of weakness, dysautonomia, bulbar weakness, and axonal GBS variants were factors potentially associated (Table 2). Two distinctive multivariable models were constructed to find independent predictors for IMV, one without considering mEGOS, EGRIS, or the GBS disability score, and the other entering these prognostic systems (Figure 2). The model without published scores yielded the time since GBS clinical features onset to hospital admission <15 days, axonal GBS variants, MRC sum score <30, and bulbar weakness. The second model including grading scales yielded the onset in lower limbs, EGRIS >4, and autonomic dysfunction as independent predictors for respiratory failure.

Table 2: Differences between patients with or without invasive mechanical ventilation (IMV)

Variables	Without IMV ($n = 52$)	With IMV ($n = 34$)	p value
Male sex, *n* (%)	32 (61.5)	20 (58.8)	0.801
Age, median (IQR), years	39 (27.25–52)	41.4 (25.5–59)	0.312
Age >40 years, *n* (%)	25 (48.1)	19 (55.9)	0.479
MRC sum score at admission, median (IQR)	39 (25.5–48)	21 (12–36)	0.004
MRC sum score at admission < 30, *n* (%)	13 (25)	20 (58.8)	0.002
mEGOS score at admission, median (IQR)	5.5 (4–9.75)	9.5 (7.5–10)	0.032
mEGOS score >4, *n* (%)	22 (42.3)	28 (82.4)	<0.001
EGRIS score at admission, median (IQR)	3 (2–4)	5 (4–6)	<0.001
EGRIS score >4, *n* (%)	6 (11.5)	24 (79.6)	<0.001
GBS disability score at admission, median (IQR)	4 (3–4)	5 (5–5)	<0.001
GBS disability score at admission >3, *n* (%)	34 (65.4)	33 (97.1)	0.001
GBS disability score at 30 days, median (IQR)	1 (0.25–3)	3 (2–4)	<0.001
GBS disability score at 30 days >3, *n* (%)	9 (17.3)	15 (44.1)	0.007
History of infection, *n* (%)	37 (71.2)	16 (47.1)	0.025
Onset of weakness in upper limbs, *n* (%)	11 (21.2)	2 (5.9)	0.053
Onset of weakness in lower limbs, *n* (%)	34 (65.4)	32 (94.1)	0.002
Onset to admission <15 days, *n* (%)	40 (76.9)	31 (91.2)	0.089
Clinical features, *n* (%)			
Paresthesias	23 (44.2)	21 61.8)	0.112
Pain	17 (32.7)	6 (17.6)	0.123
Autonomic dysfunction	7 (13.5)	14 (41.2)	0.003
Any cranial nerves involved	13 (25)	14 (41.2)	0.114
Facial palsy	9 (17.3)	25 (26.5)	0.307
Bulbar weakness	1 (1.9)	11 (32.4)	<0.001
CSF protein-cytologic dissociation, *n* (%)	41 (78.8)	14 (58.8)	0.046
Axonal subtypes, *n* (%)	24 (46.2)	28 (82.4)	0.001
Hospital stay, median (IQR), days	14 (10–20)	65 (45.25–117)	<0.001
In-hospital case fatality rate, *n* (%)	5 (9.6)	7 (20.6)	0.151

CSF = cerebrospinal fluid; EGRIS = Erasmus GBS respiratory insufficiency score; IMV = invasive mechanical ventilation; ICU = intensive care unit; IQR = interquartile range; mEGOS = modified Erasmus Guillain–Barré syndrome outcome score; MRC = Medical Research Council.

