

Characterization of Patients with Guillain-Barré Syndrome in the General Hospital of Mexicali

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Abstract

Background: Guillain-Barré Syndrome is a progressive autoimmune polyradiculoneuropathy characterized by symmetrical flaccid paralysis accompanied by areflexia, hyporeflexia or hyperreflexia on rare occasions. Worldwide, it remains the first cause of flaccid paralysis. It is usually associated with infectious disease history; however, there are various clinical variants, each with a different outcome. Prognosis is usually good, although 20% of patients could suffer a severe clinical variant of Guillain-Barré Syndrome and 5% will die despite treatment. **Methods:** This is a cross-sectional study, including the records of hospitalized patients with Guillain-Barré Syndrome at Mexicali's General Hospital within a five-year period. **Results:** In a five-year span there were 64 patients with Guillain-Barré Syndrome, most of the patients were men (70.3%), with age ranging 1 to 76 years. A total of 8 (12.5%) patients died, from which 7 (87.5%) required mechanical ventilation during hospitalization. Immunoglobulin therapy was provided to 56 (87.5%) patients, and 6 (10.7%) of them perished due to acute kidney injury. **Conclusion:** Guillain-Barré Syndrome is a common disease among male population, with no dominating onset age, however, leaning for the young and elder. Most of the patients that were hospitalized at the General Hospital of Mexicali had a history of previous infection (gastrointestinal, respiratory, or other infectious diseases). The need for mechanical ventilation represents a higher severity index, nonetheless, this does not mean that assisted ventilation is directly associated with mortality. As for treatment, immunoglobulin is the most common choice for therapy, though some of the patients died from acute kidney injury.

Key Words: Guillain-Barré Syndrome; Polyradiculoneuropathies; Immunoglobulin therapy; Mechanical ventilation; Acute kidney injury; Plasmapheresis (Source: MeSH-NLM).

Introduction

Landry-Guillain-Barré Strohl Syndrome is a progressive autoimmune polyradiculoneuropathy,¹ characterized by symmetrical flaccid paralysis with areflexia, hyporeflexia or hyperreflexia on very rare occasions.² Worldwide, it remains the first cause of flaccid paralysis. It is usually associated with a previous infectious disease; however, this is not always the case. There are various clinical variants, each with a different prognosis and mortality. Prognosis is usually good, although 20% of patients could suffer a severe clinical variant of Guillain-Barré Syndrome (GBS) and 5% will die despite treatment.³⁻⁴

Nowadays, in the post-polio era, Guillain-Barré Syndrome is the most common cause of acute flaccid paralysis of healthy individuals. It has a worldwide incidence of 1-2 adults per 100,000 per year, mainly affecting male population. There is no dominant age group, however, the incidence increases 20% every 10 years from the first decade of life.^{5,6} While in México, Domínguez-Moreno reported an incidence of 0.89-1.89/100,000 people per year,⁷ from our knowledge, there are not studies regarding Guillain-Barré Syndrome's epidemiology in the city of Mexicali, México, being the main reason for this study to be conducted.

There is not a specific etiology for the disease; however, it may occur in association with multiple viral or bacterial infections, many agents have been linked as a precipitating factor, for example, *Campylobacter jejuni*,⁸ *Escherichia coli*, *Mycoplasma pneumoniae*, and viruses like cytomegalovirus, Epstein-Barr, human immunodeficiency virus, herpes zoster, and hepatitis. A study carry out in a city of México documented

eleven cases of GBS from January to March 2017, 23% were associated with Zika virus, 7% non-polio enteroviruses and 38% *Campylobacter*.⁹ A previous infection may trigger immune response that leads to acute polyneuropathy, approximately two-thirds of the patients refer a previous gastrointestinal or respiratory infection. In other studies, a small percentage of patients who have a history of vaccination, surgery, trauma or bone marrow transplant have also developed the disease.⁶

Clinical symptoms are broad and therefore misleading during diagnosis. Typically, it appears as a rapidly progressive symmetrical muscle weakness with absent, decreased or augmented deep tendon reflexes.¹ Weakness may range from mild motor impairment to complete paralysis of facial, respiratory or bulbar muscles, and limbs. Some unusual features include papilledema, myokymia, decreased auditory acuity, meningeal signs, vocal cord paralysis, and impaired alertness.^{5,10}

In a prospective, observational, international study that included a thousand patients from Europe, America, Asia and Bangladesh with Guillain-Barré Syndrome, they identified numerous clinical variants (Table 1) and their frequency according to geographical region, concluding that in North America the most common subtype is sensorimotor (69%).¹¹

Electrophysiological studies have a crucial role in confirming the diagnosis and classifying the main variants as demyelinating or axonal. It's hard to distinguish subtypes on clinical features alone. Findings can be normal early in the course but appear to be altered two weeks after the onset of symptoms.¹²

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Editor: Mihnea-Alexandru Găman

Student Editors: David Avelar Rodríguez

Submission: Oct 1, 2019. Revisions: Oct 22, 2019; Dec 8, 2019.

