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Prevalence and Clinical Features of Epilepsy in Argentina

A Community-Based Study

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Key Words

Epilepsy screening · Positive predictive value, Junín

Abstract

Objective: To ascertain the prevalence of epilepsy in Junín, a town of 70,000–80,000 inhabitants from the Province of Buenos Aires, Argentina. **Background:** Some South American communities have reported extremely high prevalences of epilepsy. We investigated whether Junín would also have a high prevalence. **Design/Methods:** Systematic sampling was used to select 5,839 households (sampling fraction = 25%). Participating households amounted to 5,648 (97%), with 17,049 persons. A two-phase case-finding strategy was used. Phase 1 was the screening of the 17,049 persons, which was performed by trained but medically unsophisticated interviewers. Phase 2 was the neurological evaluation of the 250 persons who were screened positive for epilepsy. Diagnoses were based on defined diagnostic criteria. **Results:** As of January 1, 1991 (prevalence day), 106 persons had epilepsy, including 64 (60%) with active epilepsy. Among these, 9 (14%) were epilepsy cases newly diagnosed by survey neurologists, and 50 (78%) were on antiepileptic treatment at

the time of the survey. Regarding the same 64 persons, seizures were generalized in 37 (58%) and partial in 24 (38%). Lifetime prevalence of epilepsy was 6.2/1,000 (6.3/1,000, age adjusted to the world standard population). Total point prevalence for active epilepsy was 3.8/1,000 (4.0 for females and 3.5 for males). In addition, prevalence peaked at the ages of 40–59 for females and 0–4 for males. **Conclusions:** This is one of the first community-based studies of epilepsy in Argentina, and the prevalence results provide new epidemiological data contributing to our understanding of the different prevalence rates found in Latin America.

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Introduction

Epilepsy-related surveys have been conducted in different Latin American communities, providing a wide array of prevalence figures [1–4]. Some of the highest reported prevalence figures refer to populations with serious public health problems that may potentially contribute to relevant numbers of epilepsy cases (e.g. endemic neurocysticercosis [5, 6]). Around 90% of people with epilepsy from developing countries are not receiving appropriate treatment. Furthermore, there is a high social burden and stigma associated with epilepsy that can negatively affect an individual's quality of life and social interaction [7].

This work was partially presented at the Regional North American Annual Meeting of the World Federation of Neurology – Research Group on Neuroepidemiology, Denver, Colo., USA, April 19, 2002.

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0251-5350/07/0281-0008\$23.50/0

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We report a prevalence survey of epilepsy in an Argentine city with good sanitation facilities and ready access to healthcare services. The Junín survey, which also addressed Parkinson's disease and stroke, used a 2-phase case-finding strategy based on household screening and clinical evaluation [8]. In addition, we investigated the positive predictive value (PPV) for the disease, active and inactive status including seizure history, seizure type and the percentage of patients on antiepileptic treatment.

Methods

Population and General Design

The survey was conducted in the town of Junín, in the Province of Buenos Aires, Argentina. Junín, located in an agricultural area, has approximately 70,000–80,000 inhabitants, almost all of whom are Caucasians (mainly of Spanish or Italian ancestry). Junín County has 2,253 km² and the population density is 37 inhabitants/km² and every dwelling has an average of 3.4 inhabitants. Life expectancy at birth (period 1991–1995) is 71.3 years. Fourteen percent of the population are over 65 years old [9]. The city has good availability and high-quality medical services, including specialty care, even for low-income residents. People have access to safe drinking water in nearly every dwelling. The sewage and waste disposal system is also adequate. No endemic infectious diseases were found in the area; in particular, there was no public health problem with neurocysticercosis.

Eligibility was based on residency status. City residents living in households, as of January 1, 1991 (prevalence day), were eligible for the survey. Soldiers and college students who lived temporarily within Junín and patients from a chronic-care institution (with 129 beds), which includes patients from Junín and the surrounding region, were excluded from the study.