Discussion

In this data set with a predominance of axonal GBS electrophysiological subtypes, EGRIS was a relevant clinical tool to predict the need for IMV, irrespective of IVIg or PLEX treatments. Most published papers regarding diagnosis, prognosis, and treatment of patients with GBS derive from either exclusive or predominant cohorts with AIDP,[2,16,30–32] which might be a limitation when extrapolating results in Asian or Latin American populations regarding treatment response and outcomes.[9–15,34–36] Therefore, there is an urgent need to study whether treatment responses and outcomes apply in the same way as it has been described in patients with the classical AIDP. In our present report, we

https://doi.org/10.1017/cjn.2022.19 Published online by Cambridge University Press

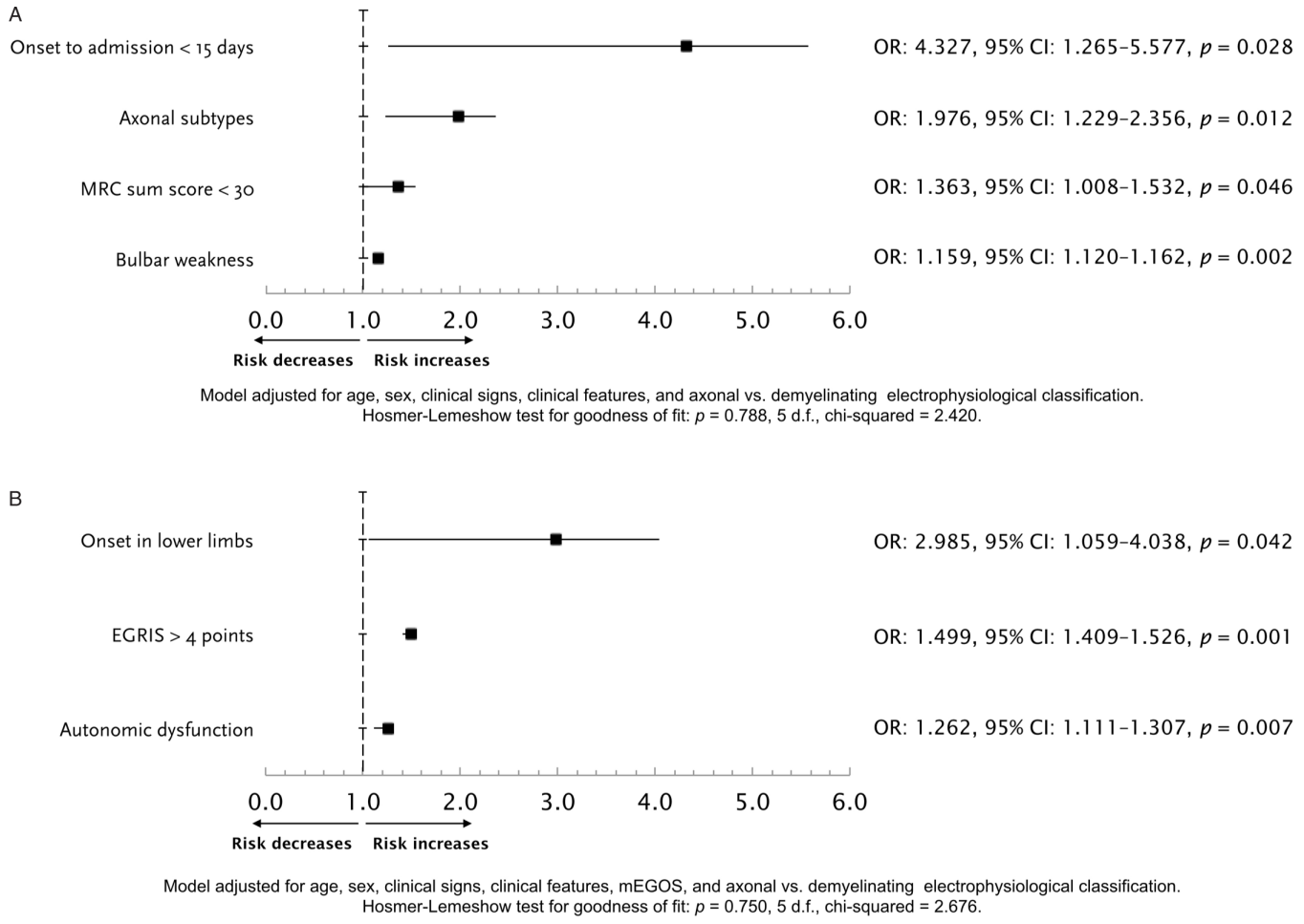

Figure 2: Logistic regression model for the prediction of respiratory failure, without including mEGOS or EGRIS as potential independent variables (A). Logistic regression model for the prediction of respiratory failure, including mEGOS or EGRIS as predictors (B). EGRIS = Erasmus GBS respiratory insufficiency score; MRC = Medical Research Council.

