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Incidence of epilepsy and seizure disorders in childhood and association with social determinants: a birth cohort study

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Abstract

Objective: To investigate the incidence and prevalence of epilepsy and seizure disorders during childhood, and their relationship to selected social determinants.

Methods: Population-based birth cohort study, with children born between January 1st and December 31st, 2003 in the city of Passo Fundo (RS), Brazil. Data were prospectively collected in two stages. In the first one, the Questionnaire of Neurologic Tracking for Epilepsy (QNT-E) was applied during a visit at the children's homes, together with the assessment of social determinants of health. Constructs of social position (economic class, mother's educational level, marital status and occupation), biological and behavioral factors (alcohol and tobacco consumption during pregnancy, number of prenatal appointments, and use of medicines during pregnancy), and psychosocial factors (religious meetings attendance) were analyzed. In the second stage, children with a positive QNT-E were submitted to neuroclinical assessment for diagnostic confirmation.

Results: Eleven cases of epilepsy, 27 of febrile seizures, 10 of neonatal seizures, 8 of single seizures, in addition to 26 patients with non-epileptic paroxysmal events, were identified. The incidence rate of epilepsy was 7/100,000 children, and the prevalence 65.2/10,000 children. Nine children had active epilepsy, giving a point prevalence of 53.3/10,000 children. After multivariate analysis, no social determinants could be significantly related to epilepsy.

Conclusions: In this study, a low incidence rate of epilepsy was reported, in contrast to almost a double incidence of febrile seizures and non-epileptic paroxysmal events. Moreover, the achievement of an accurate diagnosis of epilepsy in developing countries is still a challenge, in order to avoid misdiagnosis.

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Introduction

Epilepsy is a highly prevalent disorder around the world, particularly in developing countries, where the health care system still fails to prevent one of the most common causes of epilepsy, namely infectious diseases. Many studies assessing the prevalence of epilepsy are available in the literature, but not so many have evaluated the incidence of epilepsy in a specific child population.[1-16]

The incidence of epilepsy has been studied in several countries and in several subgroups of the population. However, due to different study designs and criteria used, the data obtained is difficult to compare, and the rates reported are hardly comparable.[6] Furthermore, since many studies were retrospective, a complete description of the cases is not available. A prospective approach allows a more

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complete ascertainment of cases, in addition to being helpful in evaluating prognosis, in counseling patients and their families, as well as in selecting patients for more intensive and investigational treatments.[6,17]

In Brazil, health facilities for the poorest social groups have increased in the last decades. However, this has unevenly happened among the different Brazilian states and cities.[18] In developing countries such as Brazil, the effect of social inequalities on epileptic seizures has remained unknown. Socioeconomic status might expose people to specific vulnerabilities and health-damaging factors, which can be evaluated using a model of inequality.[19]

Clinical markers for epilepsies have been well known. However, the same has not occurred with social determinants. This study aimed to investigate the incidence of epilepsy and seizure disorders in the first years of life in a cohort of children from a developing country followed since birth, and the occurrence of social determinants associated to epilepsy.

Methods

Investigational area and population

The study was performed in the city of Passo Fundo, southern Brazil, which currently has a population estimated at 188,303 inhabitants, 97.2% of which live in the urban area and 2.8% in the rural area. From the total number of inhabitants, 14,711 are in the age range from 0 to 4 years old.[20] The population, among which 89% are of European descent, is composed of different ethnicities – Italian, German, Portuguese, indigenous, and others. The gross domestic product *per capita* corresponds to US$ 13,880.00, and the monthly average income of residents with 10 years old or more is US$ 444.00. The weather is temperate, subtropical, with mean temperature around 63.5 °F.[20]

At the time of the study, public health facilities were available in 37 units of primary care, five units of secondary care, five emergency units and five tertiary hospitals. Furthermore, eight teams of Family Health Care were responsible for visiting poor income families at home. Pediatric facilities were available in all tertiary units and in 24 primary care units. The mean birth rate between 1996 and 2000 was 3,372, and the infant mortality rate was 18.73 deaths per 1,000 live births in 2002, 21.69 in 2003, and 14.65 in 2007. The initial cohort was established in 2003, and a total of 2,285 (94.8%) infants were monitored.[21]

Inclusion and exclusion criteria

The initial birth cohort included all newborns born in the city of Passo Fundo during the year 2003, who were followed until 2007, when the third evaluation of these population was performed. Children included in this study belonged to the 2003 birth cohort, resided in the city, and could be found until depleting all the attempts of searching for their homes and after investigating address changes in the nosocomial and municipal network of health. Exclusion criteria comprised adopted children, and those whose mothers had passed away or had exhibited any physical or mental handicap that had prevented them from participating, since there would not be any family member qualified to answer the survey.