Data were collected in 2 phases. *Phase 1* pertained to household selection and screening. Using a 2-stage systematic sampling procedure, housing units from across the city (about 1 in 4) were included in the survey. Households corresponding to these housing units were then screened to identify potential cases of epilepsy or other neurological disorders of interest. The screening procedure was a face-to-face interview, where one responsible adult in the family, preferably the mother/spouse, provided the answers for each family member living in the same household. The screening questions were adapted from those used in the Copiah County Study [10, 11]. The Spanish version was tested and improved in a series of pilot investigations [8]. The PPVs for screening items were disaggregated by sex. PPV is the percentage of persons with epilepsy among all persons screened as positive on the basis of a given item. Several questions were needed because of the various terms for epilepsy and seizures. For example, one term introduced for this survey but not used in the Copiah County Study was 'dysrhythmia' (in Spanish, disrritmia), which also refers to epilepsy. The questions performed reasonably well, sensitivity and specificity were 95 and 80%, respectively.

Phase 2 was the clinical evaluation. All persons screened as positive in phase 1 (i.e. suspected of having epilepsy or another disorder of interest) were to be clinically examined by a neurolo-

gist. Medical documentation and other relevant information were sought for those individuals who refused or were unavailable to be examined.

Definition of Epilepsy

A diagnosis of epilepsy required the occurrence of 2 or more unprovoked seizures or seizure episodes. Seizures were considered to be unprovoked and idiopathic if there was no apparent precipitating event (e.g. brain trauma or stroke). Seizures were considered to be unprovoked and symptomatic if there was a presumed precipitating event and if seizures occurred more than 14 days after this event. Epilepsy was ruled out in those cases with only a single seizure, only neonatal seizures, only febrile seizures or only provoked seizures.

There were 2 levels of diagnostic certainty: definite and possible. A definite diagnosis required (1) a clear description and history of seizures obtained from the subject, caregiver or from the physician or the medical records; (2) a suggestive description and history of seizures corroborated by electroencephalographic (EEG) findings. A possible diagnosis required only a suggestive description and history of seizures, without EEG confirmation.

Active and inactive forms of epilepsy were distinguished. The condition was active if on January 1, 1991, the subject was on antiepileptic medication, and if he/she had experienced 1 or more seizures in the 5-year period of 1986–1990. The condition was also active if on January 1, 1991, the subject was not taking antiepileptic medication, yet he/she had experienced 1 or more seizures in 1990. All other instances were considered inactive cases of epilepsy.

The definitions for seizure types were those proposed by the Commission on Classification and Terminology of the International League against Epilepsy [12]. Verbal consent was obtained from all subjects including participants and their relatives. Additional details about the survey methods and particularly verbal consent have been published elsewhere [8].

Statistical Analysis

Point prevalence with reference date January 1, 1991, was used to measure disease frequency. The denominators for prevalence calculations were based on sample data obtained in the survey. The survey was a descriptive investigation and the results correspond to the participating households of Junín. We did not extrapolate these results to other populations. The statistical analyses were accomplished using PC SAS Version 7.0, and they consisted mainly of simple comparisons of prevalence figures and PPVs. No significance tests were performed and no confidence intervals were computed. All results presented were age adjusted to the world standard population to permit international comparison [13].

Results

Data collection occurred essentially during the period between March 1991 and March 1993. After that, the principal investigator (M.O.M.) contacted some participants to solve inconsistencies in the data obtained.

Table 1. Prevalence of epilepsy, by age and sex, in the survey population

Age, years	Men		Women		Both sexes	
	cases	prevalence	cases	prevalence	cases	prevalence
<i>Active cases only</i>						
0–4	4 (744)	5.4	2 (669)	3.0	6 (1,413)	4.2
5–19	9 (2,018)	4.5	9 (2,010)	4.5	18 (4,028)	4.5
20–39	7 (1,811)	3.9	9 (2,032)	4.4	16 (3,843)	4.2
40–59	4 (1,807)	2.2	10 (2,160)	4.6	14 (3,967)	3.5
60–99	4 (1,591)	2.5	6 (2,207)	2.7	10 (3,798)	2.6
Total	28 (7,971)	3.5	36 (9,078)	4.0	64 (17,049)	3.8
<i>Active and inactive cases (lifetime prevalence)</i>						
0–4	4 (744)	5.4	2 (669)	3.0	6 (1,413)	4.2
5–19	11 (2,018)	5.5	19 (2,010)	9.5	30 (4,028)	7.4
20–39	13 (1,811)	7.2	14 (2,032)	6.9	27 (3,843)	7.0
40–59	5 (1,807)	2.8	18 (2,160)	8.3	23 (3,967)	5.8
60–99	9 (1,591)	5.7	11 (2,207)	5.0	20 (3,798)	5.3
Total	42 (7,971)	5.3	64 (9,078)	7.1	106 (17,049)	6.2