demonstrate that the clinical presentation is of utmost importance when classifying the risk of respiratory failure in GBS patients with a high frequency of AMAN and AMSAN variants. When analyzing the predictors with separate variables without including EGRIS, mEGOS, and GBS disability score at hospital admission, clinical information that can be obtained upon Emergency Department arrival (i.e., days elapsed from onset to admission, strength assessment, and bulbar weakness), and electrophysiological data (i.e., axonal variants), conform a set of early predictors of the need for IMV. When predicting scores were included in the model, EGRIS emerged as predictor, but other characteristics such as autonomic dysfunction and onset of weakness were also important. The fact that muscle strength, time from onset to admission, and bulbar weakness disappeared in the second model is predictable since these are variables included in EGRIS, but the disappearing of AMAN/AMSAN as prognosticator may be due to the relative power of a composite variable (i.e., EGRIS) that may also reflect the phenomenology of the axonal loss, such as skeletal muscle and bulbar weakness. It is also noticeable the high frequency of dysautonomia, taking into account the high frequency of axonal variants, since autonomic dysfunction has been considered more prevalent in AIDP.[3] This has also been challenged in a recent Mexican study.[10] This might also contribute to the high CFR observed in this study, together with the high proportion of AMAN/AMSAN and a high latency since symptoms onset to advanced medical care. During the study time, no differences were found with respect to CFR, and thus, no plausible effect on changes in access to technology or the quality of care can be addressed.

Respiratory failure of neuromuscular origin and access to immunotherapy is one of the major predictors influencing morbidity and mortality,[1,2,37,38] although GBS can also be self-limiting and the majority of patients recover completely. However, respiratory failure requiring IMV is a serious complication of GBS with an incidence of 14.8–50.9%.[26,39] The incidence of respiratory failure requiring IMV in our study was roughly 40%, similar with the incidence reported in India.[40] In North America and Europe, < 10% of patients have axonal subtypes of GBS,[16] which contrasts with the present relative frequency of 60% of the cases. This frequency appears to be more comparable to what was observed in non-Western populations such as Central and South America, and Asian countries, in that axonal subtypes account for 30–56% of cases.[9–15,34–36]

Despite not being an independent predictor when including in the multivariate model to published grading scales, the axonal variants had more cases of respiratory failure than the classical GBS, AIDP. This finding contrasts with other reports that patients with AIDP needed IMV significantly more frequently than those without AMAN/AMSAN.[41] Similar to ours, a retrospective study in a tertiary care center in Pakistan found that patients with the axonal variant had

https://doi.org/10.1017/cjn.2022.19 Published online by Cambridge University Press

significantly more strength impairment at hospital presentation, with the lowest scores for arm and leg strength at presentation, compared with AIDP.[16] This was also reported in a recent Mexican report.[10]

Our study confirms others' findings that respiratory failure in GBS is associated with shorter time from onset to admission.[22,23,32,39] This independent factor, included in EGRIS, may be directly linked to the requirement for IMV due to a rapid clinical worsening. Other clinical presentations have been identified as predictors for IMV in other studies. These include facial palsy[22,23] and simultaneous onset of motor weakness in the four limbs as the initial symptom. Successful management of GBS mandates anticipation of respiratory failure and timely intervention to reduce the risk of complications while improving the patients' outcome.

This study has limitations, such as being a retrospective analysis of a relatively small number of patients, as well as the fact that it was performed in a single referral medical center, which partly limits the generalization of the study results. Also, in our study no data were available on the inability to lift the head,[12] decreased vital capacity,[12,22] abnormalities in diaphragmatic needle electromyography,[40] and recent cytomegalovirus infection,[41] all previously reported to be predictors of respiratory insufficiency. Another limitation is the lack of biomarkers and serial electrodiagnostic studies, which might improve the predictive models. Nevertheless, we think that our results can be easily extrapolated to other regions of the world with limited resources in which axonal GBS variants are seen with a high frequency.