Definitions

In this study, epilepsy was defined as a condition characterized by recurrent unprovoked seizures. A single unprovoked seizure or cluster of seizures occurring in a time interval below 24 hours was considered a single seizure episode.[1,22] Cases of febrile seizures and neonatal seizures were identified and categorized separately.

Social determinants were established by using as reference the model of the Commission on Social Determinants of Health of the World Health Organization. This theoretical model has been based on *structural* determinants, such as those which generated social stratification (income, education); and on *intermediate* determinants, from which the differences in exposure and vulnerability to health-damaging conditions were derived.[19] Constructs of social position (economic class, mother's educational level, marital status, and occupation), biological and behavioral factors (alcohol and tobacco consumption during pregnancy, number of prenatal appointments, and use of medicines during pregnancy), and psychosocial factors (religious meetings attendance) were analyzed and defined as follows:

1) Income and economic class: estimates people and urban families' purchasing power and establishes the population's economic stratification as follows: classes A and B the one with monthly income from R$ 9,733.47 to R$ 2,012.67 or more, and classes C and D from R$ 1,194.53 to R$ 487.97 in agreement with Critério de Classificação Econômica Brasil (CCEB, Brazilian Economic Classification Criterion) 2003;
2) Mother's education: less than 8 years of school or more than 8 years;
3) Mother's marital status: living with or without a partner;
4) Use of alcohol and tobacco during pregnancy: yes or no, according to spontaneous report, regardless of amount;
5) Religious meeting attendance: yes (usually or always) or no, regardless of religion.

Cases ascertain

The study was performed in two steps.

The first step was the implementation of the Questionnaire of Neurologic Tracking for Epilepsy (QNT-E),

previously validated in Brazil.[23] This implementation was executed at the children's homes by trained interviewers, under the researchers' supervision. The QNT-E consists of 14 questions and is based on previous population instruments to detect epilepsy.[24,25] This questionnaire was first applied and validated in the city of Porto Alegre, south of Brazil, in 1993.[23]

The second step was diagnostic confirmation: the children with a positive questionnaire were submitted to neuroclinical assessment, performed by a pediatric neurologist by using the Neurological Diagnostic Interview for Epilepsy, that was constructed following recommendations from the International League Against Epilepsy (ILAE).[22,26]

The outcome was the diagnosis of epilepsy or seizure disorders (neonatal seizures, single seizures, or febrile seizures) based on clinical history, neurological assessment and complementary tests (electroencephalogram and/or neuroimaging), when available. All cases of epilepsy were reviewed by one of the senior researchers (MLN). Patients with non-epileptic paroxysmal events (NEPE) detected as false positive in the QNT-E were also identified in this phase.

Statistical analysis and ethical issues

Data were added to the data base of the original cohort for analysis in the statistical software SPSS version 15.0. Descriptive statistics, qui-square test, Fisher's exact test, measures of association force and logistic regression were used. Five percent random samples of the interviews were repeated by supervisors to control data quality.

This project was approved by the Research Ethics Committee of the Universidade de Passo Fundo (recorded under number 024/2007). All participants read and signed a free informed consent.

Results

From the 2,285 children who composed the initial cohort in 2003, 24 have died and 145 were excluded (8 were adopted, one mother developed mental illness and 2 have died, 134 have moved away from the city). After several attempts, it was impossible to localize 420 children, and 9 refused to participate in the study. In this stage, 1,687 children were included (73.8% of the original cohort).

The most significant losses occurred because of migration to either other neighborhoods or cities. Consequently, even if the sample size would be fixed, the sampling error for associations with epileptic seizures was estimated in 5% for relative risk (RR) = 3.0, with 90% power.

