Epidemiologic Study of Guillain-Barré Syndrome in Children <15 Years of Age in Latin America

Jean-Marc Olívé,* Carlos Castillo, Rafael García Castro, and Ciro A. de Quadros

In 1986, surveillance of acute flaccid paralysis (AFP) cases among children <15 years of age was implemented in Latin America as part of the initiative to eradicate poliomyelitis from the Western Hemisphere. Data on AFP, including Guillain-Barré syndrome (GBS), could be analyzed from a regional registry system and from specific GBS studies in seven countries. Between 1989 and 1991, 3112 cases of GBS were reported in Latin America, representing 52% of all nonpolio AFP cases. From the studies in seven countries, a total of 1527 GBS cases (49%) were studied, representing an overall annual incidence rate of 0.91/100,000 children <15 years old. Follow-up investigations showed a persistent muscular weakness at 60 days, 6 months, and 1 year after onset in 61%, 14%, and 10% of children, respectively. This study confirms that with the disappearance of polio, GBS arises as the most common cause of AFP.

In September 1985, the Pan American Health Organization (PAHO) launched the initiative to eradicate the indigenous transmission of wild type poliovirus from the Americas by the end of 1990 [1]. As a result of this initiative, the last case of poliomyelitis in the Americas was notified from Peru on 23 August 1991 and the Western Hemisphere was certified free of polio in September 1994. One of the main strategies of this initiative was the development, in all Latin American countries, of effective surveillance for acute flaccid paralysis (AFP) [2]. The development of the AFP surveillance system helped improve the clinical and virologic investigation of AFP cases and particularly Guillain-Barré syndrome (GBS). To standardize and promote proper AFP case investigation, meetings with neuropediatricians involved in the program were organized. During these meetings, specific GBS studies were proposed and standardized protocols were developed. Here we present the analysis of data collected between 1989 and 1991 from this regional AFP surveillance system and the findings of the GBS studies from seven Latin American countries.

Methods

Routine surveillance of AFP cases including GBS in Latin America. Effective surveillance of AFP in children <15 years of age is considered one of the key elements to the success of the polio eradication initiative [3]. Surveillance for AFP involves the compulsory and immediate notification of AFP cases in all Latin American countries. Every week, >20,000 health units in the Americas report on the presence or absence of AFP cases in children <15 years of age to their respective Ministry of Health and to the PAHO headquarters in Washington, DC, where the data are analyzed in a computerized registry (Polio Eradication Surveillance System: PESS) [4]. In addition to case reporting, active searches for AFP cases in the community, either through door-to-door survey or by review of the hospital’s admission and death certificates, are periodically conducted. Most of the reported AFP cases are investigated by a neuropediatrician in association with epidemiologists, neurophysiologists, physical therapists, and the reference virologic laboratory using a standardized case investigation form. Using the computerized database (PESS) available at Ministries of Health and PAHO Headquarters, general epidemiologic and clinical information could be obtained for most of the AFP and GBS cases reported.

GBS study in seven Latin American countries. More detailed GBS studies were done in El Salvador, Guatemala, Honduras, Paraguay, Peru, Mexico, and Venezuela. Cases were classified as GBS using the diagnostic criteria devised in 1978 at the request of the National Institute of Neurologic and Communicative Disorders and Stroke [5] and reaffirmed in 1990 [6]. Standard clinical criteria, investigation, and analysis procedures were established during two meetings of neuropediatricians and epidemiologists from all participating countries [7, 8]. In five of the seven countries (not Mexico and Venezuela), all cases were examined by a single neurologist.

Results

Routine surveillance of AFP cases including GBS in Latin America. From 1989 to 1991, 6304 cases of AFP were reported in Latin America; 230 (4%) were categorized as poliomyelitis, 43 (1%) as vaccine-associated poliomyelitis, and 6031 (95%) as nonpolio AFP cases. All AFP cases were investigated by a medical professional, and >80% were investigated within 48 h of notification. The total number of nonpolio AFP cases represents an annual incidence rate of >1.25 cases per 100,000 population <15 years of age. Of these, 3112 cases were diag-
GBS 52% Percent

Transverse myelitis 2%
Trauma 1%
Tumor 2%
No Dx. 10%
Others 33%

Figure 1. Distribution of diagnoses in nonpolio acute flaccid paralysis cases (total reported, 6031)—Latin America, 1989–1991. GBS, Guillain-Barré syndrome.

Figure 2. Distribution of Guillain-Barré syndrome cases by week of onset of muscular weakness—Latin America, 1989–1991.

Figure 3. Distribution of progress of muscular weakness in Guillain-Barré syndrome—Latin America, 1989–1991. Information was available for 2159 cases. Mean, 3.47 days (confidence interval, 2.8–4.1); median, 3.