Acceptance: Dec 13, 2019. Publication: Dec 17, 2019

Process: Peer-reviewed

The aim of this study was to describe the clinical features of patients with GBS who were hospitalized at the General Hospital of Mexicali in a period (2014-2019), and their relationship with mortality.

Table 1. Guillain-Barré Syndrome clinical variants.¹¹

Acute inflammatory demyelinating polyneuropathy
Acute motor axonal neuropathy (AMAN)
Acute motor and sensory axonal neuropathy (AMSAN)
Miller Fisher syndrome
Bickerstaff encephalitis
Pharyngeal-cervical-brachial weakness
Paraparesis
Acute pandysautonomia
Pure sensory GBS
Facial diplegia and distal limb paresthesia
Acute bulbar palsy with areflexia

Methods

This is a cross-sectional study, including the records of hospitalized patients with Guillain-Barré Syndrome at Mexicali’s General Hospital within a five-year period. Sensitive information, such as name, remained in anonymity. The patients involved were assessed by medical staff who evaluated the presence of the Asbury and Cornblath criteria for diagnosis.¹³

The General Hospital of Mexicali is a public institution owned by the government with the objective to grant financial protection for patients who lack of social security, ensuring their access to health services. This is one of the many public hospitals that allows medical students to learn by enrolling on their academic programs. It is empirically known that the incidence of the disease has been on the rise over the past few years, suggesting that the study of the disease may be relevant to the community.

The following variables were analyzed: age, gender, time of onset, prodromal infections (gastrointestinal, respiratory or other), mechanical ventilation use, acute kidney injury, cranial nerve affection and choice of treatment. We studied cerebral spine fluid cell count, glucose and protein level, to consider albumin-cytological dissociation (protein levels were higher than 40 mg/dL and a cell count lower than 10 cells/mm³).³

Nerve conduction studies were only performed in patients whose diagnosis was uncertain, however, the reliability for neurophysiological criteria for diagnosis early in the course of GBS has yet to be determined.¹⁴

Results were considered significant if p-value < 0.05. Tables of categorical variables were analyzed for heterogeneity by the χ^2 test, using Yates’ continuity correction for two-by-two tables, or Fisher’s exact test if expected frequencies were less than 5. Student’s t-test was conducted to compare continuous variables between two groups. Data were analyzed by the Epi-Info statistical package version 7.2.2.16 and with Microsoft Office Excel (2018).

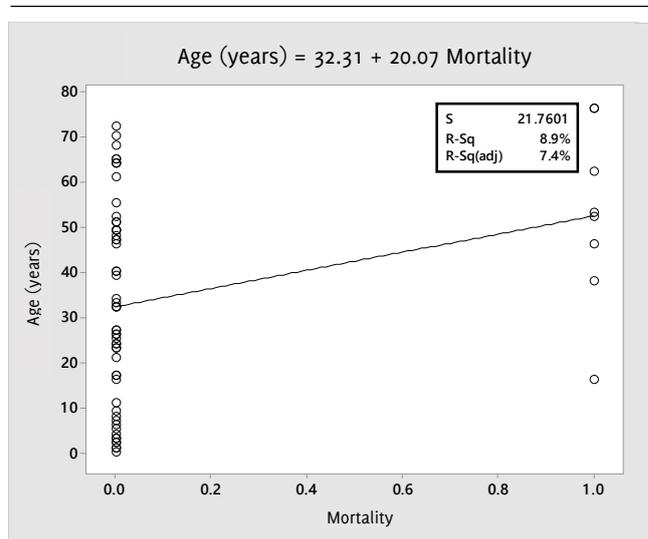
This study has been approved by the Institutional Review Board of the General Hospital of Mexicali.

Results

This study included 64 patients diagnosed with Guillain-Barré Syndrome within 5 years (2014-2019), 45 (70.3%) male patients and 19 (29.7%) female patients. Age ranged from 1 through 76 years, with an average age of onset of 35 years old. The most affected age ranges were 1-12

years and 41-59 years (21.88% both), however, the mortality rate increased with age (Figure 1). We estimated an incidence of 4 patients per 100,000 per year, meaning it has a high epidemiological impact.

Figure 1. Mortality and patients’ age at diagnosis



Some patients presented with neurological symptoms 4 days before seeking medical attention (54%) and others suffered from respiratory or gastrointestinal infection before the start of neurological symptoms (55%), 20% and 59.3% respectively, while 14.6% patients refused to have respiratory or digestive infection, but presented other infections such as urinary tract infection, HIV, and hepatitis C virus.

The global mortality rate was 12.7%. From the 70.3% males included in this study, 9% passed away, compared to the 30.16% female patients, from which 21.05% of them died. (OR=0.37 95%CI 0.8-1.6).

As for mechanical ventilation, 28% required it during the course of the disease, with an outcome of 87.5% deaths (p-value <0.01). 6.3% developed acute kidney injury during hospitalization, all of them received immunoglobulin therapy, yet the sample size of the unexposed was too small to establish a statistical significance. Of the 55 patients who received immunoglobulin, 4 (7.3%) developed acute kidney injury and 6 (10.9%) of them perished. There were 8 (12.5%) patients who did not receive any type of treatment (immunoglobulin or plasmapheresis), and 2 (25%) of them died. One of the patients who received immunoglobulin had previously received immunoglobulin therapy 15 years ago due to an earlier episode of Guillain-Barré Syndrome and had to interrupt treatment because he developed anaphylactic shock and acute kidney injury during administration. This patient did not live, despite receiving hemodialysis and plasmapheresis (Table 2).