No significant differences were observed in the characteristics of the group of children who were lost and the features of the group of children available for this step of the study. Among the 10 variables analyzed, only maternal age (below 20 years) was different ($p = 0.04$). Most of those mothers were living with their parents when the baby was born, and later became independent, which included changes of address, city or even state.

Among 1,687 children evaluated, 553 (32.8%) had a positive QRT-E, and 541 were interviewed in the confirmatory phase. In this stage, we had a 12% loss.

Eleven cases of epilepsy were identified (five boys and six girls), and characteristics of these patients are described in Table 1. In 71 patients, clinical data allowed the following diagnosis: 27 cases of febrile seizures, 10 cases of seizures restricted to the neonatal period, eight cases with one single seizure, and NEPE were suggested in 26 patients.

In this specific birth cohort population, we observed a low incidence rate of epilepsy (7/100,000 children) and a prevalence of 65.2 per 10,000 children during the 48 months of follow up. Nine children had active epilepsy, giving a point prevalence of 53.3 per 10,000 children. The incidence and prevalence of febrile seizures, single seizures, and NEPE are reported in Table 2.

The description of social determinants is presented in Table 3. The sample consisted of a population group of mothers with medium to low educational level, of which 48.5% concluded high school, 29.9% concluded basic education, and 5.7% were illiterate. In addition, 63% were housewives without any other profession, 55% belonged to the low social stratus (C/D/E) and lived in suburbs with less health facilities and with lesser availability of goods and services. Regular presence in religious meetings was high (70.4%), with a predominance of Catholic Church (70%), followed by evangelical churches (26%). Considering the use of health facilities, we have observed that 69.3% used the city network of primary care centers, 25.7% used predominantly emergency care facilities and 13.8% were covered by the system of Family Health Care teams.

The bivariate analysis showed significant differences of mother's years in school in the group of neonatal seizures ($p = 0.04$), and less perinatal visits in the group of NEPE ($p = 0.01$) (Table 3). The model of multivariate analysis did not show any association between social determinants and epilepsy (Table 4).

Discussion

According to Hauser, studies that determine prevalence of epilepsy are important tools for determination of health care needs and may allow hypothesis generation, even though they also may be misleading if used for etiologic studies or to provide information on prognosis. Studies to verify incidence of epilepsy are necessary for proper evaluation of etiologic factors, and incidence cohorts are the most appropriate groups to evaluate prognosis.[1] Based on this premise, we have conducted this birth cohort study, with children now, who are under the third evaluation period.

Table 1 - Characteristics of patients diagnosed with epilepsy

Patient	Sex	Age of first seizure*	Type of epilepsy (etiology)	EEG and/or neuroimaging	Treatment
1	F	36	Focal symptomatic (hypoxic ischemic encephalopathy)	EEG with slow basal background activity, right focal interictal discharges	PHB
2	F	24	Generalized symptomatic (hypoxic ischemic encephalopathy)	EEG with generalized epileptic activity	PHB
3	M	11	Generalized idiopathic	EEG with slow basal background activity	PHB
4	M	12	Generalized	EEG with interictal generalized discharges	PHB
5	M	48	Generalized	Normal EEG	No AED†
6	F	24	Generalized idiopathic	EEG with slow basal background, normal CT scan	CBZ
7	F	6	Generalized symptomatic (hypoxic ischemic encephalopathy)	Normal EEG	VPA
8	M	16	Generalized idiopathic	Normal CT and EEG	PHB
9	M	30	Focal	Ictal EEG with left rolandic discharges	CBZ
10	F	24	Benign rolandic epilepsy	EEG with left rolandic discharges, normal CT scan	PHB
11	F	22	Generalized symptomatic (CNS malformation)	EEG with interictal generalized discharges	OXC

AED = antiepileptic drugs; CBZ = carbamazepine; CNS = central nervous system; CT = computerized tomography; EEG = electroencephalogram; F = female; M = male; OXC = oxcarbazepine; PHB = Phenobarbital; VPA = valproate.
* In months.
† Patient never used regular medication.