The survey population includes definite and possible cases. Prevalence is expressed as number of cases per 1,000 population. Figures in parentheses indicate population size.

There were 5,839 households selected in phase 1. Of these, 5,648 were screened (97%) and 191 (3%) were lost for the study (all but 1 because of refusal). The 5,648 households contained 17,049 individuals (53% women, 47% men) who constitute the survey population (table 1). Two hundred forty-eight persons were considered significant because they screened positive in one or more questions relating to seizure experience. Additionally, 2 other persons with epilepsy called our attention because they provided positive answers to stroke-related questions. All 250 persons were evaluated in phase 2. For 244 patients, the diagnostic information gathered from examinations and other sources was adequate to rule in or rule out epilepsy. For the remaining 6 persons (all women), it was impossible to make a diagnostic determination.

Of the 248, 87 (35%) had experienced seizures that, by our definition, were not considered as epilepsy: 74 persons had only febrile seizures (5.2% of the children for the age group of 0–4 years); 5 persons only had afebrile seizures, and 8 persons only had provoked or acute symptomatic seizures (3 linked cranial trauma, 2 related to meningitis, 1 because of encephalopathic O₂ deprivation with surgery, 1 due to sepsis and 1 due to eclampsia).

A total of 106 persons had either active or inactive epilepsy, and the lifetime prevalence was 6.2 cases per 1,000 population (6.3/1,000, when age adjusted to the world standard population). The crude prevalence was some-

what higher for women than men: 7.1 versus 5.3/1,000 (7.2 vs. 5.3 age-adjusted). Regarding active epilepsy, we found 64 persons with that condition. Their prevalence was 3.8/1,000 (3.9/1,000, age adjusted to the world population), with a small gender difference: women 4.0 versus men 3.5/1,000 (4.1 vs. 3.4 age adjusted). The age-specific prevalence patterns were inconsistent between men and women, both for active and lifetime cases. For example, for active cases, the peak prevalence was at the youngest ages (0–4 years) for men but not for women (table 1).

Of the 106 persons with epilepsy, 64 (60.4%) had an active condition and 9 (8.5%) were first diagnosed for the condition by project neurologists during the survey (table 2). All 9 persons had active epilepsy. A definite diagnosis was reached for 100 persons (94.3%), and possible diagnoses were reached for the remaining 6 persons (5.7%). The PPV for any screening items was 41.9% for both sexes (table 3, in both the Spanish and English version). The PPVs for the 9 symptom-related questions ranged from 19 to 93%. The questions with the highest PPV (93%) addressed epilepsy or epileptic attacks. Of the 9 symptom questions, 6 showed the PPV for men exceeding or equaling the PPV for women. By contrast, the 3 symptom-related questions with the highest PPV for women addressed convulsions, sudden falling without loss of consciousness and repeated fainting spells. For the term ‘dysrhythmia’ the PPV (21.4%) was lower than expected (table 3).

