Journal of the Neurological Sciences 377 (2017) 102–106

Contents lists available at ScienceDirect

Journal of the Neurological Sciences

journal homepage: www.elsevier.com/locate/jns

Incidence and clinical characteristics of Guillain-Barré syndrome before the introduction of Zika virus in Puerto Rico

Jorge L. Salinas [a,*], Chelsea G. Major [b], Daniel M. Pastula [c,d], Emilio Dirlikov [a,e], Ashley Styczynski [a], Carlos A. Luciano [f], Valerie Wojna [f], Tyler M. Sharp [c], James J. Sejvar [c], Brenda Rivera-Garcia [e]

[a] Epidemic Intelligence Service, CDC, Atlanta, Georgia
[b] Office for State, Tribal, Local, and Territorial Support, CDC, Atlanta, Georgia
[c] National Center for Emerging and Zoonotic Infectious Diseases, CDC, Atlanta, Georgia
[d] University of Colorado Denver, Aurora, CO, United States
[e] Puerto Rico Department of Health, San Juan, Puerto Rico
[f] University of Puerto Rico, San Juan, Puerto Rico

ARTICLE INFO

Article history:
Received 18 January 2017
Received in revised form 3 April 2017
Accepted 6 April 2017
Available online 07 April 2017

Keywords:
Guillain-Barré syndrome
Incidence
Puerto Rico
Intravenous immunoglobulin
Polyneuropathy

ABSTRACT

Background: Zika virus has been associated with increases in Guillain-Barré syndrome (GBS) incidence. A GBS incidence estimation and clinical description was performed to assess baseline GBS epidemiology before the introduction of Zika virus in Puerto Rico.
Methods: Hospitalization administrative data from an island-wide insurance claims database and U.S. Census Bureau population estimates provided a crude GBS incidence for 2013. This estimate was adjusted using the proportion of GBS cases meeting Brighton criteria for confirmed GBS from nine reference hospitals. Characteristics of confirmed GBS cases in the same nine hospitals during 2012–2015 are described.
Results: A total of 136 GBS hospitalization claims were filed in 2013 (crude GBS incidence was 3.8 per 100,000 population). The adjusted GBS incidence was 1.7 per 100,000 population. Of 67 confirmed GBS cases during 2012–2015, 66% had an antecedent illness. Median time from antecedent illness to GBS onset was 7 days. Most cases (67%) occurred during July–September.
Conclusions: Puerto Rico's GBS incidence for 2013 was estimated using a combination of administrative data and medical records review; this method could be employed in other regions to monitor GBS incidence before and after the introduction of GBS infectious triggers.

Published by Elsevier B.V.

1. Introduction

Guillain-Barré syndrome (GBS) is an autoimmune disease of the peripheral nervous system characterized by acute, symmetric limb weakness with decreased or absent deep-tendon reflexes [1]. Nearly 70% of patients with GBS report having had symptoms of an infectious illness in the days or weeks prior to onset of neurologic illness [2]. Infectious agents most frequently associated with the development of GBS include *Campylobacter jejuni*, *Mycoplasma pneumoniae*, cytomegalovirus, and Epstein-Barr virus [1,2]. Infection with arthropod-borne viruses (arboviruses), such as dengue and chikungunya viruses, has also been associated with GBS [3,4]. Globally, the annual incidence of GBS is estimated as 1.1–1.8 cases per 100,000 population [5], but estimates may vary depending on the regional prevalence of infectious triggers.

Increased incidence of GBS has been recently reported after the introduction of an emergent arbovirus, Zika virus, in French Polynesia [6] and the Americas [7–9]. However, many of the regions where Zika virus has recently emerged lack accurate estimates of GBS incidence. Such region-specific estimates are necessary to assess potential increases in GBS incidence due to Zika virus or other pathogens.