Conclusion

In summary, our results suggest that EGRIS retains its ability as a good prognosticator of the need for IMV in GBS patients with axonal electrophysiological subtypes as the predominant variant, but our findings also suggest that in these particular populations, other early clinical data should also be considered. We wish to suggest that a bigger research effort should be made to perform a multinational study aimed to assess patients' outcomes and response to treatments for the axonal GBS subtypes.

Acknowledgements. The authors are thankful to the healthcare personnel of the Intensive Care Unit, Emergency Department, Internal Medicine, and Neurology of the *Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán* for the full commitment in caring for patients with neuromuscular disorders.

Funding. None.

Conflict of Interest. Dr Erwin Chiquete has received speaker honoraria from LFB, CSL Behring, Lilly, Novartis, Bayer, Merck, Ferrer, ApoPharma, Asopharma, and Silanes. The rest of the authors have no competing interests to declare.

Statement of Ethics. This study is consistent with the Declaration of Helsinki. This study's protocol was approved by the Ethics Committee at the First Affiliated Hospital of Harbin Medical University (No. 201314). Every patient who participated in the experiment signed informed consent before entering the experiment. Informed consent for publication was obtained from the patients.

Statement of Authorship. Conceptualization: Anaclara Michel-Chávez, Erwin Chiquete, Alfonso Gulías-Herrero, Diego Luis Carrillo-Pérez. Data curation: Anaclara Michel-Chávez, Diego Luis Carrillo-Pérez, José Aceves-Buendía, Eduardo Ruiz-Ruiz, Tatiana Bliskunova, Jennefer Portillo-Valle, Emmanuel Aguilar-Salas, Rafael Cobilt-Catana, Jorge Alberto Ortiz-Quezada, Julio Macías-Gallardo. Formal analysis: Erwin Chiquete, Emmanuel Aguilar-Salas, Salvador Durán-Coyote, Anaclara Michel-Chávez, Antonio Olivas-Martínez. Supervision: Alfonso Gulías-Herrero, Bruno Estañol, Guillermo García-Ramos, Carlos Cantú-Brito. Writing – original draft: Anaclara Michel-Chávez, Alfonso Gulías-Herrero, Diego Luis Carrillo-Pérez. Writing – review & editing: Erwin Chiquete, José Aceves-Buendía, Eduardo Ruiz-Ruiz, Salvador Durán-Coyote, Guillermo García-Ramos, Rafael Cobilt-Catana, Jorge Alberto Ortiz-Quezada, Carlos Cantú-Brito.

Data Availability Statement. The data set generated for the present analysis is available from the corresponding author on reasonable request.