Table 2. Distribution of identified epilepsy cases: selected categories by active-inactive status, Junín, January 1, 1991

Category	Active epilepsy		Inactive epilepsy		Total	
	n	%	n	%	n	%
First diagnosis of epilepsy						
Before survey	55	85.9	42	100.0	97	91.5
During survey by project neurologist	9	14.1	0	0.0	9	8.5
Total	64	100.0	42	100.0	106	100.0
AEM treatment at screening						
Yes	50	78.1	9	21.4	59	55.7
No	14	21.9	33	78.6	47	44.3
Total	64	100.0	42	100.0	106	100.0
Certainty of diagnosis						
Definite	61	95.3	39	92.9	100 ¹	94.3
Possible	3	4.7	3	7.1	6	5.7
Total	64	100.0	42	100.0	106	100.0
Seizure history						
Idiopathic only	40	62.5	33	78.6	73	68.9
Symptomatic only	24	37.5	7	16.7	31	29.2
Unknown	0	0.0	2	4.8	2	1.9
Total	64	100.0	42	100.0	106	100.0
Seizure type						
Generalized only	37	57.8	33	78.5	70	66.1
Partial only	24	37.5	7	16.7	31	29.2
Unclassified	3	4.7	2	4.8	5	4.7
Total	64	100.0	42	100.0	106	100.0

AEM = Antiepileptic medication.

¹ Includes 6 cases (3 active, 3 inactive) with a suggestive description and history but with EEG confirmation.

Regarding seizure history, 73 persons (68.9%) had idiopathic seizures, 31 (29.2%) had symptomatic seizures and 2 persons (1.9%) had seizures that could not be classified. Concerning seizure types, 106 persons were categorized as follows: 70 (66.1%) had generalized seizures, 31 (29.2%) had partial seizures and 5 (4.7%) had seizures that could not be classified. The percentage of persons with generalized seizures was lower for active epilepsy than inactive epilepsy (57.8 vs. 78.5%, table 2). By contrast, the percentage of persons with partial seizures was higher for active epilepsy than for inactive epilepsy (37.5 vs. 16.7%; table 2). Analogous patterns were observed when idiopathic and symptomatic seizures were considered separately (table 4).

If we restrict our attention to the 64 persons with active epilepsy, the median age at onset was 10.9 years for men and 16.9 years for women. Twenty-four of the 64 per-

sons (37.5%) had symptomatic seizures (table 2). The presumed remote causes were perinatal lesions (n = 5, 20.8%), CNS infections (n = 5, 20.8%), CNS tumors (n = 4, 16.7%), CNS traumas (n = 4, 16.7%), strokes (n = 4, 16.7%), chromosomal abnormalities (n = 1, 4.2%) and other conditions (n = 1, 4.2%). At screening, 50 (78.1%) persons were on antiepileptic drugs (table 2). Regarding the type of treatment, 20 (40.0%) were on monotherapy and 30 (60.0%) were on polytherapy. Phenobarbital and carbamazepine were the most common antiepileptic drugs used individually, whereas phenobarbital and phenytoin were the most common antiepileptic drugs used in polytherapy. Six patients (5.7%) reported a family history of epilepsy in first-degree relatives.

Table 3. Screening for epilepsy: PPVs from the current survey

Item in English and Spanish	PPV, %		
	men	women	both sexes
Convulsions (convulsiones)	43.2 (35/81)	53.7 (44/82)	48.5 (79/163)
Dysrhythmia (disrritmia)	25.0 (1/4)	20.0 (2/10)	21.4 (3/14)
Epilepsy or epileptic attacks (epilepsia o ataques epilépticos)	100.0 (8/8)	89.5 (17/19)	92.6 (25/27)
Sudden falling without loss of consciousness (caídas bruscas sin pérdida de conciencia)	20.0 (1/5)	46.2 (6/13)	38.9 (7/18)
Repeated fainting spells (desmayos repetidos)	38.5 (5/13)	40.5 (15/37)	40.0 (20/50)
Repeated spells of staring, confusion or inability to respond for a few moments (episodios repetidos en los que miran fijo, están confundidos o no pueden responder por unos momentos)	100.0 (4/4)	33.3 (3/9)	53.9 (7/13)
Repeated spells of being absent-minded, of appearing strange or out-of-touch, of drooling or of having unusual body movements (episodios repetidos en los que se muestran distraídos, extraños, babean o tienen movimientos inusuales del cuerpo)	83.3 (5/6)	47.1 (8/17)	56.3 (13/23)
Repeated short spells of strange or abnormal behavior (episodios repetidos y breves de conducta extraña o anormal)	100.0 (5/5)	60.0 (3/5)	80.0 (8/10)
More than one febrile seizure (más de una convulsión febril)	19.6 (11/56)	18.9 (7/37)	19.4 (18/93)
Any screening item above	39.0 (41/105) ¹	44.1 (63 /143) ¹	41.9 (104/248) ¹

Figures in parentheses indicate true-positive numbers/total positive numbers.