Zika virus transmission was first reported in Puerto Rico in December 2015, and the first GBS case with evidence of recent Zika virus infection had illness onset in January 2016 [10]. To assess the potential impact of Zika virus on GBS incidence in Puerto Rico, we sought to establish the GBS incidence prior to the widespread introduction of Zika virus using a combination of hospitalization administrative data and medical record reviews at a sample of nine reference hospitals. We also describe the clinical characteristics of patients with confirmed GBS managed at the same nine hospitals during 2012–2015.

* Corresponding author at: Centers for Disease Control, and Prevention, 1600 Clifton Road NE, Mailstop E-10, United States.
E-mail address: jsalinas@cdc.gov (J.L. Salinas).

http://dx.doi.org/10.1016/j.jns.2017.04.006
0022-510X/Published by Elsevier B.V.

2. Methods

2.1. Study population

We used 2013 data from the Puerto Rico Health Study, which includes island-wide medical insurance claims for medical encounters for approximately 90% of Puerto Rican residents [11]. Similar datasets were not available for other years. GBS cases were identified by using International Classification of Disease (ICD) discharge codes corresponding to GBS (i.e., ICD-9 code 357.0 or ICD-10 code G61.0).

2.2. Estimation of GBS incidence in 2013

To estimate the number of GBS cases in Puerto Rico in 2013, we identified all insurance claims for hospitalizations (since GBS is unlikely to be managed solely in the outpatient setting), and consolidated all claims from individual patients as providers (e.g., physicians) and ancillary services (e.g., radiology services) routinely billed separately during a single admission (Fig. 1). To calculate the annual GBS incidence in 2013, we divided the number of GBS cases in Puerto Rico in 2013 by the 2013 mid-year population estimate for Puerto Rico (3,595,839) obtained from the U.S. Census Bureau [12].

2.2.1. Proportion of confirmed GBS at nine referral hospitals during 2013

To further refine our GBS incidence estimate, we calculated the proportion of confirmed GBS cases [13] out of all cases with ICD codes for GBS from nine referral hospitals during 2013. A referral hospital was defined as having >200 inpatient beds and at least one consulting neurologist on staff. Hospitals were selected according to location within metropolitan areas of Puerto Rico: San Juan, Ponce, Manatí, and Mayagüez. Following review of medical records using a standardized abstraction tool, we used the Brighton Collaboration criteria to confirm GBS diagnoses [13]. The Brighton Collaboration is a World Health Organization (WHO)-sponsored initiative to develop standardized case definitions; the initial GBS case definitions were first published in 2010, and subsequently subjected to several reviews [13]. The Brighton Collaboration paradigm assigns a 'confirmed' GBS status (Brighton levels 1–3) in patients who meet the following clinical criteria: 1) acute onset of bilateral and relatively symmetric flaccid weakness of the limbs; 2) decreased or absent deep tendon reflexes in affected limbs; 3) a monophasic illness pattern with weakness nadir between 12 h and 28 days, followed by clinical plateau; and 4) the absence of an alternative diagnosis for weakness. Patients lacking documentation to fulfill minimal case criteria are assigned a level 4, and those with an alternative diagnosis are assigned a level 5.

Last, we applied the proportion of confirmed GBS patients in 2013 to the crude GBS incidence, estimated with administrative data from the Puerto Rico Health Study [11], to generate the adjusted GBS incidence for 2013.

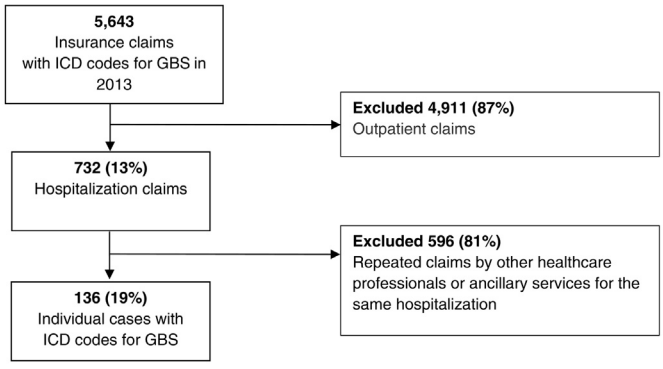

Fig. 1. Flow diagram of case identification from the Puerto Rico Health Study for Guillain-Barré syndrome incidence calculation – Puerto Rico, 2013.