Table 2 - Incidence and prevalence of epilepsy, seizures and NEPE in the birth cohort (48th month of follow-up)

Event	n	Prevalence / 10,000 patients	Incidence (patients-month)/ 100,000	Incidence (48 months)/ 100,000 patients
Epilepsy	11	65.2	11.85	7.0 (3.0-12.0)
Febrile seizures	27	160.0	29.1	16.0 (11.0-24.0)
Other seizures	18	106.7	19.39	11.0 (7.0-17.0)
NEPE	26	154.1	28.0	15.0 (10.0-23.0)
Total	82	486.1	88.34	49.0 (39.0-60.0)

NEPE = non-epileptic paroxysmal events.

Table 3 - Comparison of social determinants in patients with QNT-E negative and positive

Variables	QNT-E negative (n = 460)	Epilepsy n = 11 (%)	Febrile sz. n = 27 (%)	Neonatal sz. n = 10 (%)	Single sz. n = 8 (%)	NEPE n = 26 (%)
Economic status		p* = 0.545	p* = 1.00	p* = 0.752	p = 0.146	p = 0.06
A/B	199 (87.3)	6 (2.6)	11 (4.8)	5 (2.2)	1 (0.4)	6 (2.6)
C/D/E	249 (82.7)	5 (1.7)	15 (5.0)	5 (1.7)	7 (2.3)	20 (6.6)
Mother's years in school		p = 0.108	p = 0.184	p = 0.04*	p = 0.145	p = 0.426
≥ 8	150 (82.4)	10 (2.9)	13 (7.1)	3 (0.9)	3 (0.9)	19 (5.5)
< 8	297 (85.8)	1 (0.6)	14 (4.0)	7 (3.6)	5 (2.6)	7 (3.6)
Mother's marital status		p = 1.00	p = 1.00	p = 0.217	p = 0.129	p = 0.524
With partner	388 (85.7)	10 (2.2)	23 (5.1)	7 (1.5)	5 (1.1)	20 (4.4)
Without partner	72 (80.9)	1 (1.1)	4 (4.5)	3 (3.4)	3 (3.4)	6 (6.7)
Mother work out of home		p = 0.114	p = 0.363	p = 0.749	p = 0.270	p = 1.00
No	284 (85.3)	4 (1.2)	14 (4.2)	7 (2.1)	7 (2.1)	16 (4.8)
Yes	176 (84.2)	7 (3.4)	13 (6.3)	3 (1.5)	1 (0.5)	10 (4.9)
Use of alcohol†		p = 1.00	p = 0.783	p = 0.664	p = 0.619	p = 0.586
No	387 (85.1)	10 (2.2)	23 (5.1)	8 (1.8)	6 (1.3)	21 (4.6)
Yes	73 (84.9)	1 (1.2)	3 (3.5)	2 (2.3)	2 (2.3)	5 (5.8)
Use of tobacco†		p = 0.472	p = 0.137	p = 1.00	p = 1.00	p = 0.633
No	359 (84.3)	10 (2.3)	24 (5.6)	8 (1.9)	7 (1.6)	19 (4.5)
Yes	101 (87.8)	1 (0.9)	2 (1.7)	2 (1.7)	1 (0.9)	7 (6.1)
Number of prenatal visits		p = 1.00	p = 0.635	p = 0.212	p = 0.495	p = 0.01*
< 7	211 (81.8)	5 (1.9)	11 (4.3)	7 (2.7)	5 (1.9)	19 (7.4)
≥ 7	237 (87.5)	6 (2.2)	15 (5.5)	3 (1.1)	3 (1.1)	7 (2.6)
Use of medication†		p = 0.702	p = 0.896	p = 0.122	p = 0.205	p = 0.257
No	88 (80.7)	1 (0.9)	6 (5.5)	4 (3.7)	5 (1.2)	18 (4.2)
Yes	372 (86.1)	10 (2.3)	20 (4.6)	6 (1.4)	3 (2.8)	8 (7.3)
Religious meetings		p = 1.00	p = 0.242	p = 0.690	p = 0.192	p = 0.172
No	131 (84.0)	3 (2.1)	11 (4.2)	1 (0.9)	4 (1.1)	21 (5.6)
Yes	326 (85.1)	8 (1.9)	16 (7.1)	7 (1.9)	3 (2.8)	2 (1.8)

NEPE = non-epileptic paroxysmal events; QNT = Questionnaire of Neurologic Tracking for Epilepsy; sz. = seizure.
* $p < 0.05$.
† During pregnancy.