Figure 4. Mean annual age-specific Guillain-Barré syndrome incidence rate in 7 Latin American countries, 1989–1991.

It was diagnosed as GBS, representing 52% of all nonpolio AFP cases reported during this period (figure 1) and an annual incidence rate of 0.67 case per 100,000 population <15 years of age. There were no geographic clusters of GBS. A large majority of the GBS cases (80%) received at least three doses of oral polio vaccine (OPV). When cases were plotted by week of onset, the mean weekly GBS incidence did not show significant seasonal variation (figure 2). The same figure shows that there was no temporal association with the organization of mass OPV immunization campaigns, as most of those activities occur between March and November. The mean and median number of days of muscular weakness progression were, respectively, 3.47 days (confidence interval, 2.8–4.1) and 3 days (range, 0–60) (figure 3).

Epidemiologic study of GBS in seven Latin American countries. Between 1989 and 1991, 1527 GBS cases were studied, 4 of which were relapses. The total cases from these studies represent 49% of all GBS cases reported through routine surveillance during the same period. In the countries under study, the overall GBS annual incidence rate was 0.91/100,000 children <15 years of age and ranged from 0.72 in Peru to 1.83 in El Salvador. Only 28 cases (2%) occurred in children <1 year of age, and for all countries, the most affected age group was 1–4 years of age, with 47% of all cases (figure 4). The overall male-to-female ratio was 1.36, ranging from 1.23 in Mexico to 1.83 in El Salvador.

More than 90% of all cases led to hospitalization. Respiratory support was necessary in 16% of these, ranging from 6% in Paraguay to 26% in Guatemala. No patients were given plasmapheresis or intravenous immunoglobulin treatment.

The overall case-fatality rate was 7%, ranging from 1% in Venezuela to 13% in Guatemala. When calculated by age group, the highest case-fatality rate was 9% in children 1–4 years of age and the lowest was 5% in those 10–14 years of age.

The clinical presentation in GBS patients was preceded by an infectious illness, generally a mild upper respiratory infection, in 67% of all cases. On average, the muscular weakness peaked at 3.4 days. Major clinical features are shown in table 1. Fever at onset of the weakness was observed in 29% of all the cases.

The majority of the children had progressive muscle weakness, in a roughly symmetrical distribution, with areflexia in

Number of Cases

<table>
<thead>
<tr>
<th>Weeks</th>
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<tbody>
<tr>
<td>1</td>
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<tr>
<td>2</td>
</tr>
<tr>
<td>3</td>
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<tr>
<td>4</td>
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<tr>
<td>9</td>
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<tr>
<td>10</td>
</tr>
<tr>
<td>11</td>
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% Distribution

<table>
<thead>
<tr>
<th>Age at Onset of Disease (year)</th>
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</thead>
<tbody>
<tr>
<td>&lt; 1</td>
</tr>
<tr>
<td>1-4</td>
</tr>
<tr>
<td>5-9</td>
</tr>
<tr>
<td>10-14</td>
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</tbody>
</table>
Table 1. Prevalence of clinical signs of GBS in children in a study of 1527 cases in 7 Latin American countries compared with a review of 175 patients.

<table>
<thead>
<tr>
<th>Clinical feature</th>
<th>Prevalence (%)</th>
<th>LatAm study, 1527 cases</th>
<th>Review of 175 cases*</th>
</tr>
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<tbody>
<tr>
<td>Weakness</td>
<td>100</td>
<td>100</td>
<td></td>
</tr>
<tr>
<td>Legs</td>
<td>99</td>
<td>98</td>
<td></td>
</tr>
<tr>
<td>Arms and legs</td>
<td>71</td>
<td>84</td>
<td></td>
</tr>
<tr>
<td>Arms → legs</td>
<td>1</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Proximal → distal</td>
<td>5</td>
<td>11</td>
<td></td>
</tr>
<tr>
<td>Descending → ascending</td>
<td>4</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td>Cranial nerves involvement</td>
<td>21</td>
<td>39</td>
<td></td>
</tr>
<tr>
<td>Respiratory paralysis</td>
<td>16</td>
<td>18</td>
<td></td>
</tr>
<tr>
<td>Hyporeflexia or areflexia</td>
<td>100</td>
<td>100</td>
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</tbody>
</table>

Sensation
- Pain or perithesias: 57% (38%)
- Sensory loss: 31% (46%)
- Autonomic disorders: 20% (20%)
- Incomplete recovery: 10% (28%)
- Death: 7% (4%

NOTE. GBS, Guillain-Barré syndrome. NA, not available.