2.3. Clinical description of GBS cases, 2012–2015

We used a standardized medical record abstraction form to collect demographics, clinical features, antecedent symptoms, and treatment characteristics of confirmed GBS patients from the nine referral hospitals during 2012–2015. Antecedent illness was defined as a non-neurologic symptom(s) or syndrome that occurred within 4 weeks before the onset of neurologic manifestations. Antecedent illness was categorized as respiratory illness (i.e., having either rhinorrhea, sore throat, ear pain, nasal congestion, cough, or shortness of breath), gastrointestinal illness (i.e., nausea, vomiting, diarrhea, abdominal pain, or unspecified "gastrointestinal distress"), or viral-like illness (i.e., fever, chills, malaise, joint pain, rash, headache, "flu-like syndrome," or "viral syndrome"). We present less frequent symptoms as "uncategorized." Cytoalbuminologic dissociation was defined as cerebrospinal fluid white blood cells < 50 cells/mm^3 and protein ≥ 45 mg/dL. Where available, electrodiagnostic study results were transcribed. We recorded any immunizations given in the 4 weeks before neurologic illness onset. GBS treatments recorded were intravenous immunoglobulin (IVIG) and plasmapheresis or plasma exchange. Hospital stay outcomes were transcribed from discharge summaries.

2.4. Statistical analysis

We present categorical variables as counts and proportions, and continuous variables as medians and ranges. We managed all data using the Research Electronic Data Capture (REDCap) tool, and analyses were performed using Stata version 14 (College Station, Texas). Institutional review at the Centers for Disease Control and Prevention determined the investigation to be public health practice and not research, and as such did not require Institutional Review Board approval.

3. Results

3.1. Estimation of GBS incidence in 2013

Of 5643 insurance claims made in 2013 corresponding to GBS, 732 (13%) were for hospitalizations of 136 individual patients (Fig. 1). These 136 patients resulted in a crude GBS incidence of 3.8 per 100,000 population in 2013.

A total of 40 patients from the nine selected referral hospitals had inpatient codes for GBS in 2013. Of these, 18 (45%) met Brighton Collaboration criteria for confirmed GBS. After applying the proportion of confirmed cases from the nine hospitals (45%) to the previously calculated crude GBS incidence (3.8 per 100,000), we estimated the adjusted GBS incidence in 2013 as 1.7 per 100,000 population.

3.2. Clinical description of GBS cases, 2012–2015

We identified a total of 202 hospitalizations at the nine selected referral hospitals during 2012–2015 with ICD codes corresponding to GBS. We excluded 16 (10%) hospitalizations for patients with no available medicals record and 37 (20%) that were repeated admissions. The remaining hospitalizations represented 149 individual patients. Patients without confirmed diagnosis of GBS were excluded (i.e., Brighton Collaboration criteria levels 4 [$n = 25$, 17%] and 5 [$n = 57$, 38%]), leaving 67 (45%) patients confirmed as GBS cases, meeting Brighton Collaboration criteria levels 1–3 (Fig. 2).

Among the 67 confirmed GBS cases that were hospitalized during 2012–2015, 17 (25%), 34 (51%), and 16 (24%) met Brighton collaboration criteria levels 1, 2, and 3, respectively. Of these patients, 17 (26%) were hospitalized in 2012, 18 (27%) in 2013, 15 (22%) in 2014, and 17 (25%) in 2015. Most patients (67%) had neurologic illness onset in July, August, or September. Median age of confirmed GBS patients was 51 years (range = 3–82 years), and 36 were male (54%). GBS patients were residents of 41 (53%) of the 78 total municipalities (Fig. 3).