Table 4 - Social determinants of patients with epilepsy (n = 11), multivariate analysis

Variable	RR (raw) (95%CI)	p	RR (adjusted) (95%CI)	P
Medium-low income	1.56 (0.48-5.05)	0.55	1.12 (0.27-4.70)	0.87
Mother < 8 years in school	0.19 (0.02-1.49)	0.11	5.12 (0.63-41.49)	0.13
Single mother	1.97 (0.26-15.16)	1.00	0.50 (0.62-4.05)	0.52
Mother housewife	2.79 (0.83-9.41)	0.12	0.36 (0.09-1.43)	0.15
Use of alcohol during pregnancy	1.89 (0.25-14.58)	1.00	0.60 (0.07-4.88)	0.64
Use of tobacco during pregnancy	2.70 (0.35-20.87)	0.47	0.42 (0.50-3.47)	0.42
Irregular prenatal care	1.13 (0.34-3.77)	1.00	1.42 (0.36-5.54)	0.62

95%CI = 95% confidence interval; RR = relative risk.

Prospective incidence studies help in the proper selection of cases and the exclusion of non-epileptic disorders.[4] This was observed in this study, as before clinical evaluation 553 children (32.8%) had a positive QNT-E, but in the end only 11 cases of epilepsy were confirmed. Most of the instruments used had open questions, which increased the sensibility for positive cases. Furthermore, they cannot differentiate NEPE that often occur in the pediatric population.

Many previous prevalence and incidence studies of epilepsy have been published before, with results varying from 0.9 to 57 cases per 1,000 inhabitants for prevalence, and 26 to 190 cases per 100,000 inhabitants for incidence.[1-16] Most of these variations are due to methodological differences, as definition of epilepsy, diagnose criteria, or prospective or retrospective evaluation of data.[27] In this study, data were prospectively collected, definitions were previously determined based on ILAE recommendations,[22,26] and all positive cases screened with the questionnaire were submitted to clinical evaluation for diagnostic confirmation.

In this birth cohort, a very low incidence and prevalence of epilepsy was reported. A predominance of idiopathic epilepsy in relation to symptomatic was observed (64%), results similar to previous reports.[8,12,13] However, other authors have observed a predominance of cryptogenic and/or symptomatic epilepsy.[2,3,6,7,14,15] Differences among studies might be due to the fact that some cases could not be classified into the detailed categories of ILAE classification.[28]

Furthermore, a predominance of generalized epilepsy (63%) was also reported. In previous studies assessing only child population, some authors have reported a predominance of focal epilepsy[2,3,5,8,11-14] and others of generalized,[6,7,9,10,15] as in our study.

It is important to say that the two steps of our study allowed us to identify patients with seizures that could not be classified as epilepsy, namely febrile seizures, neonatal seizures and single seizures, and that had higher prevalence and incidence than epilepsy. In addition, the identification of NEPE, such as breath-holding spells, allowed us to disclose misdiagnosed cases.

Considering the social determinants analyzed in this study, we were able to identify a predominantly low-income and very religious population, with few years of formal education. However, after the model of multivariate analysis, none of these determinants could be related to epilepsy and seizures. Possible explanations might be due to the low incidence of epilepsy observed, and also to the fact that, although belonging to the medium-low socioeconomic level of the society, the majority of the study population had access to health facilities from primary to tertiary care.

In a previous study developed in southern Brazil, a higher prevalence of seizures was reported (45.2/1,000 children), and the absence of tap water and precarious housing were significantly associated with the outcome.[29] Differently from our study, this one was performed in one single section of the city, considered very poor. In other two epilepsy population surveys developed in southeast Brazil (São Paulo), it was observed, in children aged from 0 to 4 years, a lifetime prevalence of epilepsy of 2.8 per 1,000 children, and of active epilepsy of 2.3 per 1,000 children, which was a little lower than the outcomes reported in our study.[30,31]

In conclusion, a low incidence rate of epilepsy was reported in this specific birth cohort population, in contrast to almost a double incidence of febrile seizures and NEPE. Additionally, the achievement of an accurate diagnosis of epilepsy in developing countries is a challenge, and misdiagnosis should be avoided in order to establish the correct treatment. Moreover, population-based studies assessing the prevalence of epilepsy are relevant to better planning of health care activities.

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