¹ Two persons (1 man, 1 woman) with epilepsy were screened positive in the part of the survey pertaining to stroke, but were not screened positive for any of the items considered here.

Discussion

We performed a household screening and clinical evaluation, using a 2-phase design. Household screening for epilepsy was considered feasible because we expected a high level of cooperation from the target population. In addition, adult residents had experience with structured questionnaires from previous censuses and health surveys.

The use of household screening allowed the study neurologists to concentrate their efforts on individuals who were more likely to have possible or definite epilepsy. Generally, the study neurologists did not observe seizures directly. They had to gather information from the subjects and/or from reliable observers (usually close relatives). This information included seizure experiences and

epilepsy-related conditions or disorders (e.g. perinatal lesions, encephalitis and traumatic brain injury). The study neurologists performed neurological evaluations to identify signs of epilepsy-related conditions (e.g. in children, cerebral palsy or mental retardation; in adults, stroke or brain tumor). History information together with neurological evaluations generally took at least 1 h. However, some patients needed to be checked more than once in order to have a clearer diagnosis. One advantage of the household screening was the possibility to find undiagnosed cases. Nine patients – 14% of all active cases – who already had the disease were diagnosed for the first time by project neurologists.

For the clinician, the dilemma is to determine whether or not the patient has the disease, based on the clinical interview related to the history of seizures. In our study,

Table 4. Distribution of identified epilepsy cases: seizure type by seizure history by active-inactive status, Junín, January 1, 1991

Seizure type	Seizure history						
	idiopathic only		symptomatic only		unknown	total	
	n	%	n	%	n	n	%
<i>Active epilepsy</i>							
Generalized only	25	62.5	12	50.0	0	37	57.8
Partial only	13	32.5	11	45.8	0	24	37.5
Undetermined	2	5.0	1	4.2	0	3	4.7
Total	40	100.0	24	100.0	0	64	100.0
<i>Inactive epilepsy</i>							
Generalized only	28	85.0	5	71.4	0	33	78.6
Partial only	5	15.0	2	28.6	0	7	16.7
Undetermined	0		0		2	2	4.7
Total	33	100.0	7	100.0	2	42	100.0

Of the 24 symptomatic cases that are active, 46% are partial. Of the 7 symptomatic cases that are inactive, 29% are partial.

the survey had some questions with a high PPV for both sexes. Almost half of the patients (42%) screened positive for epilepsy during the first phase of the study. In developing countries, where other diagnostic procedures are not always available, such information remains very useful.

Operational Problems and Sampling Error

Elderly patients from 'local geriatric group homes' were excluded due to practical reasons. The geriatric group homes had no medically trained personnel. Geriatric homes personnel were unfamiliar with the clinical condition of the residents, and no medical records were kept at these homes [14]. Another problem is that elderly persons who experienced seizures might not recognize these events, especially when the seizures are subtle. Such seizures may be overlooked not only by the elderly, but also by their physician and close relatives. The above-mentioned problems may underestimate final results due to a less than total representation of the elderly.

Another problem we encountered in our study was the false-negative cases. The diagnosis of epilepsy is usually associated with considerable prejudice. Although there was no systematic evaluation of persons who screened negative for epilepsy, a few false-negative results came to our attention. We knew about 5 persons with epilepsy (3 inactive, 2 active) who concealed their condition during the screening. They were worried about the consequences the disease could have in their job situation. These individuals, who were the patients of some of the project

neurologists, were not included in the prevalence counts [15].

