

Age may contribute to the increased frequency of Axonal Guillain-Barré syndrome

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DISCLOSURES

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ETHICAL PUBLICATION STATEMENT

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ABSTRACT




Introduction



The frequency of axonal Guillain-Barré Syndrome (GBS) varies among countries. The study supporting the high frequency of axonal GBS in South America was performed on a pediatric population. We aimed to study the frequency of axonal GBS in both children and adults in South America.




Methods



This was a retrospective cohort analysis of patients diagnosed with GBS between January 2006 and December 2013 in a neurological center in Buenos Aires, Argentina. Adults and children with a diagnosis of GBS were included and classified applying Ho and colleagues' ¹ criteria for axonal GBS.



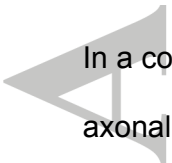
Results



There were 105 patients with GBS. Among 58 adults, only 5 individuals presented were classified as axonal GBS compared to 16 of 47 children. The frequency of axonal GBS was significantly higher in children than in adults (34% vs 8.6%, $P=0.0001$).



Discussion



In a cohort of South American patients, age may impact the frequency of axonal GBS.

INTRODUCTION

Guillain-Barré Syndrome (GBS) is a potentially life threatening immune-mediated polyradiculoneuropathy. It is the most common cause of acute flaccid paralysis worldwide², with a reported incidence of 0.6 to 4 per 100,000 persons per year³. GBS was regarded as a demyelinating neuropathy from the time of its original description until an axonal subtype was identified in the early 1990s³. Acute inflammatory demyelinating polyneuropathy (AIDP) and the “axonal variants” are now considered the two main electrophysiological subtypes of GBS⁴. Acute motor axonal neuropathy (AMAN) and acute motor and sensory axonal neuropathy (AMSAN) share similar pathological processes and immunological profiles. For this reason, they are grouped together as “axonal variants”, with AMSAN considered a more severe form of axonal GBS⁴. Because demyelinating and axonal GBS variants have different pathogeneses, clinical features and patterns of recovery, it has been proposed that they may also have differential responses to treatment³.

Since its original description in children and young adults, the variable frequency of axonal GBS has been largely associated with geographic location and levels of sanitation⁵. It is low in North America and Europe (3-17%), intermediate in Israel (22%) and Japan (38%), and high in Bangladesh (67%) and China (75%)^{3,6}. South America and Mexico have an intermediate frequency, accounting for 30-38% of all cases of GBS³. Remarkably, only two pediatric series support this statement^{7,8} and no data is available on axonal

GBS frequency in adult South American populations. Furthermore, previous studies about epidemiology of GBS subtypes did not explore a possible association between axonal GBS frequency and age. Our aim was to study the frequency of axonal GBS in South American children and adults with similar levels of sanitation.

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MATERIALS AND METHODS

We conducted a retrospective cohort analysis of patients diagnosed with GBS between January 2006 and December 2013 in our hospital located in Buenos Aires, Argentina. Age, gender, living area, clinical features, diagnostic studies, and treatment were assessed in all cases. Electrodiagnostic studies were reviewed applying Ho and colleagues' criteria for axonal GBS¹ (Supplementary Table 1). The frequency of axonal GBS in adults (>18 years old) was compared to that in children using a Fisher's exact test. P values <0.05 were considered as significant. Statistical analysis was conducted using Stata V12.1. The study was approved by the local ethics committee.

RESULTS

The overall frequency of axonal variants among 105 patients diagnosed with GBS was 20% (n=21). Fifty-eight patients (55 %) were adults (57% males, median age 49 yr., range 20 to 83) and the remaining 47 (45%) were children (53% males, median age 10 yr., range 3 to 17). All patients lived in urban or suburban areas with similar levels of sanitation. The median number of days from disease onset (sensory or motor symptoms) to admission was 8, with a range of 3-23. Electrodiagnostic studies were performed within the first week of admission in all cases. Applying Ho and colleagues' criteria, only 5 adults (8.6%) had axonal GBS (AMAN), whereas the majority was classified as AIDP.

No patients remained unclassified. On the other hand, 16 children (34%) presented with axonal GBS, consisting of 19% (n=9) with AMSAN, and 15% (n=7) with AMAN. AIDP was diagnosed in 51% of children (n=24) and Miller-Fisher in 10% (n=5). Two patients (4%) remained unclassified. Axonal variants were significantly more frequent in children than in adults (P=0.0001).

DISCUSSION

We found in our cohort an overall frequency of axonal GBS of 20%. In children, the frequency was 34%, similar to previous studies in our country and Mexico^{7,8}. However, in adults, the frequency of axonal variants was significantly lower (8.6%), and similar to what is found in some European countries and North America³.

Remarkably, adults and children in our population had similar levels of sanitation. Previous studies pointed to the geographical location, closely related with the level of sanitation, as the main determinant of the probability *a priori* that a patient would have an axonal GBS variant^{3,9}. Evidence in prior studies about age distribution and its relationship with axonal GBS is scarce. Of note, those studies that included only adults had the lowest frequency of axonal GBS (summarized in Supplementary Table 2). On the other hand, studies of only pediatric populations and those in which there was a preponderance of children and younger adults, showed the highest frequencies of axonal variants. Nonetheless, the role of the age has not been specifically addressed until now. Our data suggests that, besides the level of sanitation, age could be a major determinant of the probability of having an axonal vs. a demyelinating GBS variant.

Campylobacter jejuni infections have a central role in the pathogenesis of axonal GBS. It is well known that the immune response against this *bacteria* induces the production of antibodies that cross-react with gangliosides present in peripheral nerves, causing direct damage to the axon in axonal

GBS variants³ Infections caused by *C. jejuni*, mostly diarrhoeas, are also the most important trigger for AMAN and AMSAN, with positive serology in 27-65 % of these patients³. Thus, we hypothesize that the epidemiology of *C. jejuni* infections could explain, at least in part, the relationship between age and frequency of axonal GBS in our cohort.

C. jejuni is a leading cause of diarrhoea in children in developing countries with an estimated incidence of ~30,000/100,000 population. In developed countries, its incidence is markedly lower (~300/100,000 population), possibly related to improved levels of sanitation⁹. However, in both cases, it is significantly higher than what is found in adults (~90/100,000)¹⁰. This data clearly shows that, regardless of the level of sanitation, *C. jejuni* affects primarily children. Also, as *C. jejuni* infections can be asymptomatic, the exposure to it during childhood could be a protective factor against this infection later in life¹¹.

The present study has some limitations. As some of our patients were referred from other institutions, a referral bias may have been introduced.

However, this bias should affect both the adult and pediatric populations equally. In addition, a prior study⁷ in our country confirms the frequency of axonal variants found in our pediatric population. Unfortunately, we were not able to find data about the prevalence of axonal variants of GBS in adult South American populations. The lack of serology against *C. jejuni* is another limitation. This is not routinely done in our centre since it is unlikely to change the management of individual patients.

CONCLUSION

In conclusion, in our cohort, age seems to have an impact on the frequency of axonal GBS. We hypothesize that the pathogenic relationship between *C. jejuni* infections and axonal GBS, and the epidemiology of *C. jejuni* infections could explain our findings. This should be taken into account and addressed in further epidemiological studies. Our data also shows that adult-onset axonal GBS in a South American cohort had a similar frequency than those reported in North America and some European countries.

ABBREVIATIONS

Guillain-Barré Syndrome (GBS)

Acute inflammatory demyelinating polyneuropathy (AIDP)

Acute motor axonal neuropathy (AMAN)

Motor and sensory axonal neuropathy (AMSAN)

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