References

1. Shang P, Zhu M, Baker M, Feng J, Zhou C, Zhang HL. Mechanical ventilation in Guillain-Barré syndrome. Expert Rev Clin Immunol. 2020;16:1053–64.
2. Leonhard SE, Mandarakas MR, Gondim FAA, et al. Diagnosis and management of Guillain-Barré syndrome in ten steps. Nat Rev Neurol. 2019;15:671–83.
3. Shahrizaila N, Lehmann HC, Kuwabara S. Guillain-Barré syndrome. Lancet. 2021;397:1214–28.
4. Martic V, Bozovic I, Berisavac I, et al. Three-year follow-up study in patients with Guillain-Barré syndrome. Can J Neurol Sci. 2018;45:269–74.
5. Rajabally YA, Uncini A. Outcome and its predictors in Guillain-Barre syndrome. J Neurol Neurosurg Psychiatry. 2012;83:711–8.
6. Panda PK, Sharawat IK. Predictors of unfavorable outcome in Guillain-Barre syndrome. J Clin Neurosci. 2020;81:52–3.
7. Sejvar JJ, Baughman AL, Wise M, Morgan OW. Population incidence of Guillain-Barré syndrome: a systematic review and meta-analysis. Neuroepidemiology. 2011;36:123–33.
8. Domínguez-Moreno R, Tolosa-Tort P, Patiño-Tamez A, et al. Mortality associated with a diagnosis of Guillain-Barré syndrome in adults of Mexican health institutions. Rev Neurol. 2014;58:4–10.
9. Choi SJ, Hong YH, Kim JS, Shin JY, Sung JJ. HyperCKemia in Guillain-Barré syndrome. Eur Neurol. 2020;83:415–20.
10. López-Hernández JC, Colunga-Lozano LE, Garcia-Trejo S, et al. Electrophysiological subtypes and associated prognosis factors of Mexican adults diagnosed with Guillain-Barré syndrome, a single center experience. J Clin Neurosci. 2020;80:292–7.
11. Bazán-Rodríguez L, López-Hernández JC, Jorge de Saráchaga A, et al. Classic and overlapping Miller-Fisher syndrome: clinical and electrophysiological features in Mexican adults. Neurol Sci. 2021;42:4225–9.
12. Shafqat S, Khealani BA, Awan F, Abedin SE. Guillain-Barré syndrome in Pakistan: similarity of demyelinating and axonal variants. Eur J Neurol. 2006;13:662–5.
13. Granieri E, Andreasi NG, De Martin P, et al. Incidence study of Guillain-Barré syndrome in the province of Ferrara, Northern Italy, between 2003 and 2017. A 40-year follow-up. Neurol Sci. 2019;40:603–9.
14. Gongora-Rivera F, Grijalva I, Infante-Valenzuela A, et al. Zika virus infection and Guillain-Barré syndrome in Northeastern Mexico: a case-control study. PLoS One. 2020;15:e0230132.
15. de Andrade da Silva R, Cremaschi RC, Rebello Pinho JR, de Oliveira JB, Coelho FM. Guillain-Barré syndrome-the challenge of unrecognized triggers. Neurol Sci. 2019;40:2403–4.
16. Hadden RD, Cornblath DR, Hughes RA, et al. Electrophysiological classification of Guillain-Barré syndrome: clinical associations and outcome. Plasma Exchange/Sandoglobulin Guillain-Barré Syndrome Trial Group. Ann Neurol. 1998;44:780–8.
17. Liu MQ, Wang J, Huang CN, et al. Elevated cerebrospinal fluid levels of beta-2-microglobulin in patients with Guillain-Barré syndrome and their correlations with clinical features. Neurol Sci. 2021;42:4249–55.
18. Prada V, Massa F, Salerno A, et al. Importance of intensive and prolonged rehabilitative treatment on the Guillain-Barrè syndrome long-term outcome: a retrospective study. Neurol Sci. 2020;41:321–7.
19. Korinthenberg R, Sejvar JJ. The Brighton Collaboration case definition: comparison in a retrospective and prospective cohort of children with Guillain-Barré syndrome. J Peripher Nerv Syst. 2020;25:344–9.
20. Walteros DM, Soares J, Styczynski AR, et al. Long-term outcomes of Guillain-Barré syndrome possibly associated with Zika virus infection. PLoS One. 2019;14:e0220049.
21. Berisavac I, Arsenijevic M, Bozovic I, et al. Disability and quality of life in Guillain-Barré syndrome - longitudinal study. J Clin Neurosci. 2020;78:185–8.
22. Lawn ND, Fletcher DD, Henderson RD, Wolter TD, Wijdicks EFM. Anticipating mechanical ventilation in Guillain-Barré syndrome. Arch Neurol. 2001;58:893–8.

https://doi.org/10.1017/cjn.2022.19 Published online by Cambridge University Press