A review [16] showed that in Latin America the median lifetime prevalence for all countries was 17.8 (range 6–43.2) per 1,000 people. A multivariate linear-regression model found no association between prevalence rates and possible explanatory variables. Our values of 6.2/1,000 for lifetime prevalence (6.3/1,000, age adjusted to the world standard population) are within the minimum prevalence rates. One of the objectives of this study was to compare our prevalence figures with those obtained in Argentina and other studies with similar case-finding methods. A primary school group of children from Buenos Aires [4] showed no differences in prevalence, sex, seizure type and percentage of patients on antiepileptic treatment when compared with the same age group from our study. Also we compared prevalence rates from the Junín study with the Copiah County (white only) [10, 11] and the Sicily surveys [17, 18]. The prevalence of active epilepsy of those surveys was similar to our results, and these figures are close to those reported in developed countries [19].

Regarding other rural and suburban areas in Latin America, e.g. Bolivia with 12.3/1,000 (11.1/1,000 for active epilepsy) [20, 21], Ecuador with 14.3/1,000 (8.0/1,000 for active epilepsy) [22, 23] and Uruguay with 11.6/1,000 inhabitants (6.4/1,000 for active epilepsy [pers. commun., 24], results show remarkably higher prevalence rates for both lifetime and active prevalence. Figure 1 shows the age-specific prevalence comparison of 3 surveys.

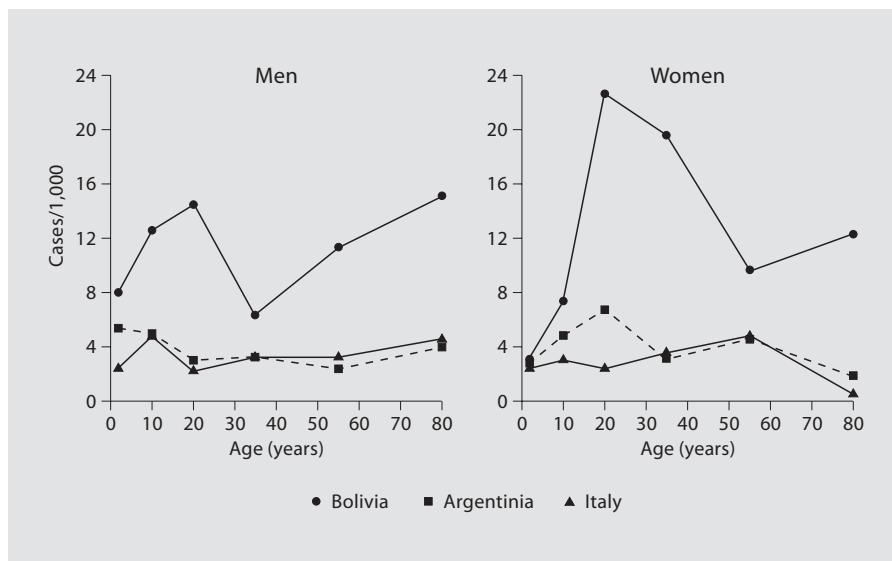


Fig. 1. Age-specific prevalence of epilepsy. Comparison of 3 studies: Cordillera Province, Bolivia, November 1, 1994; Junín, Argentina, January 1, 1991, and Sicily, Italy, November 1, 1987.

Health differences vary from country to country and even within the same country. Population growth resulting from different mortality and fertility rates characterizes the demographic transition in the Americas. Four typologies have been used to identify the level of this transition in the corresponding countries. Argentina is in group 4: advance transition (moderate or low birth rate and mortality; low natural growth, 1%) together with Canada, the USA, Chile, Cuba, Puerto Rico and others [25].

The low epilepsy prevalence in Junín may be due to many factors, e.g. the absence of some epilepsy-related condition (e.g. neurocysticercosis), good-quality public health programs and related services, demographic transition and lower treatment gaps. Epilepsy is a complex

disease and final prevalence results will depend upon the interaction of environmental conditions and genetic factors, as well as remission-related therapeutic response.

Acknowledgments

This project was financially supported by the Fundación para la Investigación en Neuroepidemiología (FINEP), Junín, Buenos Aires Province, Argentina. The authors thank Dr. Cecilia Pardini, who conducted some of the neurological evaluations for the survey. Our special thanks go to Dallas W. Anderson and Jack Panossian for their significant contributions to our study and to Lorenna Allemandi for the thoughtful assistance in the preparation of this article.

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