Discussion

This is the first population-based study on the reported incidence of AFP, particularly GBS. We believe that the standardization of the specific GBS studies in the seven countries, representing 49% of the GBS cases reported in Latin America from 1989 to 1991, and the handling of the information produced reliable data but may not be representative of all GBS cases reported during the same period, as no attempts in other countries were made to develop specific GBS studies as part of the AFP surveillance system developed. The multiplicity of observers in some countries may have produced interobserver variability. However, in five countries, a single neurologist examined each case, thereby eliminating this variability. Also, because the study involved children, some signs and symptoms, particularly pain, paresthesia, and loss of sensitivity, may have been more difficult to ascertain. Furthermore, the presence of fever at onset may have been difficult to assess and may also have been due to concomitant infection.

Nevertheless, the epidemiologic and clinical features of GBS in children in the seven-country study are similar to previous descriptions from Latin America [9, 10] and from other parts of the world [11, 12]. The overall incidence of 0.91 case of GBS per 100,000 population <15 years of age in the seven countries participating in the study is similar to that reported in hospital-based studies [13–15]. With <2% of the cases, GBS in children <1 year of age represents a small proportion of all cases. As found in other studies, the most affected age group in children was 1–4 years [12, 16].

The male-to-female ratio of 1.36 found in children seems to be lower than that usually found in adults, estimated at ~2:1 [17, 18].

The overall 7% case-fatality rate is higher than figures previously published in developed countries [14, 19]. This difference was mainly due to unavailable or deficient respiratory support once the child was admitted to an intensive care unit. The mean duration of muscle weakness progression of 3.47 days from the routine surveillance study and the average dura-

![Figure 5](https://example.com/figure5.png)

**Figure 5.** Proportion of Guillain-Barré syndrome cases with persistent non-polio-compatible muscular weakness during follow-up in 7 Latin American countries, 1989–1991.
tion of 3.4 days found in this study is shorter than the average of 28 days found in GBS cases in adults [19]. This would indicate that in children, the course of the disease is shorter than in adults, which should represent a better prognosis for rapid recovery, as it is found that increasing duration of paralysis is associated with slower recovery [20, 21]. Results may confirm findings from previous studies that GBS in children may have a better prognosis than in adults [22, 23].

In the GBS cases studied, the presence of fever at onset of paralysis was found in a much higher proportion of cases (29%) than normal [24, 25]. Several factors may have contributed to this difference: delay in clinical evaluation when secondary infections, particularly in the respiratory tract, could be present or environmental and socioeconomic factors that increase the risk of concomitant infections.

Follow-up investigation demonstrated that 44% of GBS cases still had persistent motor weakness at 60 days after onset. The presence of motor weakness at 60 days is one of the criteria that the poliomyelitis eradication program uses for case confirmation in absence of adequate stool samples (2 stool samples taken 24 h apart within 2 weeks of muscular weakness onset). This high rate of residual paralysis among GBS cases 60 days after paralysis onset may result in a misclassification of GBS cases as confirmed polio and underscores the importance of virus isolation from adequate stools as the preferred method to confirm cases of polio [26].

Elevated CSF protein level with normal cell count was encountered in 56% of all GBS cases during the first week of disease onset. This demonstrates the necessity to study multiple CSF samples when GBS is suspected.

Even if electrodiagnostic studies are a valuable diagnostic tool, as described elsewhere, ~20% of the patients had normal nerve conduction velocity studies, which may not become abnormal until several weeks of illness [27–30].

This study confirms that with the disappearance of polio, GBS arises as the most common cause of AFP. It also reiterates the importance of a standardized clinical investigation of all cases of AFP in children, which can be achieved only through a well-organized coordination between epidemiologists, neurologists, pediatricians, virologists, and specialists in rehabilitation. These findings emphasize that stool specimen collection for virus isolation is superior to clinical examinations for residual paralysis 60 days after onset for case confirmation, particularly when the incidence of polio is low. Each case of GBS should be considered a probable case of polio and should be subjected to adequate investigation, including collection of stool samples as early as possible after paralysis onset. This is important, as poliomyelitis can easily be misdiagnosed as GBS, as happened during the poliomyelitis outbreak in Finland in 1984 [31].

It is hoped that these findings can be useful in other regions of the world, where polio is still endemic and AFP surveillance is being established, in improving the diagnosis of GBS and thus easing the task of attaining the goal of global eradication of poliomyelitis by the year 2000 [32].

Acknowledgments

We particularly thank the national staff of the Ministries of Health of the countries of the Americas and the PAHO field staff involved in this effort, whose commitment, creativity, and enthusiasm has made possible the objective to eradicate poliomyelitis from this continent, and all clinicians and neuropediatricians participating in the seven-country study, particularly Hilda Alcala (Mexico), Patricia Campos (Peru), Marco Molinero (Honduras), Hernan Paublini (Venezuela), Ruben Posadas and Carlos Ramirez (Guatemala), Laura Rojas (Paraguay), and Gustavo Roman (United States).

References