23. Sharshar T, Chevret S, Bourdain F, Raphaël JC. French cooperative group on plasma exchange in Guillain-Barré syndrome. Early predictors of mechanical ventilation in Guillain-Barré syndrome. Crit Care Med. 2003;31:278–83.
24. Leung J, Sejvar JJ, Soares J, Lanzieri TM. Guillain-Barré syndrome and antecedent cytomegalovirus infection, USA 2009-2015. Neurol Sci. 2020;41:885–91.
25. Aladawi M, Elfil M, Abu-Esheh B, et al. Guillain barre syndrome as a complication of COVID-19: a systematic review. Can J Neurol Sci. 2022;49:38–48.
26. Wu X, Li C, Zhang B, et al. Predictors for mechanical ventilation and short-term prognosis in patients with Guillain-Barré syndrome. Crit Care. 2015;19:310.
27. Umer SR, Nisa Q, Kumari M, Abbas S, Mahesar SA, Shahbaz NN. Clinical features indicating the need for mechanical ventilation in patients with Guillain Barre syndrome. Cureus. 2019;11:e5520.
28. Green C, Baker T, Subramaniam A. Predictors of respiratory failure in patients with Guillain-Barré syndrome: a systematic review and meta-analysis. Med J Aust. 2018;208:181–8.
29. Asbury AK, Cornblath DR. Assessment of current diagnostic criteria for Guillain-Barré syndrome. Ann Neurol. 1990;27.
30. Hughes RA, Newsom-Davis JM, Perkin GD, Pierce JM. Controlled trial prednisolone in acute polyneuropathy. Lancet. 1978;2:750–3.
31. van Koningsveld R, Steyerberg EW, Hughes RA, Swan AV, van Doorn PA, Jacobs BC. A clinical prognostic scoring system for Guillain-Barré syndrome. Lancet Neurol. 2007;6:589–94.
32. Walgaard C, Lingsma HF, Ruts L, et al. Prediction of respiratory insufficiency in Guillain-Barré syndrome. Ann Neurol. 2010;67:781–7.
33. Zhang J, Yu KF. What's the relative risk? A method of correcting the odds ratio in cohort studies of common outcomes. JAMA. 1998;280:1690–1.
34. Shalman A, Savir S, Mechnik Steen Y, et al. Albumin levels as a biomarker for second Intravenous Immunoglobulin (IVIG) treatment in Guillain-Barre syndrome (GBS). J Clin Neurosci. 2020;74:247–9.
35. Cárdenas-Rodríguez MA, Meléndez-Flores JD, Villarreal-Garza E, et al. SARS-CoV-2-associated Guillain-Barré syndrome: a descriptive and comparative analysis. Can J Neurol Sci. 2021, 1–3. DOI 10.1017/cjn.2021.504. Epub ahead of print.
36. Tiwari I, Alam A, Kanta C, et al. Clinical profile and predictors of mechanical ventilation in Guillain-Barre syndrome in North Indian children. J Child Neurol. 2021;36:453–60.
37. Beydoun HA, Beydoun MA, Hossain S, Zonderman AB, Eid SM. Nationwide study of therapeutic plasma exchange vs intravenous immunoglobulin in Guillain-Barré syndrome. Muscle Nerve. 2020;61:608–15.
38. Ganesh A, Reis IR, Varma M, Patry DG, Cooke LJ. Neurological and head/eyes/ears/nose/throat manifestations of COVID-19: a systematic review and meta-analysis. Can J Neurol Sci. 2021;72:1–18.
39. Durand MC, Porcher R, Orlikowski D, et al. Clinical and electrophysiological predictors of respiratory failure in Guillain-Barré syndrome: a prospective study. Lancet Neurol. 2006;5:1021–8.
40. Zifko U, Chen R, Remtulla H, Hahn AF, Koopman W, Bolton CF. Respiratory electrophysiological studies in Guillain-Barré syndrome. J Neurol Neurosurg Psychiatry. 1996;60:191–4.
41. Visser LH, van der Meché FG, Meulstee J, et al. Cytomegalovirus infection and Guillain-Barré syndrome: the clinical, electrophysiologic, and prognostic features. Dutch Guillain-Barré Study Group. Neurology. 1996;47:668–73.

https://doi.org/10.1017/cjn.2022.19 Published online by Cambridge University Press