Table 2. Study results

Variable	Freq. (%)	Death (%)	OR (95% CI)
Total	64 (100)	8 (12.7)	
Men	45 (70.3)	4 (9)	1
Women	19 (30.16)	4 (21.05)	0.37 (0.8-1.6)
Previous infection	55 (86)	7 (12.7)	1.16 (0.12-10.8)
Gastrointestinal	38 (59.3)	6 (15.7)	2.2 (0.4-12.1)
Respiratory	13 (20)	2 (25)	1.3 (0.2-7.7)
Other	9 (14)	1 (12.5)	0.8 (0.09-7.9)
Mechanical ventilation	18 (28.5)	7 (87.5)	28 (3.11-251)
Acute kidney injury	4 (6.3)	1 (25)	2.5 (0.22-27.2)
Cranial nerve affection	20 (31.25)	1 (5)	0.2 (0.03-2.4)

Discussion

This study reviewed 64 cases of patients with GBS from 2014 through 2019, 70.3% were male and 30.16% were female with an obvious incline for males just like Carrillo-Pérez et al stated.¹⁵ The average age of onset was 35 years, unlike Medina-Benites et al who reported an average of 43.85 years;³ no predominant age range was observed for the onset of the disease, however, there is an increased incidence in young and elderly patients. While analyzing the data, an association between age and mortality was observed, demonstrating that age is directly proportional to mortality ($p < 0.0001$).

From the total of patients, 86% reported having had a previous infection from which 59.3% were gastrointestinal and 20% respiratory, unlike other studies where only 77% presented a previous infectious disease.¹⁶ During characterization no patients were found with a history of trauma, surgery or vaccination, however, different studies reported there is an increased incidence after vaccination or surgery.¹⁷

Mechanical ventilation is associated to a poor outcome, and it is not a predictor for prognosis, yet, it is an indicator of a severity of the disease. It is well elucidated that the need for mechanical ventilation for acute respiratory failure translates severity. In this study 7 (10.9%) patients perished while on mechanical ventilation. In other studies the need for mechanical ventilation was compared to the history of previous infections, 52% presented a respiratory infection from which 28% required mechanical ventilation.¹⁶ Furthermore, another study mentioned that only 13% of the study population (total of 8,364 patients) needed mechanical ventilation, although they had a larger number of patients.¹⁷

Regarding treatment, immunoglobulin was administered to 56 (87.5%) patients, 6 expired as they developed acute kidney injury, unfortunately, the sample size does was not enough to establish a

relationship between acute kidney injury and the use of immunoglobulin, moreover, only one patient was treated with plasmapheresis ending in death since he had severe clinical disease and similarly developed acute kidney injury. In other studies treatment is divided into supportive measures, immunoglobulin and plasmapheresis (19%, 57%, 23% respectively) with a total of 21 without relating to mortality,³ whereas in another study with 25 patients where most received plasmapheresis (52%) no significant change was found in disease progression.¹⁴ The decision to administer immunoglobulin may be affected by the fact that ours is a public hospital, sometimes with limited resources, therefore, the availability of supplies may be affected.

This is a retrospective study, with obvious weaknesses involved. For example, the lack of information on some patients' records. Similarly, the score of Erasmus for outcome in Guillain-Barré Syndrome or the modified disability scale for GBS was not applied in this study.³

The incidence rate for GBS in our city is 4 per 100,000 individuals per year, being twice as much as a previous study conducted in our country. We noted a higher prevalence among male sex, just like the rest of the studies regarding GBS, this without being a risk factor for mortality. Also, there is no prevailing onset age. The need for mechanical ventilation represents a higher severity index, nonetheless, this does not mean that assisted ventilation is directly associated with mortality. As for therapy, the use of immunoglobulin as first-choice treatment was associated with acute kidney injury, without an increment in mortality, though results were not statistically significant due to the size of our sample.

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Acknowledgments

Special recognition to Juan José Valencia Calderón who facilitated all the data needed during the project.

Conflict of Interest Statement & Funding

The Authors have no funding, financial relationships or conflicts of interest to disclose.

Author Contributions

Conceptualization: JHR, and HJR. Methodology: FMMG, and JHR. Validation: JHR, RG, and HJR. Formal Analysis: FMMG, JHR, AG, AB, and HJR. Investigation: FMMG, and AG. Resources: FMMG, AG, and AB. Writing – Original Draft: JHR, and HJR. Writing – Review & Editing: FMMG. Visualization: FMG. Supervision: JHR, RG, and HJR.

Cite as:

Martínez-González FM, Hernández-Ríos J, Gutiérrez A, Beltrán A, González R, Jaramillo-Ramírez H. Characterization of Patients with Guillain-Barré Syndrome in the General Hospital of Mexicali. *Int J Med Students.* 2019 Sep-Dec;7(3):58-61.

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ISSN 2076-6327

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